UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2025

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 001-41742

Sagimet Biosciences Inc.
(Exact name of registrant as specified in its charter)

Delaware	**20-5991472**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
155 Bovet Road, Suite 303 San Mateo, California	**94402**
(Address of principal executive offices)	(Zip Code)

(650) 561-8600
(Registrant's telephone number, including area code)

N/A
(Former name, former address and former fiscal year, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Series A Common Stock, $0.0001 par value per share	SGMT	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant on June 30, 2025, the last business day of the registrant's last completed second quarter was $228.4 million (based on the closing price for shares of the registrant's Series A common stock as reported on the Nasdaq Global Market on that date).

The number of shares of the registrant's Series A and B common stock, $0.0001 par value per share, outstanding at March 5, 2026 was 32,017,613 and 567,494, respectively.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to the 2026 Annual Meeting of Stockholders, which will be filed with the Securities and Exchange Commission within 120 days after the end of the registrant's fiscal year ended December 31, 2025, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K (this Annual Report) contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). All statements other than statements of historical facts contained in this Annual Report, including statements regarding our future results of operations and financial position, business strategy, drug candidates, planned preclinical studies and clinical trials, results of preclinical studies, clinical trials, research and development costs, regulatory approvals, timing and likelihood of success, as well as plans and objectives of management for future operations, are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that are in some cases beyond our control and may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "would," "expect," "plan," "anticipate," "could," "intend," "target," "project," "believe," "estimate," "predict," "potential," or "continue" or the negative of these terms or other similar expressions. Forward-looking statements contained in this Annual Report include, but are not limited to, statements about:

- our financial performance;
- our ability to obtain additional cash and the sufficiency of our existing cash, cash equivalents and marketable securities to fund our future operating expenses and capital expenditure requirements;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the scope, progress, results and costs of developing denifanstat, TVB-3567 or any other drug candidates or combination therapies we may develop, and conducting preclinical studies and clinical trials;
- our ability to advance drug candidates into, and successfully complete, clinical trials within anticipated timelines;
- the timing and costs involved in obtaining and maintaining regulatory approval of denifanstat, TVB-3567 or any other drug candidates or combination therapies we may develop, and the timing or likelihood of regulatory filings and approvals, including our expectation to seek special designations or accelerated approvals for our drug candidates for various indications;
- current and future agreements with third parties in connection with the development and commercialization of denifanstat, TVB-3567 or any other future drug candidate or combination therapy;
- our estimate of the number of patients in the United States who suffer from the diseases we target and the number of subjects that will enroll in our clinical trials;
- our relationship with Ascletis BioScience Co. Ltd. (Ascletis), and its affiliate Gannex Pharma Co., Ltd. (Gannex), and the success of their development and registration efforts for denifanstat in China;
- the ability of our clinical trials to demonstrate the safety and efficacy of denifanstat, TVB-3567 and any other drug candidates or combination therapies we may develop;
- our plans relating to commercializing denifanstat, TVB-3567 and any other drug candidates or combination therapies we may develop, if approved, including the geographic areas of focus and our ability to build a commercial organization;
- the success of competing therapies that are or may become available;
- developments relating to our competitors and our industry, including competing drug candidates and therapies;
- our plans relating to the further development and manufacturing of denifanstat, TVB-3567 and any other drug candidates or combination therapies we may develop, including additional indications that we may pursue for denifanstat, TVB-3567 or other drug candidates or combination therapies;

- our ability to obtain sufficient funding or enter into a strategic collaboration to initiate future clinical trials for our combination of denifanstat and resmetirom in metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH);

- existing regulations and regulatory developments in the United States and other jurisdictions;

- our potential and ability to successfully manufacture and supply denifanstat, TVB-3567 and any other drug candidates or combination therapies we may develop for clinical trials and for commercial use, if approved;

- the rate and degree of market acceptance of denifanstat, TVB-3567 and any other drug candidates or combination therapies we may develop, as well as the pricing and reimbursement of denifanstat, TVB-3567 and any other drug candidates or combination therapies we may develop, if approved;

- our expectations regarding our ability to obtain, maintain, protect and enforce intellectual property protection for denifanstat, TVB-3567 and for any other future drug candidate or combination therapy;

- our ability to realize the anticipated benefits of any strategic transactions;

- our ability to attract and retain the continued service of our key personnel and to identify, hire, and then retain additional qualified personnel and our ability to attract additional collaborators with development, regulatory and commercialization expertise;

- the impact of macroeconomic conditions and geopolitical turmoil on our business and operations;

- our expectations regarding the period during which we will qualify as an emerging growth company under the JOBS Act; and

- our anticipated use of our existing cash, cash equivalents and marketable securities.

We have based these forward-looking statements largely on our current expectations and projections about our business, the industry in which we operate and financial trends that we believe may affect our business, financial condition, results of operations and prospects, and these forward-looking statements are not guarantees of future performance or development. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of risks, uncertainties and assumptions described in Part I, Item 1A. “Risk Factors” and elsewhere in this Annual Report. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein until after we distribute this Annual Report, whether as a result of any new information, future events or otherwise.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely upon these statements.

PART I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company developing novel therapeutics called fatty acid synthase (FASN) inhibitors that target dysfunctional metabolic and fibrotic pathways in diseases resulting from the overproduction of the fatty acid, palmitate. Our lead drug candidate, denifanstat, is an oral, once-daily pill and selective FASN inhibitor in development for the treatment of metabolic dysfunction-associated steatohepatitis (MASH), acne and select forms of cancer. Our second FASN inhibitor, TVB-3567, is a potent and selective small molecule FASN inhibitor in development for acne.

FASN inhibition for the treatment of MASH

The critical role of FASN overactivity in MASH makes it an attractive target for drug therapy. Our FASN inhibitor, denifanstat, targets multiple drivers of MASH by reducing steatosis, inflammation and fibrosis.

MASH: A growing epidemic

MASH is an aggressive form of metabolic dysfunction-associated steatotic liver disease (MASLD), a condition where an abnormal buildup of excess fat, known as steatosis, occurs in the liver unrelated to the consumption of alcohol. According to a study published in 2023, MASH is a growing epidemic that affected more than 265 million people worldwide in 2019. It is often associated with insulin resistance, type 2 diabetes, cardiovascular disease, and an increase in overall mortality. Left untreated, damage to the liver can lead to cirrhosis or liver cancer, potentially making liver transplantation necessary. There are few approved treatments for non-cirrhotic MASH (stages F1, F2 and F3 fibrosis) and no approved treatments for cirrhotic MASH (F4). We believe FASN inhibition may offer a meaningful therapeutic solution for this unmet need. The therapeutic potential of our FASN inhibitor, denifanstat, stems from its differentiated mechanism of action directly targeting the three key drivers of MASH pathogenesis: steatosis, inflammation, and fibrosis.

Phase 2b FASCINATE-2 clinical trial of denifanstat in MASH

Denifanstat met all primary and multiple secondary endpoints in the Phase 2b FASCINATE-2 clinical trial evaluating denifanstat in 168 biopsy-confirmed MASH patients with stage F2 or F3 fibrosis compared to placebo at week 52. We announced topline results in January 2024 and published the trial results in *The Lancet Gastroenterology & Hepatology* in October 2024. Denifanstat also demonstrated anti-fibrotic activity, including in patients with advanced fibrosis, as seen in the F3 modified intention to treat (mITT) population and qF4 patients (qF4 patients are artificial intelligence (AI)-defined F4, based on the second harmonic generation (SGH) HistoIndex platform, which may encompass late stage F3 as well as F4 patients):

- Fibrosis improvement by ≥ 1 stage with no worsening of MASH (F3 mITT population: denifanstat 49% vs. placebo 13%, p=0.0032).
- Fibrosis improvement by ≥ 2 stages with no worsening of MASH (mITT population: denifanstat 20% vs. placebo 2%, p=0.0065; F3 mITT population: denifanstat 34% vs. placebo 4%, p=0.0065).
- A statistically significant difference in progression to cirrhosis (F4) (mITT population: denifanstat 5% vs. placebo 11%, p=0.0386).
- A statistically significant difference in fibrosis improvement by ≥ 1 stage with no worsening of MASH for patients on a stable background dose of a GLP-1 Receptor Agonist (mITT population: denifanstat 42% vs. placebo 0%, p=0.034).
- Decrease of 1 or 2 qFibrosis stages in 85% of qF4 patients as measured by AI-based pathology (SGH, HistoIndex).
- Statistically significant liver fibrosis regression in the portal and peri-portal regions (observed with AI-based digital pathology), which have been recently linked to major adverse liver outcomes (MALO) and mortality as measured by AI-based composite scores.

As in prior studies, denifanstat was generally well tolerated. No treatment-related serious adverse events (SAEs) were observed, and the majority of adverse events (AEs) were mild to moderate in nature (Grades 1 and 2). There were no Grade ≥3 treatment-related AEs and no drug-induced liver injury (DILI) signal in the study. The most common treatment-related AEs by system organ class (observed in ≥5% of patients in the study) were eye disorders, gastrointestinal disorders, and skin and subcutaneous tissue disorders. The incidence of treatment emergent adverse events (TEAEs) leading to treatment discontinuation was 19.6% in the denifanstat group compared to 5.4% in placebo.

Combination of denifanstat and resmetirom for the treatment of MASH

We are developing a combination of our oral once-daily FASN inhibitor, denifanstat, and the thyroid hormone receptor beta (THR-β) agonist, resmetirom (commercially available as Rezdiffra), for cirrhotic patients living with F4-stage MASH.

Phase 1 pharmacokinetic (PK) clinical trial of a combination of denifanstat and resmetirom

In December 2025, we announced completion of our Phase 1 PK trial of a combination of denifanstat and resmetirom. The Phase 1 PK trial was an open-label, 2-cohort study that enrolled 40 healthy adult participants. The trial objectives were to evaluate multiple-dose and single-dose pharmacokinetics, identify any potential drug-drug interactions (DDI), and assess the safety and tolerability of the combination. The combination of denifanstat and resmetirom was generally well-tolerated over the duration of the study, with no safety signals. No SAEs were reported, and there were no clinically significant laboratory AEs and no treatment-related discontinuations.

Our combination program builds upon preclinical data we presented at the European Association for the Study of the Liver (EASL) Congress in 2024 for two mouse models of MASH, showing that the combination of a FASN inhibitor (TVB-3664, a surrogate for denifanstat) and resmetirom, had a synergistic effect on important liver disease markers, including improvement of NAS by histologic analysis and more robust improvement in hepatic collagen content compared to the single agents. Synergistic activity of the combination was demonstrated in the rate of histological improvement (NAS ≥2 points), which was 33% for FASN inhibitor monotherapy, 25% for resmetirom monotherapy, and 80% for the combination of the two, a level of improvement that greatly exceeds a simple addition of the activity of the two drugs.

We plan to use these data to advance the development of the combination into a Phase 2 proof-of-concept efficacy trial for patients living with MASH with F4 fibrosis, expected to initiate in the second half of 2026, subject to consultation with regulatory authorities.

Biomarker strategy

Given the inherent complexity of MASH and other diseases caused by dysregulated lipogenesis, our development strategy includes precision medicine approaches using non-invasive tests (NITs), which we also refer to as biomarkers, to identify indications that can be treated by denifanstat as well as patients who are most likely to respond to denifanstat. This approach includes the development of blood-based pharmacodynamic biomarkers, such as tripalmitin, to confirm FASN inhibition and pathway engagement by denifanstat, as well as predictive biomarkers incorporating metabolomic and single nucleotide polymorphism (SNP) blood profiling to identify a biomarker signature that predicts improvements in markers of MASH disease in patients taking denifanstat. Furthermore, we may apply such predictive tests complementary to therapeutic intervention with denifanstat to better understand the patients who partially respond to denifanstat. Identifying these potential non-responders may help clinicians determine if, for instance, a combination of denifanstat and another non-FASN inhibitor therapeutic may optimize clinical outcomes. We anticipate developing complementary diagnostic tools to benefit patients, clinicians and payors. Ultimately, we intend to leverage these non-invasive biomarkers to ensure FASN biology is informing both the diseases we investigate and the patients who receive treatment.

Acne

In addition to MASH, we are evaluating our FASN inhibitors in acne, a disorder in which dysregulation of fatty acid metabolism also plays a key role. Denifanstat is being developed for acne in China by our license partner for China, Ascletis BioScience Co. Ltd. (Ascletis), a subsidiary of Ascletis Pharma Inc. (Ascletis Pharma). Our potent and selective small molecule FASN inhibitor, TVB-3567, is currently in a first-in-human Phase 1 clinical trial for development of an acne indication. Acne is a promising therapeutic area for application of FASN inhibitors because FASN is required for sebum production, which is upregulated in acne and leads to exacerbation of acne lesions including development of nodules and cysts.

Phase 3 clinical trial of denifanstat in acne

In January 2026, Ascletis reported positive topline results in the open-label Phase 3 trial evaluating the long-term safety of ASC40 (denifanstat) tablets in patients with moderate to severe acne in China.

In December 2025, Ascletis announced that the China National Medical Products Administration (NMPA) accepted its New Drug Application (NDA) for denifanstat for the treatment of moderate to severe acne.

In June 2025, Ascletis announced that denifanstat met all primary and secondary endpoints in its Phase 3 trial in moderate to severe acne vulgaris in China. The Phase 3 clinical trial was a randomized, double-blind, placebo-controlled, multicenter clinical trial of 480 enrolled patients randomized 1:1 to receive denifanstat 50mg or placebo, once daily for 12 weeks.

Ascletis reported the following efficacy data from the Phase 3 trial:

- All primary endpoints were met, including:
    - the percentage of treatment success (defined as an Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with at least a 2-point decrease from baseline) (denifanstat 33.2% vs. placebo 14.6%, $p<0.0001$).
    - the percentage change in total lesion count (denifanstat -57.4% vs. placebo -35.4%, $p<0.0001$).
    - the percentage change in inflammatory lesion count (denifanstat -63.5% vs. placebo -43.2%, $p<0.0001$).
- The secondary endpoint of change in non-inflammatory lesion count was also met (denifanstat -51.9% vs. placebo -28.9%, $p<0.0001$).

Ascletis reported that denifanstat was generally well-tolerated. Following 12 weeks of once-daily oral administration at 50mg, the incidence rates of TEAEs were comparable between denifanstat and placebo.

Phase 1 clinical trial of TVB-3567

In June 2025, we initiated a first-in-human Phase 1 clinical trial of our potent and selective small molecule FASN inhibitor, TVB-3567, for development of an acne indication. The Phase 1 clinical trial is a randomized double-blind placebo-controlled trial designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of TVB-3567 in healthy participants with or without acne. The trial is comprised of several parts, including single ascending dose cohorts and multiple ascending dose cohorts in participants without acne, followed by testing in participants with acne including evaluation of pharmacodynamic biomarkers.

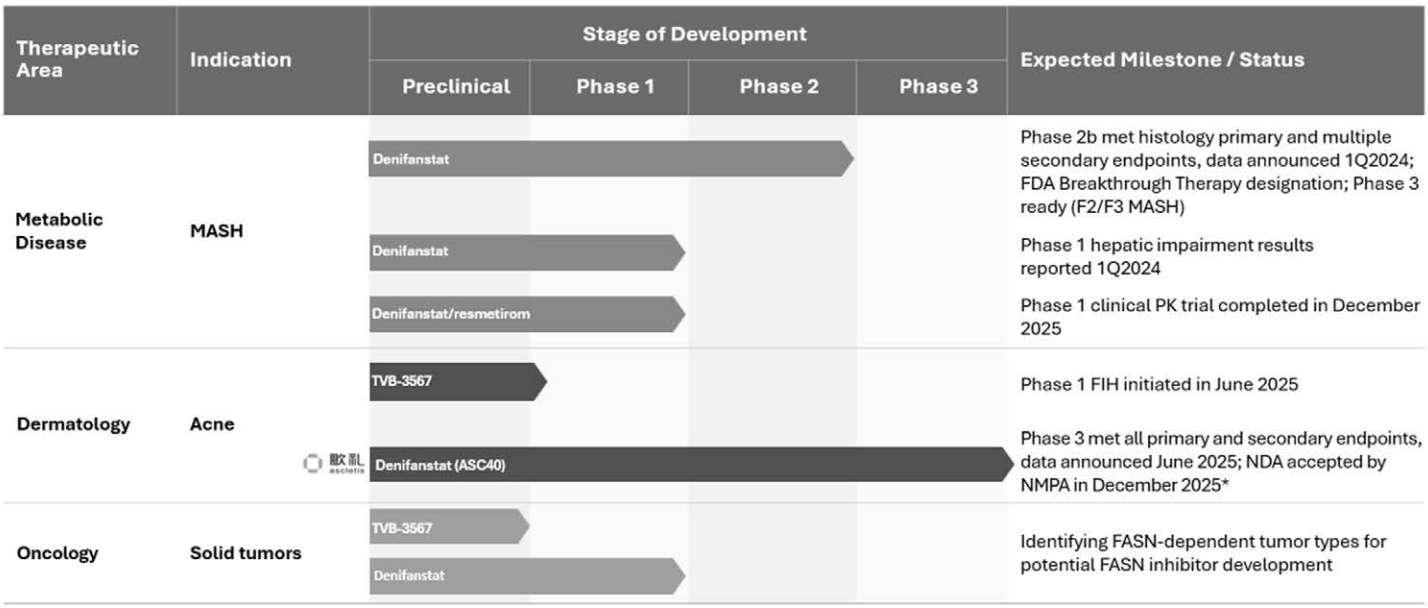
Subject to consultation with regulatory authorities, and contingent on the results of the Phase 1 trial, we anticipate initiating the Phase 2 trial of TVB-3567 in 2026.

Our FASN inhibitor pipeline

The critical role of FASN overactivity in MASH, acne and cancer has made it an attractive target for drug therapy. Early generations of FASN inhibitor compounds made by others were limited by their off-target activities, inappropriate localization to the brain and poor pharmaceutical properties. Most of these compounds never entered clinical development, and the few that did, failed in early-stage clinical trials due to these limitations. We selected denifanstat and TVB-3567 from our library of over 1,200 internally discovered and wholly owned FASN inhibitors after a rigorous medicinal chemistry and preclinical development effort. We advanced denifanstat and TVB-3567 into clinical development, based upon their oral administration, high selectivity for FASN, and excellent pharmacokinetic and pharmaceutical properties, including restricted penetration of the blood-brain barrier. FASN is a large protein with six different enzymatic domains. The selectivity of denifanstat and TVB-3567 is a consequence of binding to the protein in an area that is not an

enzymatic active site and unique to the structure of FASN. This selectivity is critical for preventing off-target effects that plagued earlier generations of FASN inhibitor compounds.

The following table summarizes our development programs for multiple diseases with high unmet need:



**Trials conducted in China by Ascletis, who has licensed development and commercialization rights to all indications in Greater China.*
***First-in-human (FIH).*
Figure 1. Development pipeline

Our strategy

Our goal is to develop and commercialize our selective FASN inhibitors in therapeutic areas where upregulation of FASN plays a central role in the development or progression of disease. We intend to achieve this goal by pursuing the following key strategic objectives:

- ***Progress the combination of denifanstat and resmetirom through clinical development for the treatment of MASH.*** We have tested a combination of a FASN inhibitor (TVB-3664, a surrogate for denifanstat) and a THR-ß agonist in two in vivo preclinical MASH models, and data showed that the combination of a FASN inhibitor and resmetirom had a synergistic effect on important liver disease markers, including improvement of NAS (NAFLD Activity Score) by histologic analysis and more robust improvement in hepatic collagen content compared to the single agents. We hypothesize that the complementary mechanisms of denifanstat (inhibiting fat synthesis) and THR-ß (increasing fat removal) may normalize liver fat in MASH patients and may improve clinical activity on fibrosis endpoints. In December 2025, we announced completion of our Phase 1 PK trial of a combination of denifanstat and the THR-β agonist resmetirom. We plan to advance the development of the combination into a Phase 2 proof-of-concept efficacy trial for patients living with MASH with F4 fibrosis, expected to initiate in the second half of 2026, subject to consultation with regulatory authorities.

- ***Establish the combination of denifanstat and resmetirom as a potential backbone therapy for the treatment of MASH.*** Given the disease complexity of MASH, as well as the heterogeneity and large size of the MASH patient population, we believe a combination of denifanstat and resmetirom has the potential to address multiple MASH indications. Subject to data from our clinical trials, we intend to seek approval of the combination of denifanstat and resmetirom for the treatment of cirrhotic MASH (F4) and pediatric MASH to maximize denifanstat's full clinical and commercial potential.

- ***Advance our precision medicine strategy to identify patients who will benefit from denifanstat***. Given that MASH is a complex, progressive disease for which there are two recently approved treatments in the United States and only one currently

approved treatment in Europe, our precision medicine strategy to develop non-invasive biomarkers complements our clinical development efforts for denifanstat. This includes the development and application of pharmacodynamic biomarkers to confirm drug response to denifanstat and predictive biomarkers to select the patients most likely to have a clinical response. We expect to continue to validate these biomarkers with results emerging from our ongoing clinical development, including our planned Phase 2 proof-of-concept efficacy trial for patients living with MASH with F4 fibrosis, expected to initiate in the second half of 2026, subject to consultation with regulatory authorities.

- ***Advance TVB-3567 clinical development for the treatment of moderate to severe acne.*** In June 2025, we initiated a first-in-human Phase 1 clinical trial of TVB-3567, a potent and selective small molecule FASN inhibitor, for development of an acne indication. This builds upon the clinical trial results of denifanstat in acne reported by our license partner for China, Ascletis. In June 2025, Ascletis announced that denifanstat met all primary and secondary endpoints in its Phase 3 trial in moderate to severe acne vulgaris in China. In December 2025, Ascletis announced that the China NMPA has accepted its NDA for denifanstat for the treatment of moderate to severe acne. In January 2026, Ascletis reported positive topline results in the open-label Phase 3 trial evaluating the long-term safety of ASC40 (denifanstat) tablets in patients with moderate to severe acne in China. Subject to consultation with regulatory authorities, and contingent on the results of our Phase 1 trial, we anticipate initiating the Phase 2 trial of TVB-3567 in 2026.

- ***Expand pipeline in indications beyond MASH and acne, where FASN plays a central role in disease pathogenesis.*** Based on our seminal work around FASN biology and the broad potential of this mechanism in diseases beyond MASH and acne, we have also prioritized oncology in our initial development pursuits for denifanstat. In oncology, we are developing FASN inhibitors to treat specific subsets of solid tumors that are FASN-dependent. We are exploring the potential of denifanstat in combination with other classes of oncology drugs. We conducted our first-in-human Phase 1 clinical trial for denifanstat in patients with advanced solid tumors. We will maintain a focused and disciplined strategy in evaluating potential indications beyond MASH and acne that may merit further advancement.

- ***Develop and commercialize our drug candidates independently in indications and geographies where we believe we can maximize value and benefit to patients.*** Because we believe our FASN platform and drug candidates have the potential to treat a broad range of diseases, we will independently develop drug candidates in indications and geographies where we believe we can successfully commercialize on our own if they are approved. We will collaborate on drug candidates that we believe have promising utility in disease areas, patient populations or geographies that are better served by the resources or specific expertise of other biopharmaceutical companies. Our license agreement with Ascletis for the development, manufacturing and commercialization of denifanstat in Greater China is an example of this strategy.

Overview of MASH

MASH is an aggressive form of MASLD, a condition where an abnormal buildup of excess fat (known as steatosis) occurs in the liver unrelated to the consumption of alcohol. MASLD encompasses a progressive and histologically-defined range of liver diseases including simple steatosis (the presence of excess liver fat without inflammation or fibrosis) to MASH without fibrosis (excess liver fat with inflammation), to MASH with fibrosis and may ultimately lead to cirrhosis or cancer of the liver. Patients with moderate to severe disease, who have advanced fibrosis (F3) or cirrhosis (F4), have the highest risk of liver-related outcomes such as decompensation, hepatocellular carcinoma, and liver transplantation. There are few approved treatments for non-cirrhotic MASH (stages F1, F2 and F3 fibrosis) and no approved treatments for cirrhotic MASH (F4).

MASH is initiated and propagated through several processes driven by excess fat in liver cells.

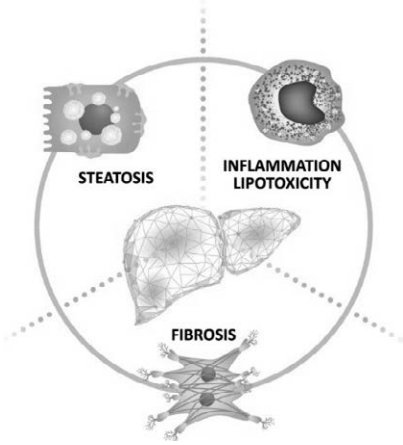


Figure 2. Excess liver fat drives three key diseases processes

Excess intracellular fat damages hepatocytes, the predominant cell type in the liver, leading to apoptosis, or cell death. Hepatocyte apoptosis triggers the stimulation of specialized immune cells. The increased activity of these cells drives inflammation in the liver. Additionally, as more hepatocytes are destroyed and inflammation increases, hepatic stellate cells are stimulated and induce fibrotic scarring. As this progressive cycle continues, the functions of the liver become compromised, potentially necessitating transplantation.

The diagnosis and severity of the disease can be assessed by histological analyses of liver tissue taken by biopsy which examine the degree of steatosis, inflammation and fibrosis using a microscope. For example, NAS is the most widely used histological grading and staging score and is a compilation of scores measuring steatosis, ballooning and inflammation. Additionally, the severity of fibrosis is scored on a 5-level scale of F0 (no fibrosis) to F4 (cirrhosis). NAS, along with the fibrosis stage, indicate the degree of progression of an individual's disease. In addition to liver biopsy, non-invasive approaches for the diagnosis of MASH are becoming increasingly prevalent and may eventually replace liver biopsy as further data becomes available. As part of its December 2018 MASH draft guidance, the U.S. Food and Drug Administration (FDA) emphasized the importance of non-invasive biomarkers in accurately diagnosing and assessing various degrees of MASH. The FDA encouraged sponsors to include non-invasive biomarkers in clinical trials for MASH with the goal of ultimately supplanting liver biopsy. Recently, in August 2025, the FDA accepted a Letter of Intent (LOI) for vibration-controlled transient elastography (VCTE) as a reasonable surrogate endpoint for assessing response to investigational drugs in non-cirrhotic MASH.

MASLD is a growing epidemic. According to a study published in 2023, MASLD affected more than 1.6 billion people worldwide as of 2019, 265 million of whom had MASH. In a separate study published in 2018, the prevalence of MASH in the United States was estimated at 17.3 million in 2016 and expected to grow to 27.0 million by 2030. Of the MASH patients in the United States, 1.4 million had cirrhotic MASH (F4) in 2016, which is our initial target patient population for the combination of denifanstat and resmetirom, if approved. The number of cirrhotic MASH (F4) patients is expected to grow to 3.5 million in 2030. According to a study published in 2022, when MASH is left unchecked, over time approximately 10%-20% of patients with MASH will progress to liver cirrhosis (histological stage F4). Once cirrhosis has developed, the risk of developing a major complication is 17%, 23%, and 52% at one, three, and 10 years, respectively. The survival of patients with MASH cirrhosis falls markedly once decompensation occurs, with a median survival of approximately two years. Conversely, histological regression of cirrhosis has been shown to reduce the risk of cirrhosis-related complications by six-fold. According to a study published in 2022, in the United States alone, the economic burden of MASH has been estimated to be over $222 billion.

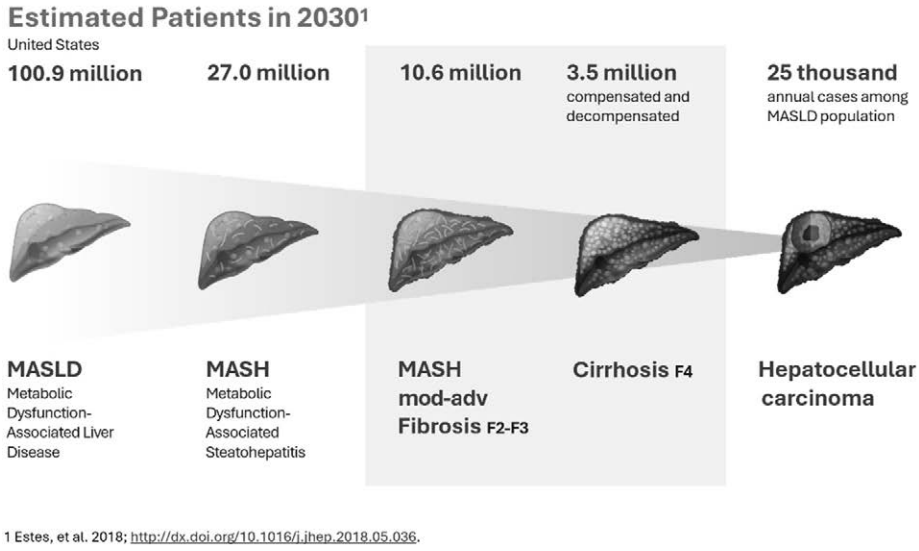


Figure 3. MASLD disease progression and epidemiology

MASH treatment landscape

MASH is characterized by the build-up of fat in the liver and various degrees of inflammation and fibrosis along with systemic metabolic changes including dyslipidemia (increased fat levels in blood) and insulin resistance. These parameters provide a framework to classify the various treatments under development and their mechanisms of action, many of which have significant limitations or address only a subset of MASH patients. Treatments that primarily address the build-up of fat in the liver and systemic metabolic changes include enzyme-specific inhibitors, nuclear receptor modulators, gene expression modulators, growth factor analogs and drugs that induce weight loss. Other approaches attempt to directly target only inflammation and fibrosis.

Enzyme-specific inhibitors in the lipid synthesis pathway target an enzyme in the de novo lipogenesis (DNL) pathway to return lipid synthesis to a normal level, reduce liver fat, and minimize the ongoing inflammation and fibrosis in MASLD and MASH patients, ultimately allowing the liver tissue to regain its normal cellular structure and function. FASN and acetyl-CoA carboxylase (ACC) are examples of enzyme inhibitors, both of which have shown significant clinical improvements in fat reduction, and improvements in biomarkers of liver enzymes, inflammation and fibrosis. ACC inhibitors, unlike FASN inhibitors, have also been shown to increase plasma triglyceride levels in MASH patients. This is particularly problematic for MASH patients who typically have an elevated risk for cardiovascular disease.

Nuclear receptor modulators alter the gene expression pattern of cells, affecting multiple biochemical pathways, which can lead to unintended changes beyond the target pathway of interest. Examples of nuclear receptor modulators studied as therapeutic targets in MASH include farnesoid X receptor (FXR) agonists, peroxisome proliferator-activated receptor (PPAR) agonists, and thyroid hormone receptor beta (THR-ß) agonists. FXR is expressed in a number of tissues throughout the body, including the liver. It serves as a receptor for bile acids and participates in regulating their metabolism, including synthesis, conjugation, absorption, and secretion. The PPAR family of receptors modulate fatty acid metabolism and energy homeostasis. FXR and PPAR agonists have had mixed clinical results to date. The FDA approval of THR-ß agonist Rezdiffra (resmetirom) in March 2024 and by the European Commission in August 2025 for the treatment of MASH in patients with moderate to advanced liver fibrosis represents a significant advancement in the MASH space. Activation of hepatic THR-ß is associated with systemic lipid lowering, increased bile acid synthesis, and fat oxidation. These results suggest that directly targeting liver fat metabolism can be a successful therapeutic strategy in MASH. However, it should be noted that therapeutic nuclear receptor modulation is not without safety risk. FXR agonists can affect pathways leading to excess bile acids, which have long been shown to be toxic. This can cause pruritus, or itching of the skin. PPAR agonists have been associated with weight gain. THR-ß agonists need to be highly selective for the beta isoform of this receptor and avoid binding the alpha isoform, which exists in the heart and kidneys. If not highly selective, they can result in significant, potentially life-threatening complications.

Growth factor analogs attempt to mimic natural proteins, such as FGF21, to bring several disordered systems back to normal levels. In two clinical trials in patients with F2-F3 fibrosis, FGF21 analogs showed evidence of MASH resolution and improvement in liver fibrosis after 48 or 96 weeks of treatment, respectively. Data showed that an FGF21 analog administered for 96 weeks induced regression

of histological cirrhosis (F4). Gastrointestinal side effects are common with injected FGF21, nausea and diarrhea being the most common. Data from two clinical trials, one in patients with F2-F3 fibrosis and the other in patients with F4 fibrosis, demonstrated that an FGF21 analog was associated with a decrease in bone density that can potentially lead to an increased risk of fractures. Because of the large size of proteins, the mode of delivery is typically limited to injection. Growth factor analogs are also more expensive to manufacture compared to small molecules. We believe there is a possibility that patients will develop neutralizing antibodies against these therapeutics with chronic treatment.

Glucagon-like peptide 1 (GLP-1) analogs are approved to treat diabetes and obesity; and one GLP-1 analog is approved for the treatment of MASH in adult patients with moderate to advanced liver fibrosis in the United States. In Phase 2 and Phase 3 clinical trials in F2-F3 fibrosis, treatment with a GLP-1 analog or GLP-1-containing medications, reduced body weight, demonstrated histological MASH resolution, reduced biomarkers associated with MASH and achieved improvement in fibrosis compared to placebo. In addition, a Phase 2 clinical trial with a GLP-1 receptor agonist failed to demonstrate improvement in F4 fibrosis. Gastrointestinal side effects are common with injected or oral GLP-1 medications, with nausea and vomiting being the most common.

Our lead drug candidate—denifanstat in MASH

Denifanstat, formerly known as TVB-2640, an oral, once-daily pill, is our selective FASN inhibitor currently being developed for the treatment of MASH. Following a robust translational research program in multiple preclinical models that demonstrated FASN inhibition reduced liver fat, decreased inflammatory cells and molecules and blunted fibrosis and a proof-of-mechanism Phase 1b clinical trial that demonstrated inhibition of hepatic DNL in humans, we initiated two Phase 2 clinical trials in patients with MASH: FASCINATE-1 and FASCINATE-2. Treatment with denifanstat favorably altered biomarkers of MASH in our Phase 2 clinical trials as shown in the figure below.

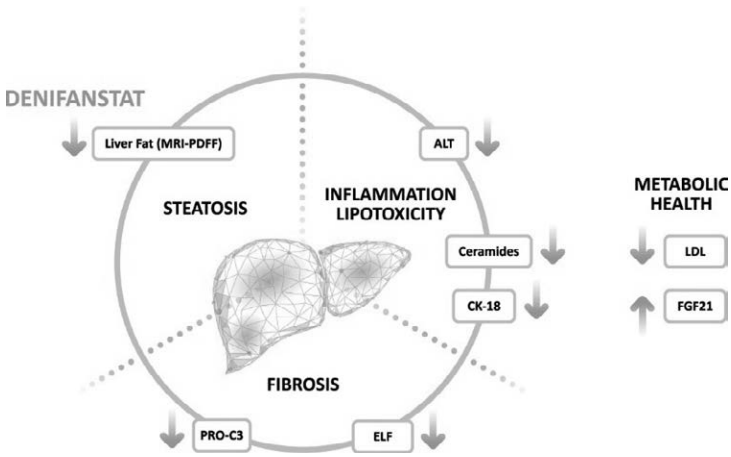


Figure 4. Comprehensive improvement across biomarkers

The Phase 2 FASCINATE-1 clinical trial examined multiple doses of denifanstat, ranging from 25mg to 75mg daily, administered for 12 weeks compared to placebo in 142 patients in the United States and China. Denifanstat caused a rapid and robust reduction in liver fat that was statistically significant in the 50mg cohort, as well as improvements in inflammatory, fibrotic and cardiometabolic components of the disease in this short time period and was generally well tolerated at dose levels of 25mg and 50mg once-daily in these diverse populations. The 50mg dose was selected for further study.

Our Phase 2b FASCINATE-2 clinical trial examined the impact of 50mg denifanstat for one year on the livers of biopsy confirmed MASH patients with moderate to advanced fibrosis (F2-F3). In January 2024, we announced that denifanstat had met both primary endpoints and multiple secondary endpoints in the Phase 2b FASCINATE-2 clinical trial evaluating denifanstat in 168 biopsy-confirmed MASH patients with stage F2 or F3 fibrosis compared to placebo at week 52. The trial results were published in October 2024 in *The Lancet Gastroenterology & Hepatology*.

- Both primary endpoints were met:

- A ≥2-point reduction in NAS (NAFLD Activity Score) without worsening of fibrosis in both modified intention to treat (mITT) and intention to treat (ITT) populations (mITT population: denifanstat 52% vs. placebo 20%, p=0.0003; ITT population: denifanstat 38% vs. placebo 16%, p=0.0035), and

- MASH resolution without worsening of fibrosis with ≥2-point reduction in NAS (mITT population: denifanstat 36% vs. placebo 13%, p=0.0044; ITT population: denifanstat 26% vs. placebo 11%, p=0.0173).

- Multiple secondary endpoints were met, including:

  - The 2 histology endpoints used by the FDA for accelerated approval in Phase 3 programs; fibrosis improvement by ≥ 1 stage with no worsening of MASH (mITT population: denifanstat 41% vs. placebo 18%, p=0.0102) and MASH resolution with no worsening of fibrosis (mITT population: denifanstat 38% vs. placebo 16%, p=0.0043). MRI-derived proton density fat fraction (MRI-PDFF) response relative to placebo (mITT population: denifanstat 65% vs. placebo 21%, p<0.0001). MRI-PDFF responders are patients with ≥8% liver fat content at baseline who achieve a ≥30% relative reduction of liver fat at the end of treatment.

Denifanstat demonstrated anti-fibrotic activity, including in patients with advanced fibrosis, based on results in the F3 mITT population and qF4 patients (qF4 patients are AI-defined F4, based on the second harmonic generation (SGH) HistoIndex platform, which may encompass late stage F3 as well as F4 patients):

- Fibrosis improvement by ≥ 1 stage with no worsening of MASH (F3 mITT population: denifanstat 49% vs. placebo 13%, p=0.0032).

- Fibrosis improvement by ≥ 2 stages with no worsening of MASH (mITT population: denifanstat 20% vs. placebo 2%, p=0.0065; F3 mITT population: denifanstat 34% vs. placebo 4%, p=0.0065).

- A statistically significant difference in progression to cirrhosis (F4) (mITT population: denifanstat 5% vs. placebo 11%, p=0.0386).

- A statistically significant difference in fibrosis improvement by ≥ 1 stage with no worsening of MASH for patients on a stable background dose of a GLP-1 Receptor Agonist (mITT population: denifanstat 42% vs. placebo 0%, p=0.034).

- Decrease of 1 or 2 qFibrosis stages in 85% of qF4 patients as measured by AI-based pathology (SGH, HistoIndex).

- Statistically significant liver fibrosis regression in the portal and peri-portal regions (observed with AI-based digital pathology), which have been recently linked to MALO and mortality as measured by AI-based composite scores.

- A statistically significant VCTE improvement (VCTE <= -30% and VCTE < 10KPa) at week 26 (mITT population: denifanstat 32% vs. placebo 13%, p=0.02) and at week 52 (mITT population: denifanstat 42% vs. placebo 13%, p=0.0009).

Other key results of the Phase 2b FASCINATE-2 clinical trial included:

- A statistically significant increase in polyunsaturated triglycerides (potential for cardiovascular benefit) at the end of 52 weeks of treatment (mITT population: +42% denifanstat vs. -4% placebo, p<0.001).

- A biomarker of denifanstat activity (tripalmitin) showed an early and sustained reduction in de novo lipogenesis at 4-weeks (-2.4ug/mL with denifanstat vs. -0.4ug/mL placebo, p=0.001) and 13-weeks (-2.2ug/mL with denifanstat vs. -0.1ug/mL placebo, p=0.005) in the ITT population.

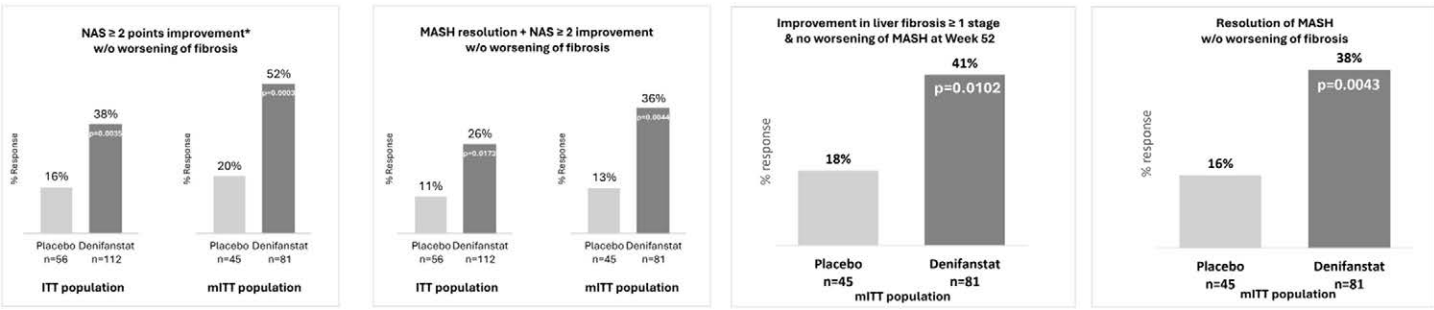


Figure 5. FASCINATE-2 liver biopsy analysis at Week 52, primary and secondary endpoints
Cochran-Mantel-Haenszel Test – two sided at the 0.05 significance level. * ≥1-point improvement in ballooning or inflammation.
Loomba R, et al. Lancet Gastroenterol Hepatol. 2024;9(12):1090-1100

Fibrosis Endpoints	Subgroup	Placebo	Denifanstat	p-value
≥1 stage improvement in fibrosis w/o worsening of MASH	ITT	14%	30%	0.040**
	mITT	18%	41%	0.0102**
	F3	13%	49%	0.0032**
≥2 stage improvement in fibrosis w/o worsening of MASH	mITT	2%	20%	0.0065**
	F3	4%	34%	0.0065**
Progression to cirrhosis (F4)	mITT	11%	5%	0.0386*

*One sided at the 0.05 significance level, **Two sided at the 0.05 significance level

Figure 6. FASCINATE-2 liver biopsy analysis at Week 52, secondary endpoints

In the study, the ITT definition was consistent with the FDA's historical recommendation that patients without a second biopsy be considered treatment failures.

As in prior studies, denifanstat was generally well tolerated. No treatment-related SAEs were observed, and the majority of AEs were mild to moderate in nature (Grades 1 and 2). There were no Grade ≥3 treatment-related AEs and no drug-induced liver injury (DILI) signal in the study. The most common treatment-related AEs by system organ class (observed in ≥5% of patients in the study) were eye disorders, gastrointestinal disorders, and skin and subcutaneous tissue disorders. The incidence of TEAEs leading to treatment discontinuation was 19.6% in the denifanstat group compared to 5.4% in placebo.

In October 2024, the FDA granted Breakthrough Therapy designation to denifanstat for the treatment of non-cirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). Treatments that receive Breakthrough Therapy designation must target a serious or life-threatening disease and preliminary clinical evidence must indicate that the drug may demonstrate a substantial improvement over existing therapies on one or more clinically significant endpoints. Breakthrough Therapy designation of denifanstat was supported by positive data from the Phase 2b FASCINATE-2 clinical trial in biopsy-confirmed MASH patients with stage 2 or stage 3 fibrosis. In October 2024, we completed successful end-of-Phase 2 interactions with the FDA.

Mechanisms of action in MASH

FASN is a key enzyme in the DNL pathway that converts metabolites of dietary sugars such as fructose into palmitate, a saturated fatty acid. Excess DNL activity and palmitate drive the hallmarks of MASH through accumulation of triglyceride in hepatocytes, and induction of inflammatory responses. The amount of FASN expressed and the DNL pathway activity are increased in the livers of patients with metabolic syndrome or MASLD compared to healthy individuals. Increased DNL activity in hepatocytes leads to the

accumulation of excess fat (steatosis) in the liver. This initiating event drives MASH, and causes liver inflammation, tissue damage, and fibrosis. In addition, inflammatory cells require DNL for pro-inflammatory function, and hepatic stellate cells, which generate fibrotic scar tissue in the liver, require DNL to express profibrotic genes including procollagen. Furthermore, palmitate, the product of FASN, is used to synthesize pro-inflammatory and pro-fibrotic molecules called lipotoxins which contribute to the mechanisms driving the progressive nature of MASH. This places FASN at the nexus of three major drivers of liver damage in MASH: excess intracellular fat synthesis, inflammation and fibrosis.

We believe that inhibiting FASN has the potential to minimize side effects in MASH patients for several reasons. First, the enzymatic inhibition of FASN is targeted and directly acts within the DNL pathway, unlike nuclear receptor modulators such as THR-ß or FXR agonists that activate multiple transcription pathways. Second, FASN is aberrantly overactivated in the liver in MASH, and normalizing activity through inhibition of FASN may avoid side effects. Furthermore, mice genetically engineered to have the FASN gene knocked-out in their livers appear normal, whereas mice with the ACC gene, an enzyme one step earlier in the lipid synthesis pathway, knocked-out have high liver and plasma triglycerides.

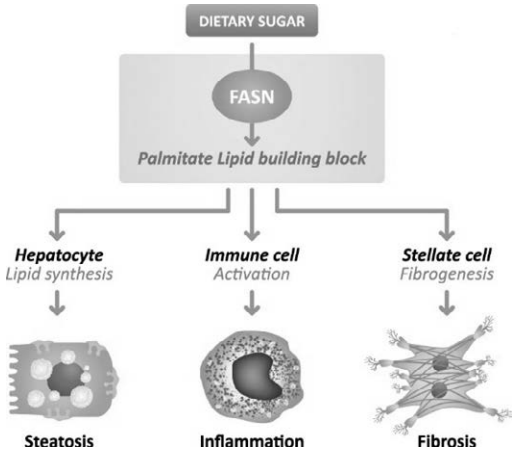


Figure 7. Denifanstat impacts key drivers of MASH

We believe that denifanstat has the potential to alleviate MASH by inhibiting FASN and thereby impacting key drivers of MASH by:

1. Blocking liver fat accumulation (steatosis) by reducing liver fat synthesis in hepatocytes;
2. Minimizing inflammation by blocking the activation and cytokine secretion by inflammatory cells; and
3. Reducing fibrosis by blocking the activation and fibrogenic activity of stellate cells.

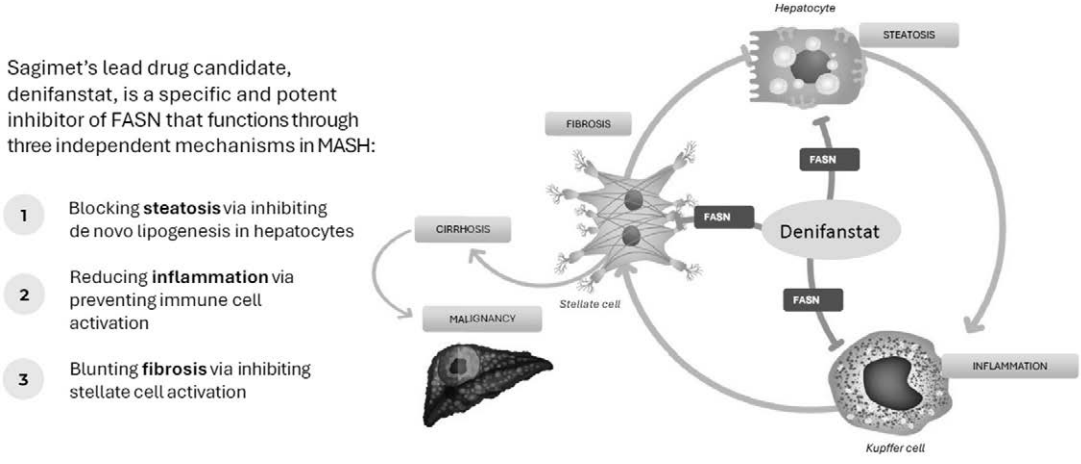


Figure 8. The cycle of MASH pathogenesis

The diagram above of the cycle of MASH pathogenesis shows how excess dietary sugar, particularly in someone with decreased sensitivity to insulin, produces excess palmitate in hepatocytes leading to fatty hepatocytes. The high level of palmitate, a lipotoxin, creates metabolic stress in these cells, leading to ballooned hepatocytes, which is evidence of cellular damage. These damaged hepatocytes undergo apoptosis. The cellular debris resulting from apoptosis stimulates inflammatory cells in the liver, eliciting an inflammatory response. This damage and inflammation in the liver stimulates hepatic stellate cells, which trigger fibrotic responses. As additional excess sugars come in via the diet, this process continues, leading to build up of fibrotic scar tissue. If the damaging environment is removed, the liver has the potential to regenerate healthy tissue over time. However, if the damaging environment continues to persist, some patients will progress to cirrhosis and may develop hepatocellular carcinoma.

Recent studies, including evidence presented at the European Association for the Study of the Liver in Paris, France in 2018 and a clinical trial that measured DNL in MASH patients with cirrhosis (2022; Lawitz et al.), have shown that the liver also continues to produce fat in the later stages of MASLD, including in patients with early stages of cirrhosis. This broadens the number of patients who could benefit from FASN inhibition. These late-stage patients can progress to liver cirrhosis, which can lead to acute liver decompensation events that can be life threatening, require hospitalization, and in the case of decompensated cirrhosis, liver transplant. We believe the three-pronged potential mechanism of action of denifanstat could address these patients with MASH cirrhosis, preventing further liver damage.

Combination therapy for MASH treatment

Currently there are few approved treatments for non-cirrhotic MASH (stages F1, F2 and F3 fibrosis) and no approved treatments for cirrhotic MASH (F4). Clinical results of single agent trials have often been modest, with the majority of patients not responding. Combination therapy may increase the depth and breadth of clinical response across patient populations and decrease tolerability concerns for the treatment of MASH. The magnitude of patients combined with the disease complexity support the concept that multiple combinations of drugs targeting different mechanisms will be required to effectively manage this disease in a large, diverse population.

Based on its proposed mechanism of action, we believe that denifanstat, if successfully developed and approved, has the potential to be a backbone therapy and improve clinical activity in combination with a broad set of other drugs. Denifanstat's convenient once-a-day oral administration and tolerability profile make it a potentially desirable combination partner. The activity of denifanstat may be further empowered by additional drugs targeting other aspects of MASH or metabolic disease.

Our combination strategy is to use preclinical models to mechanistically evaluate the combination potential prior to considering clinical studies with the combination. We focused on combination partners that have clinical validation in MASH, and complementary mechanism of action to denifanstat. We have experience with models of human liver microtissues, human liver slices, and murine models; these models and others continue to be refined in order to provide information that guides identification of mechanisms and drugs that would exhibit a significant benefit for combination therapy.

We have tested a combination of a FASN inhibitor (TVB-3664, a surrogate for denifanstat) and a THR-ß agonist in two in vivo preclinical MASH models, and data showed that the combination of a FASN inhibitor and resmetirom had a synergistic effect on important liver disease markers, including improvement of NAS (NAFLD Activity Score) by histologic analysis and more robust improvement in hepatic collagen content compared to the single agents. Synergistic activity of the combination was demonstrated in the rate of histological improvement (NAS $\geq$2 points). The FASN inhibitor monotherapy showed 33% improvement, resmetirom monotherapy showed 25% improvement, and the combination of the two showed an 80% improvement, a level of improvement that greatly exceeds a simple addition of the activity of the two drugs. Therefore, the complementary mechanisms of denifanstat (inhibiting fat synthesis) and THR-ß (increasing fat removal) might further normalize liver fat in MASH patients and might improve clinical activity on fibrosis endpoints. Building on the combination data, we initiated in October 2025 a Phase 1 clinical trial to evaluate the PK of a combination of denifanstat and resmetirom. The Phase 1 PK trial of denifanstat and resmetirom was an open-label, 2-cohort study that enrolled 40 healthy adult participants. The objectives were to evaluate multiple-dose and single-dose pharmacokinetics, identify any potential DDIs, and assess the safety and tolerability of the combination. In December 2025, we announced the completion of the Phase 1 PK trial. The combination of denifanstat and resmetirom was generally well-tolerated over the duration of the study, with no safety signals. No SAEs occurred, and there were no clinically significant laboratory AEs, and no treatment-related discontinuations. We plan to use these data to advance the development of the combination into a Phase 2 proof-of-concept efficacy trial for patients living with MASH with F4 fibrosis, subject to consultation with regulatory authorities.

We have also evaluated a GLP-1 agonist in a preclinical mouse combination study. In November 2023, at the 7th Obesity and NASH Drug Development Summit, we presented the results of a study assessing treatment with FASN inhibitor alone, semaglutide alone, or combination of FASN inhibitor with semaglutide for 12 weeks in a MASH mouse model. FASN inhibitor or semaglutide alone improved

NAS and decreased several biomarkers associated with MASH. Only the FASN inhibitor, but not semaglutide, showed significant reduction of liver fibrosis by a digital AI pathology assessment. FASN inhibitor and semaglutide in combination showed further histological improvement of NAS and liver fibrosis compared to treatment with FASN inhibitor alone or semaglutide alone. In addition, data from the Phase 2b FASCINATE-2 trial in a small subset of patients on a stable GLP-1 dose showed a statistically significant superior response in liver fibrosis improvement by more than one stage without worsening of MASH when patients received denifanstat in addition to GLP-1 therapy, versus with placebo. We believe such data support further clinical evaluation of denifanstat and GLP-1 combination therapy for MASH.

We may conduct exploratory clinical trials with relatively short durations to evaluate combinations of denifanstat and other complementary mechanisms. These trials would allow us to evaluate potential improvements in non-invasive biomarkers directly in MASH patients and select combinations for further development.

MASH clinical program

Denifanstat has been studied in over 1,200 people to date including healthy volunteers, patients with solid tumors, patients with acne, and patients with MASH. In MASH, we completed a Phase 2 clinical trial, FASCINATE-1, which examined multiple doses of denifanstat from patients in both the United States and China. We completed a Phase 2b trial, FASCINATE-2, in patients with biopsy-confirmed MASH with moderate to advanced fibrosis (F2-F3). FASCINATE-1 examined doses ranging from 25mg to 75mg daily for 12 weeks and demonstrated improvement in non-invasive measurements of steatosis, inflammation, fibrotic and metabolic parameters. FASCINATE-2 evaluated the 50mg dose daily for one year. In January 2024, we announced positive topline results at week 52 from our Phase 2b FASCINATE-2 clinical trial. The Phase 2b FASCINATE-2 clinical trial achieved statistically significant results on primary and multiple secondary endpoints at week 52 in 168 biopsy-confirmed MASH patients. Further, in December 2025, we announced completion of our Phase 1 PK trial of a combination of denifanstat and a THR-β agonist, resmetirom.

Phase 1 PK clinical trial of a combination of denifanstat and resmetirom

In December 2025, we announced the completion of the Phase 1 PK trial of a combination of denifanstat and a THR-β agonist, resmetirom. The Phase 1 PK trial of denifanstat and resmetirom was an open-label, 2-cohort study that enrolled 40 healthy adult participants. The trial objectives were to evaluate multiple-dose and single-dose pharmacokinetics, identify any potential DDI, and assess the safety and tolerability of the combination. The combination of denifanstat and resmetirom was generally well-tolerated over the duration of the study, with no safety signals. No SAEs occurred, and there were no clinically significant laboratory AEs, and no treatment-related discontinuations.

Our combination program builds upon preclinical data we presented at the EASL Congress in 2024 for two mouse models of MASH, showing that the combination of a FASN inhibitor (TVB-3664, a surrogate for denifanstat) and resmetirom had a synergistic effect on important liver disease markers, including improvement of NAS by histologic analysis and more robust improvement in hepatic collagen content compared to the single agents. Synergistic activity of the combination was demonstrated in the rate of histological improvement (NAS ≥2 points), which was 33% for FASN inhibitor monotherapy, 25% for resmetirom monotherapy, and 80% for the combination of the two, a level of improvement that greatly exceeds a simple addition of the activity of the two drugs.

We plan to use these data to advance the development of the combination into a Phase 2 proof-of-concept efficacy trial for patients living with MASH with F4 fibrosis, subject to consultation with regulatory authorities.

Phase 2b FASCINATE-2 clinical trial

Phase 2b FASCINATE-2 clinical trial design

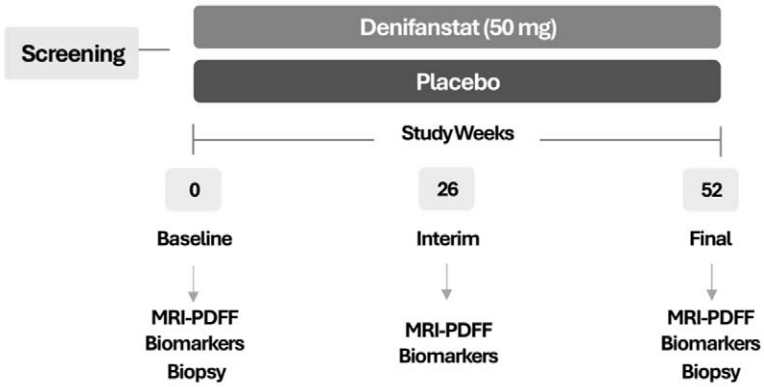


Figure 9. Phase 2b FASCINATE-2 clinical trial design

The Phase 2b FASCINATE-2 clinical trial was a randomized, placebo-controlled, double-blind clinical trial, which enrolled 168 biopsy-confirmed MASH patients with F2-F3 fibrosis confirmed by liver biopsy and randomized overall 2:1 to receive 50mg of denifanstat or placebo for 52 weeks. Following 52 weeks of therapy, a second liver biopsy was obtained. A central pathologist who is unaware of the patients' assignment to denifanstat or placebo cohorts evaluated these biopsies. Patients were followed for an additional four weeks after the biopsy for safety. The primary efficacy endpoints were histological improvement at week 52 in NAS ≥2 points (with ≥1 point improvement in ballooning or inflammation) and without worsening of fibrosis (by NASH Clinical Research Network (CRN) fibrosis score); OR resolution of steatohepatitis and no worsening of liver fibrosis (by NASH CRN fibrosis score) and ≥2 points improvement in NAS at Week 52. Resolution of steatohepatitis is defined as absence of fatty liver disease or isolated or simple steatosis without steatohepatitis and a NAS of 0 or 1 for inflammation, 0 for ballooning, and any value for steatosis. The study also had multiple secondary endpoints including fibrosis improvement without worsening of MASH and MASH resolution without worsening of fibrosis, as well as AI-based digital pathology assessment of liver biopsies.

Phase 2b FASCINATE-2 clinical trial results

In January 2024, we announced positive topline results at week 52 from our Phase 2b FASCINATE-2 clinical trial. The Phase 2b FASCINATE-2 clinical trial achieved statistically significant results on primary and multiple secondary endpoints in 168 biopsy-confirmed MASH patients with stage F2 or F3 fibrosis compared to placebo at week 52, including statistically significant improvements in MASH resolution without worsening of fibrosis with ≥2-point reduction in NAS (denifanstat 36% vs. placebo 13%, p=0.0044), and ≥2-point reduction in NAS without worsening of fibrosis (denifanstat 52% vs. placebo 20%, p=0.0003). Denifanstat-treated patients showed statistically significant fibrosis improvement by ≥ 1 stage with no worsening of MASH (denifanstat 41% vs. placebo 18%, p=0.0102) showed statistical significance in fibrosis improvement as measured by an AI digital pathology-based qFibrosis assessment. Analyses of liver fat showed a greater proportion of MRI-PDFF ≥30% responders relative to placebo (denifanstat 65% vs. placebo 21%, p<0.0001).

The p-value is a measure that states the probability that a comparable or better result would be produced purely by chance. Differences with a p-value of <0.05 are generally considered statistically significant, indicating a high degree of confidence that the measured result was due to administration of the drug and not due to chance.

Liver fibrosis and MASH resolution

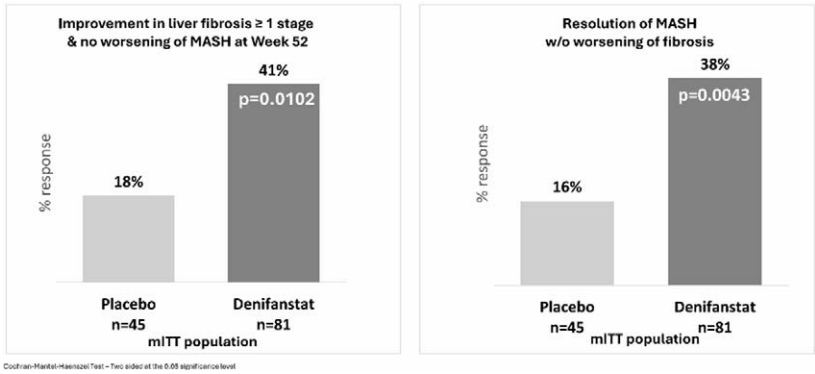


Figure 10. Liver fibrosis and MASH resolution

Liver fibrosis is associated with prognosis in MASH. As shown in Figure 11 below, denifanstat demonstrated a decrease of 0.3 (p=0.0023) in qFibrosis Continuous Value (HistoIndex, plc) versus an increase of 0.1 in placebo at week 52. AI-based digital pathology further corroborates and expand the findings from conventional pathology.

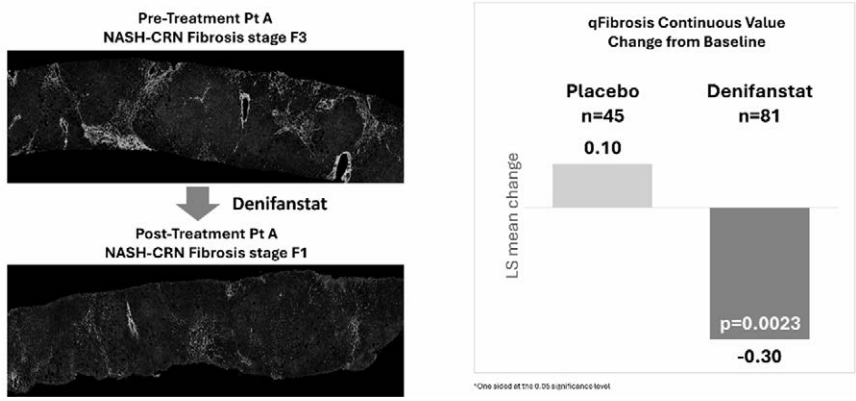


Figure 11. Fibrosis analysis using AI-based digital pathology

Vibration-controlled transient elastography

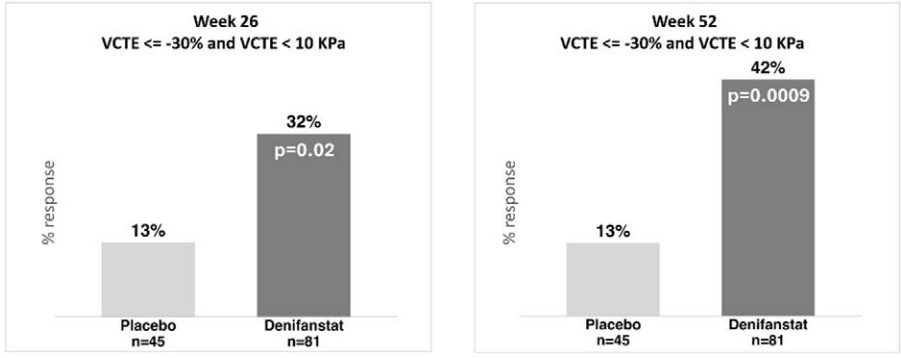


Figure 12. Vibration-controlled transient elastography

Treatment with denifanstat resulted in 32% (p=0.02) of patients becoming VCTE responders compared with 13% in placebo at week 26, and 42% (p=0.0009) of patients becoming VCTE responders compared with 13% in placebo at week 52. VCTE measures liver stiffness and responders above are defined as patients who achieve ≥30% relative reduction of VCTE score from baseline, and a score

of <10kPa. Longitudinal data supports the use of liver stiffness measured by VCTE as a pragmatic noninvasive indicator of treatment response in MASH. A >=30% reduction in VCTE has been associated with improved clinical outcomes, while an achievement of an absolute VCTE <10 KPa corresponds to regression into a lower risk disease category.

Liver fat biomarker: MRI-PDFF imaging

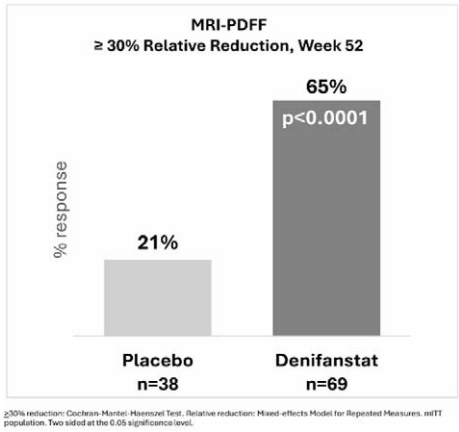


Figure 13. Liver fat biomarkers

Treatment with denifanstat resulted in 65% (p<0.0001) of patients becoming MRI-PDFF responders compared with 21% in placebo. MRI-PDFF responders achieve ≥30% relative reduction of liver fat. A meta-analysis of several clinical trials showed that patients who experience a ≥30% relative reduction of liver fat had a 7-fold higher likelihood that the biopsied liver tissue in these responders would show a ≥2 point improvement in NAS and a 5-fold higher rate of MASH resolution.

In addition to liver fat, several inflammation/lipotoxicity, fibrosis and metabolic health biomarkers that are important to MASH were assessed.

Inflammation biomarkers

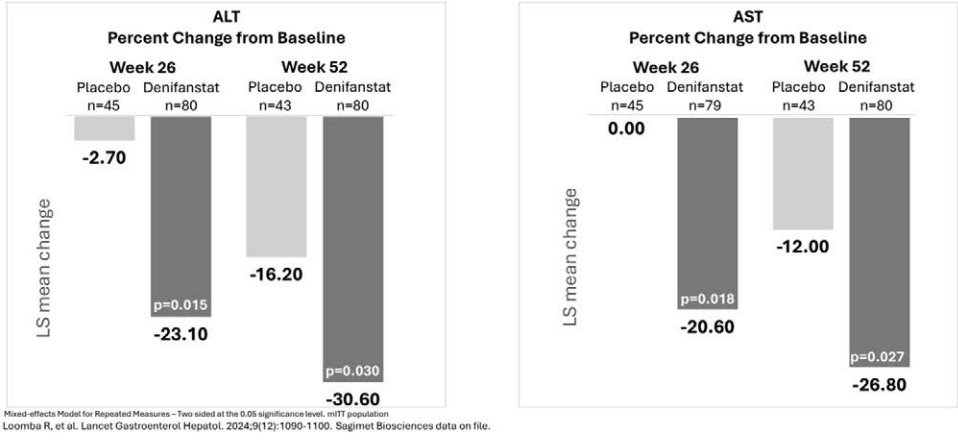


Figure 14. ALT and AST

- ***ALT.*** Denifanstat showed a statistically significant decrease of ALT by 30.6% (p=0.03) versus 16.2% for placebo at week 52. ALT is a liver enzyme often elevated in MASH patients and indicative of hepatic inflammation and damage. Decreasing ALT levels in MASH patients has been shown to correlate with improvements in liver health.

- ***AST.*** Denifanstat showed a statistically significant decrease of AST by 26.8% (p=0.027) versus 12% for placebo at week 52. AST is a liver enzyme often elevated in MASH patients and indicative of hepatocyte injury and is associated with fibrosis.

Fibrosis biomarkers

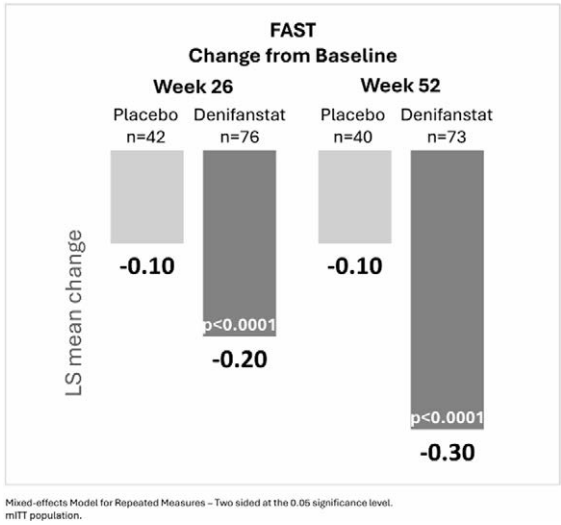


Figure 15. FAST score

- **FAST score**. Denifanstat showed a statistically significant decrease of 0.3 ($p<0.0001$) versus 0.1 in placebo at week 52. The FAST score combines liver stiffness and fat content by Fibroscan® with AST, and is a validated noninvasive marker of fibrosis.

Lipid biomarkers

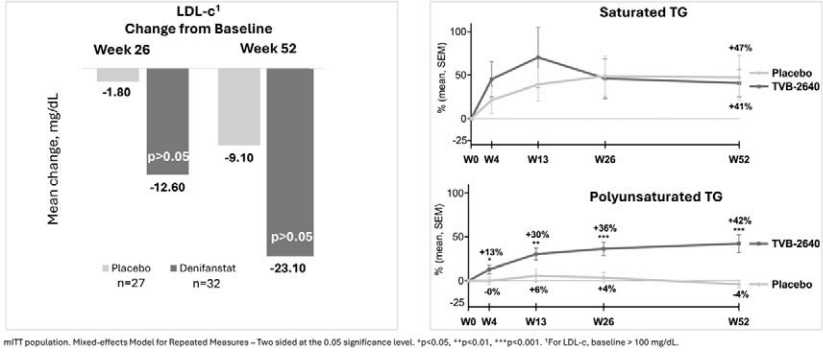


Figure 16. Lipid biomarkers

- ***LDL-cholesterol***. Denifanstat showed a decrease in LDL-cholesterol levels of 23.1 mg/dL ($p>0.05$), compared to a decrease of 9.1 mg/dL, with placebo at week 52 in the subset of patients with baseline LDL-c greater than 100 mg/dL. Elevated LDL-cholesterol levels are associated with increased risk of cardiovascular disease and often elevated in MASH patients.

- ***Total plasma triglycerides***. Denifanstat showed a statistically significant increase in polyunsaturated triglycerides of 42%, compared to a decrease of 4.0% with placebo at week 52. Polyunsaturated fatty acids are a class of fatty acids that include omega-3 and omega-6 fatty acids that have been shown to reduce the risk of cardiovascular disease.

We also assessed other laboratory values in patients in the interim cohort as described below:

- ***Tripalmitin.*** Denifanstat decreased tripalmitin levels by 2.2 µg/mL ($p=0.005$) after 13 weeks of treatment compared to -0.1 µg/mL with placebo. Tripalmitin is a triglyceride in which all three fatty acid chains are palmitate. We believe this reduction reflects the reduction of excess palmitate resulting from the inhibition of FASN.

Safety data

In the FASCINATE-2 clinical trial, the safety population included all 168 subjects enrolled. As in prior clinical trials of denifanstat, no treatment-related SAEs were observed, and the majority of AEs were mild to moderate in nature (Grades 1 and 2). There were no Grade ≥3 treatment-related AEs. The most common treatment-related AEs by system organ class (observed in ≥5% of patients in the study) were eye disorders (denifanstat 15.2%, placebo 16.1%), gastrointestinal disorders (denifanstat 11.6%, placebo 8.9%), and skin and subcutaneous tissue disorders (denifanstat 22.3%, placebo 7.1%). The incidence of TEAEs leading to treatment discontinuation was 19.6% in the denifanstat group compared to 5.4% in placebo. None of the SAEs (denifanstat 12%, placebo 5%) were considered drug-related. Additionally, there was no evidence of DILI and no deaths in the trial.

Phase 2 FASCINATE-1 clinical trial

We completed our Phase 2 FASCINATE-1 clinical trial in 2021 and demonstrated that a once-daily oral dose of 50mg denifanstat for 12 weeks was well tolerated and led to a statistically significant reduction in excess liver fat in patients with MASH, the study's primary and key secondary endpoints. The 25mg dose level was also well tolerated, and led to non-statistically significant improvements in comparison to placebo. The 75mg dose level was a small, open-label, non-randomized cohort, which was not powered to show statistical significance.

Denifanstat demonstrated improvements in biomarkers across all three hallmarks of MASH:

- Liver fat (steatosis): MRI-PDFF
- Inflammation/lipotoxicity: alanine transaminase (ALT), ceramides, CK-18
- Fibrosis: PRO-C3, ELF

Denifanstat also improved multiple biomarkers of metabolic health, including LDL-cholesterol and FGF21. We believe the concordance of improvements observed across multiple parameters in this relatively short time frame supports the potential of denifanstat to treat MASH patients.

Phase 2 FASCINATE-1 clinical trial design

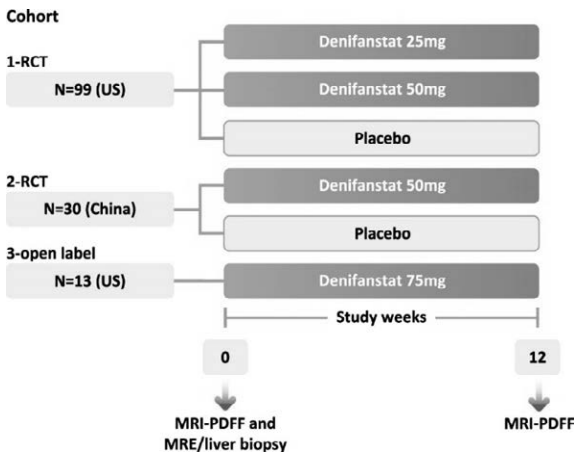


Figure 17. Phase 2 FASCINATE-1 trial design

The Phase 2 trial was conducted over three cohorts. Cohort 1 and Cohort 2 were randomized, placebo-controlled, single-blind, dose escalation clinical trials based in the United States and China. Cohort 3 was a small, open-label, non-randomized trial in the United States to evaluate a higher 75mg dose level which did not demonstrate a discernable benefit and was less well tolerated. Based on these results, we selected the 50mg dose to advance into further clinical development.

Key enrollment criteria included male and female subjects aged ≥18 years with either biopsy-proven MASH within two years before randomization or magnetic resonance elastography (MRE) ≥2.5 kPa (Cohorts 1 and 2 only); and MRI-PDFF ≥8%. A total of 142 patients were enrolled across the three cohorts, with 112 patients enrolled in the United States and 30 patients enrolled in China.

Cohort 1 clinical activity—United States

Baseline demographics. The median age of patients in Cohort 1 was 55 years, 46% were female, and 93% were white with 72% identifying as Hispanic or Latino. As expected for a MASH population, the median liver fat was 15.6%, the majority of patients had type 2 diabetes and the median body mass index (BMI) was 32.6 kg/m2. Safety data was reported for all 99 patients enrolled in the clinical trial. The primary analysis of clinical activity was performed on 85 patients that had an end-of-treatment MRI-PDFF. Two patients discontinued the trial early due to a TEAE and five patients had an end of treatment MRI-PDFF later than planned between 12 and 16 weeks of treatment as a result of COVID-19 visit restrictions; they were not included in the primary efficacy analysis.

Liver fat biomarker: MRI-PDFF imaging

The primary endpoint of this clinical trial was the percent change in relative liver fat following 12 weeks of treatment, and was statistically significant at 50mg of denifanstat. The patients in the placebo group, on average, had a 4.5% relative increase in liver fat over 12 weeks. In contrast, there was a dose-dependent relative reduction of liver fat of 9.6% (p=0.053) in patients treated with 25mg of denifanstat and of 28.1% (p<0.01) in patients treated with 50mg.

The secondary endpoint of this clinical trial was percentage of subjects with at least a 30% reduction in liver fat at week 12, and was statistically significant at 50mg of denifanstat; 23% of patients in the 25mg arm achieved an MRI-PDFF response (p=ns), defined as ≥30% relative reduction of liver fat, and 61% of patients treated with 50mg of denifanstat achieved a response (p<0.001), compared with 11% of the placebo group, as depicted below.

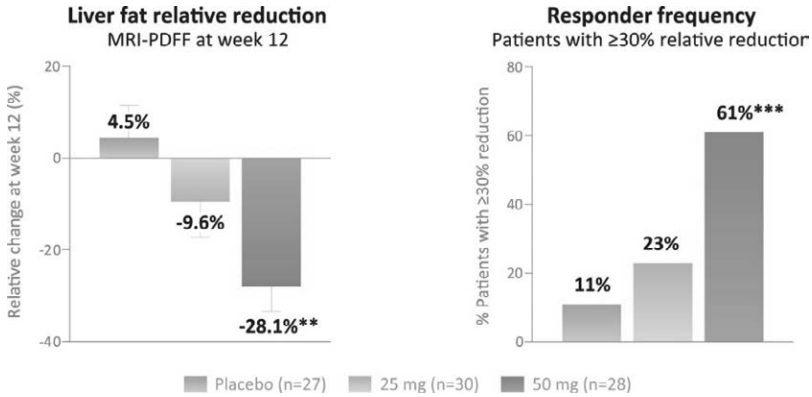


Figure 18. Liver fat biomarkers. **p<0.01, *** p<0.001

MRI-PDFF images for one patient treated with 50mg of denifanstat are shown below. The two images were taken 12 weeks apart from one another at the same horizontal position in the patient's body. The image on the left shows substantial liver fat content, represented by the yellow-green colored portion of the image. After 12 weeks of treatment, this same area no longer had a substantial amount of liver fat, as shown by the lack of yellow-green coloration and presence of the blue background color in the image on the right.

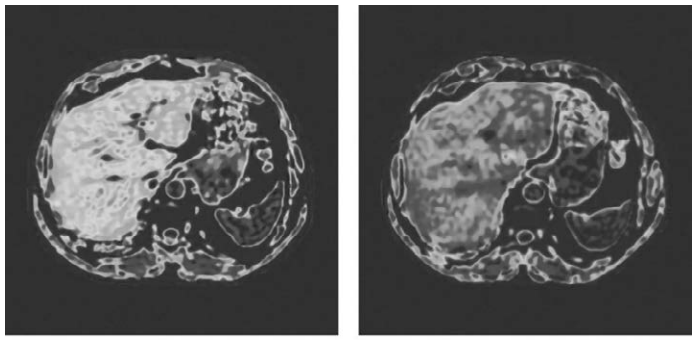


Figure 19. MRI-PDFF images for one patient treated with 50mg denifanstat

In addition to liver fat, several inflammation/lipotoxicity, fibrosis and metabolic health biomarkers that are important to MASH were assessed in this clinical trial.

Inflammation/lipotoxicity biomarkers

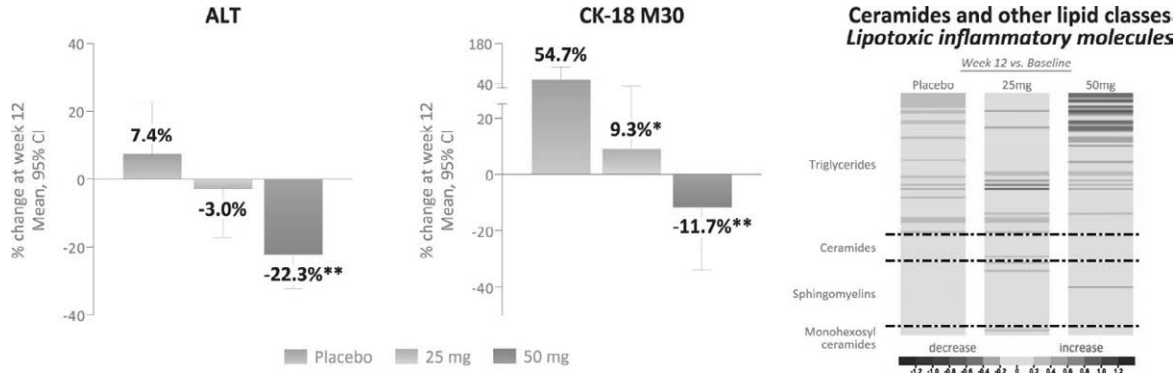


Figure 20. Inflammation / lipotoxicity biomarkers. *p<0.05, **p≤0.01

- ***ALT.*** Denifanstat showed a statistically significant decrease of ALT up to 22.3% (p<0.01) in a dose-dependent manner. Approximately one-third of the patients in each arm had abnormal ALT levels at baseline. In this subgroup, 33% of placebo patients normalized ALT post-treatment compared to 60% of the patients treated with 50mg of denifanstat.

- ***CK-18(M30).*** Denifanstat showed a statistically significant decrease of CK-18(M30) up to 11.7% (p<0.01) in a dose-dependent manner.

- ***Ceramides.*** Denifanstat showed a statistically significant decrease in multiple ceramides. Excess accumulation of ceramides, a type of fat often increased in MASH patients, is toxic and leads to inflammation and fibrosis. The decrease in ceramide levels likely reflects the reduction of excess palmitate and suggests an improved inflammatory environment.

Fibrosis biomarkers

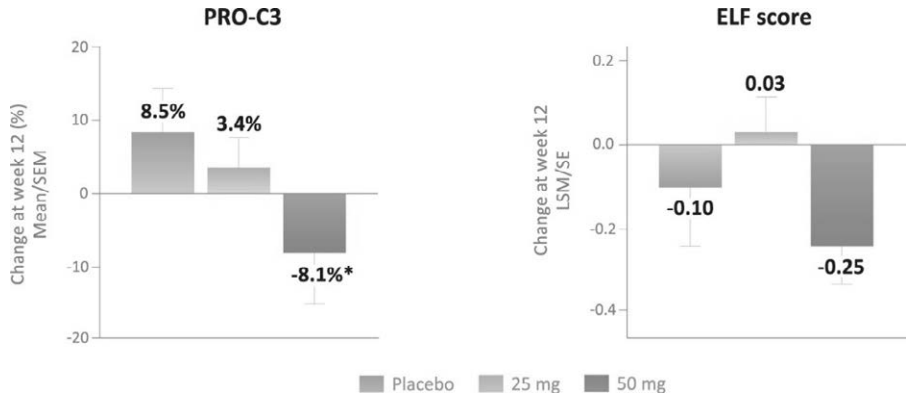


Figure 21. Fibrosis biomarkers. *p<0.05

- ***PRO-C3***. Denifanstat showed a statistically significant decrease in PRO-C3 levels (measured by ELISA) in a dose-dependent manner. PRO-C3 levels increased in the placebo group by 8.5% and decreased in the denifanstat 50mg-treated group by 8.1% ($p < 0.05$).

- ***ELF Score***. Denifanstat showed a 0.25 decrease in ELF score compared to a decrease of 0.1 with placebo (p = ns).

Metabolic/lipid biomarkers

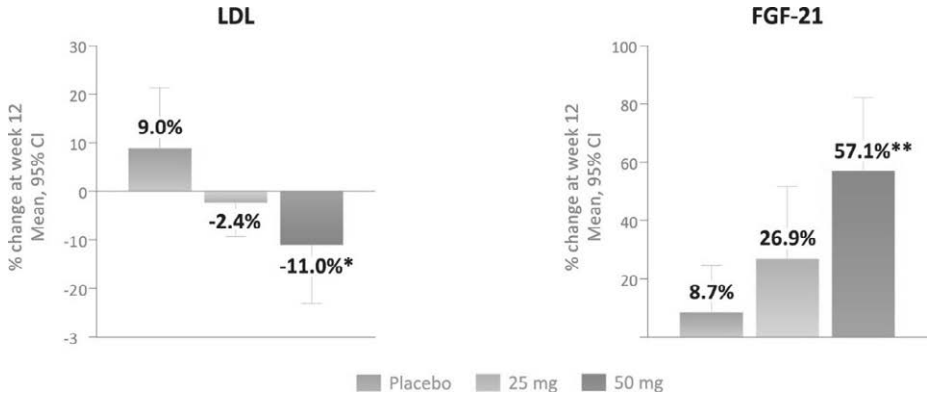


Figure 22. Metabolic / lipid biomarkers. *p<0.05 **p<0.01

- ***LDL-cholesterol***. Denifanstat showed a statistically significant decrease in LDL-cholesterol levels up to 11% ($p<0.05$) in a dose- dependent manner.

- ***FGF-21.*** Denifanstat showed a statistically significant increase in FGF-21 levels up to 57% ($p<0.01$) in a dose-dependent manner.

Over the course of the clinical trial, we also assessed other laboratory values in the patients as described below:

- ***Tripalmitin.*** Denifanstat decreased tripalmitin levels up to 40% ($p<0.0001$) in a dose-dependent manner.

- ***Total plasma triglycerides***. There were minor elevations of triglyceride levels of 22mg/dL (p=ns) and 13mg/dL (p=ns) in the 25mg and 50mg arms, respectively. In FASCINATE-2, it was observed that the increase in triglycerides was due to a change in composition towards a beneficial polyunsaturated content in the pool of triglycerides.

- ***Total and HDL cholesterol***. Denifanstat decreased total cholesterol levels up to 5.1% ($p<0.05$) and HDL-cholesterol up to 4.4% ($p<0.01$) in a dose dependent manner. The ratio of total-cholesterol and HDL-cholesterol (4.4-4.6) did not change in any

arm in the clinical trial during 12 weeks of treatment, suggesting that the reduction of HDL-cholesterol was indicative of lowered total-cholesterol levels in the blood.

Cohorts 2 and 3

Cohort 2—China. As part of our collaboration with our license partner Ascletis, we evaluated the profile of denifanstat (designated ASC-40 in China) in a small cohort of MASH patients under our FASCINATE-1 protocol in China. We enrolled 30 MASH patients who received either 50mg of ASC40 (n=21) or placebo (n=9) once-daily for 12 weeks. The median age of patients in the China cohort in this clinical trial was 34 years, 23.3% were female, 100% were Asian, median liver fat was 18.0%, and the median BMI was 28.9 kg/m2. In March 2021, we and Ascletis announced results showing ASC40 reduced liver fat with a 50% responder rate in patients treated with ASC40. ASC40 also demonstrated a decrease of ALT by 28% (p=ns) (mean decrease of 31 U/L at week 12). 63% of patients had at least a 17 unit decrease in ALT, a threshold that has been associated with liver fibrosis biopsy response.

Cohort 3—75mg Open-Label. A small, open-label 75mg once-daily cohort was conducted in the United States (N=13 patients) to explore the safety and efficacy of denifanstat at this dose level. The median age of Cohort 3 in this clinical trial was 48 years, 38.5% were female, 100% were Hispanic/Latino, median liver fat was 14.0%, and the median BMI was 28.4 kg/m2. At the end of 12 weeks of treatment, denifanstat 75mg led to a mean relative decline of liver fat content by MRI-PDFF of 35.8% and a responder rate of 57.1%. The liver fat decline was mostly driven by one single patient that had a decline of 82.6%. Denifanstat 75mg once-daily also decreased ALT by 3.2% (9.6 U/L) and LDL cholesterol by 13.5%.

Safety data

	Cohort 1			Cohort 2		Cohort 3
Treatment Emergent Adverse Event (TEAE) Classification	US Placebo N=31	US 25mg N=33	US 50 mg N=35	China Placebo N=9	China 50 mg N=21	US 75mg N=13
Any TEAE	Gr 1: 12 (38.7%) Gr 2: 7 (22.6%)	Gr 1: 18 (54.5%) Gr 2: 7 (21.2%)	Gr 1: 12 (34.3%) Gr 2: 6 (17.1%)	Gr 1: 3 (33%) Gr 2: 2 (22%)	Gr 1: 11 (52%) Gr 2: 4 (19%) Gr 3: 2 (10%)	Gr 1: 3 (23%) Gr 2: 6 (46%)
TEAE leading to drug withdrawal	0	2 (6.1%)	0	0	0	4 (31%)
Treatment Emergent Serious Adverse Event (SAE)	0	0	0	0	0	0
Drug related TEAE	Gr 1: 3 (9.7%) Gr 2: 1 (3.2%)	Gr 1: 10 (30.3%) Gr 2: 2 (6.1%)	Gr 1: 9 (25.7%) Gr 2: 1 (2.9%)	0	Gr 1: 9 (43%) Gr 2: 4 (19%)	Gr 1: 1 (8%) Gr 2: 6 (46%)

Figure 23. FASCINATE-1 safety summary

Denifanstat was considered well tolerated in the Phase 2 FASCINATE-1 trial at the 25mg and 50mg dose levels, with AEs that were mostly mild and similar among the cohorts. Safety data were collected from all 99 patients, of whom 68 were treated with denifanstat. Overall, 62 (63%) patients experienced at least one TEAE, all of which were assessed by the investigator as Grade 1 or mild except one incidence of Grade 2 urinary tract infection, one incidence of Grade 2 increased appetite at 25mg, and one incidence of Grade 2 shortness of breath at 50mg. All three of these Grade 2 TEAEs resolved without dose adjustment. No denifanstat-related SAEs occurred in any dose group. Overall, the most common TEAEs, regardless of drug-relatedness, among denifanstat-treated patients included headache (six patients; 9%), peripheral edema, rash, and upper respiratory tract infection (four patients; 6%); bronchitis, diarrhea, nausea, and urinary tract infection (four patients; 6%); and hypertriglyceridemia (noted as unrelated to treatment; two patients; 5.7%). Two (3%) patients discontinued denifanstat due to a TEAE: (1) mild eye allergy on day two of the clinical trial and (2) mild conjunctivitis. Both events occurred at the 25mg dose and resolved following discontinuation. No discontinuations for a TEAE were observed in the 50mg dose cohort.

In the Chinese cohort of 30 patients, 21 and nine of whom were treated with denifanstat and placebo, respectively, the 50mg denifanstat daily dose was well tolerated with a benign adverse event profile and no SAEs. Most TEAEs were Grade 1 (11 patients: 52% on denifanstat and 3 patients; 33% on placebo) or Grade 2 (four patients; 19% on denifanstat and two patients; 22% on placebo). No patients in the China cohort discontinued due to a TEAE. Treatment-related AEs, as determined by the investigator, were observed in 13 patients (62%) on denifanstat.

In the 75mg open-label cohort of 13 patients, there was an increased incidence of TEAEs compared to U.S. patients who received 25mg or 50mg, 23% of TEAES were Grade 1 and 46% of TEAES were Grade 2, including four cases of dry skin (30.8%, including possible palmar-plantar erythrodysesthesia (PPE) syndrome), five cases of dry eye (38.5%) and four cases of hair thinning (30.8%). Hair thinning was not observed in the 25mg or 50mg cohorts. The 75mg cohort had an overall discontinuation rate of 46.2% (N=6) due to AEs. Four patients discontinued treatment due to more than one on-target AE; hair thinning (N=4; 30.8%), dry skin (N=4; 30.8%, including possible PPE syndrome), dry eye (N=2; 15.4%). Two patients (15.4%) discontinued due to one or more AEs of headache, lower abdominal pain, constipation, and diarrhea. All TEAEs were Grades 1 or 2, and there were no SAEs. While the 75mg dose demonstrated clinical activity, the adverse effects, which were reversible, were not balanced by the clinical activity observed. As such, this dose level was not pursued in the Phase 2b FASCINATE-2 trial.

The results from the Phase 2 FASCINATE-1 trial showed that a once-daily, oral dose of 25mg or 50mg of denifanstat for 12 weeks was well tolerated and led to rapid and robust reduction in excess liver fat in patients with MASH, which was statistically significant in the 50mg cohort, in a dose-dependent manner. Additionally, these data showed improvements across steatosis, inflammation/lipotoxicity and fibrosis biomarkers associated with MASH and multiple biomarkers of metabolic health. Based on the results, we elected to use the once-daily, oral 50mg dose in the Phase 2b FASCINATE-2 trial.

Phase 1 DNL clinical trial results

To evaluate the impact of denifanstat on liver fat synthesis in 12 healthy male adults with characteristics of metabolic syndrome, we collaborated with the University of Missouri. Liver fat synthesis was quantified by measuring the conversion of acetate into the product of FASN, palmitate. This measurement was done in each subject once before the subject received denifanstat and again after 10 days of taking a once-daily oral dose of either 50mg, 100mg or 150mg of denifanstat. This second measurement was taken approximately 10 hours after the last dose in order to measure the impact of steady-state drug levels on liver fat synthesis. This trial showed there was a significant reduction of liver fat synthesis at all doses and such reduction occurred in a dose-dependent manner. The 50mg dose reduced peak liver fat synthesis by approximately 26% and the 150mg dose inhibited liver fat synthesis by 78%, as shown in the graphic below. The drug was well-tolerated; one of the four subjects given 100mg and one of the two subjects given 150mg of denifanstat experienced some hair thinning that returned to normal after the drug was stopped. These changes correlated with significant reduction of their skin sebum while on treatment, which returned to normal after drug was stopped.

Denifanstat inhibited DNL in human volunteers

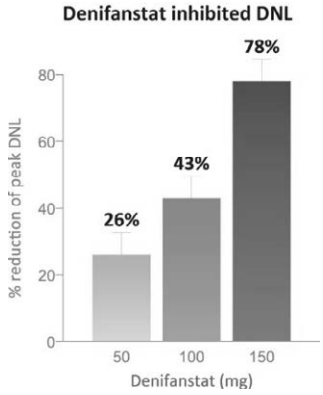


Figure 24. Inhibition of liver fat synthesis in Phase 1 DNL trial

We believe the results from this clinical trial established the clinical proof of mechanism for denifanstat. The results showed that an oral dose of denifanstat reached the liver of adults who were overweight. By inhibiting FASN, fat synthesis was reduced in the liver. Prior studies have shown subjects with increased amounts of liver fat have an approximately 3-fold higher rate of FASN-mediated DNL compared to subjects with lower liver fat. The conceptual goal of denifanstat treatment in MASH patients is to normalize the rate of DNL; the goal does not include ablation of the pathway. The data from this Phase 1 trial suggested that doses below 100mg should be evaluated for their ability to reduce liver fat by reducing the rate of DNL.

Phase 1 open-label study in subjects with hepatic impairment

In March 2024, we announced completion of our Phase 1, open-label, pharmacokinetic study of denifanstat in subjects with mild, moderate, or severe hepatic impairment compared to subjects with normal hepatic function.

This Phase 1 hepatic impairment study was designed to test the safety and pharmacokinetics of denifanstat in subjects with hepatic impairment, a standard requirement of the ongoing development program in MASH. This was a non-randomized parallel group study in which 38 subjects were enrolled and completed the study. The study population comprised 8 subjects in each category of mild, moderate or severe hepatic impairment, and 14 healthy subjects with normal hepatic function demographically matched to the hepatic impaired subjects for age, body weight and gender. Subjects received oral denifanstat 50mg a day for 4 days. Denifanstat was generally well-tolerated, and no safety signals were reported. The pharmacokinetic results from the study demonstrated that denifanstat can be studied with patients with F4 fibrosis.

Preclinical studies in MASH models

We characterized the effect of FASN inhibitors in preclinical models of MASH using a comprehensive strategy. We performed mechanistic *in vitro* studies in isolated human cell types to confirm the mode of action of FASN inhibitors. The *in vitro* results demonstrated that FASN inhibition via DNL pathway directly targets a) liver fat accumulation in hepatocytes, the initiating event of MASH, b) pro-inflammatory signaling in immune cells, and c) fibrogenesis by hepatic stellate cells, as described below. We used several different *in vivo* mouse models of MASH that encompass the full physiology of diet induced MASH and liver histology. These models showed consistently that FASN inhibitors had in vivo activity and improved liver health biomarkers including ALT, pro-inflammatory cytokines, and liver histology endpoints of steatosis, inflammation and fibrosis. Collectively, these preclinical results suggest that FASN inhibitors effect change in the histologic parameters of MASH resolution and fibrosis improvement in two distinct ways. Not only do they act by preventing inflammation and fibrosis secondary to the excess accumulation of fat, but they also act by inhibiting inflammation and fibrosis mechanisms directly. In preclinical models of MASH we have also tested FASN inhibitors in combination with other drug classes including a THR- β agonist (resmetirom) and GLP-1 agonist (semaglutide), to evaluate the potential for additive or synergistic effect.

Disease models—direct impact on steatosis, inflammation and fibrosis

Steatosis—FASN inhibition directly reduced lipid accumulation in liver models. In human liver microtissues, denifanstat decreased cellular triglycerides, a marker of lipid accumulation or steatosis. This is a consequence of FASN inhibition leading to decreased hepatic DNL. These findings were extended in animal models where decreased lipid content was observed after FASN inhibitor treatment by Oil Red staining or steatosis by histology.

Inflammation—FASN inhibition directly reduced pro-inflammatory activity in immune cells. Two types of immune cells relevant for inflammation in the liver were used to test the effect of FASN inhibitors on pro-inflammatory activity: human white blood cells and human primary CD4+ T-cells. Human white blood cells were activated with lipopolysaccharide (LPS) or related stimulants, treatment with FASN inhibitors dramatically decreased production of interleukin-1 beta, a pro-inflammatory cytokine. A similar effect was observed in mice fed with a high fat, high cholesterol diet where interleukin-1 beta plus several other pro-inflammatory cytokines and chemokines were reduced. Th17 cells are immune cells that can cause pro-inflammatory damage in the liver and the DNL pathway is important for Th17 cell differentiation and function. In human primary CD4+ T cells, denifanstat significantly reduced the number of Th17 cells and increased the number of regulatory T-cells (Treg). Treg cells are more common in healthy livers and expected to blunt the damage caused by the inflammation producing Th17 and other immune cells.

Fibrosis—FASN inhibition directly reduced activation and fibrogenic activity of human hepatic stellate cells (HSCs). HSCs are the main cell type responsible for fibrosis and the deposition of scar tissue in the liver. HSCs need the DNL pathway to become activated to accomplish fibrogenic activity, which leads to production of fibrotic scar. In the human HSC cell line LX-2, FASN inhibitor decreased expression of several fibrogenic genes, as seen below. This includes the genes encoding collagen 1α1, αSMA, two important markers of HSC activation and pro-fibrogenic activity. The protein levels of collagen 1α1 and SMA were also decreased by FASN inhibitor treatment. These results provide mechanistic evidence that FASN inhibition can directly reduce fibrogenic activity in HSCs. We believe that this would be expected to reduce fibrosis. In more complex disease models such as mice with MASH, decreased expression of fibrogenic markers was also observed after FASN inhibitor treatment.

	% inhibition of gene expression in hepatic stellate cells at 48hr vs baseline	
Gene	50 nM FASNi	150 nM FASNi
Col1α1	37%**	68%****
αSMA	37%	60%**
TGFβ-R1	0%	53%*
PDGF-Rβ	0%	54%**
TIMP1	19%	9%
TIMP2	12%	24%
MMP2	0%	50%**

Figure 25. Expression of fibrogenic genes
in a human stellate cell line. *p<0.01, **p<0.05, ****p<0.0001

FASN inhibition not only directly inhibits the fibrogenic activity of stellate cells, but it also removes the fibrogenic stimuli required to activate these cells. These stimuli result from excess fat in hepatocytes. By reducing liver fat via FASN inhibition, the levels of fibrogenic stimuli, including lipotoxins, are reduced. We believe this is an important and unique facet of using FASN inhibition to treat MASH.

Disease models—in vivo activity in MASH

We evaluated the effect of FASN inhibitors in three different mouse models of MASH spanning the spectrum of disease severity: a prevention model, a therapeutic model with diet-induced MASH, and a therapeutic model with diet-induced MASH and advanced fibrosis and tumor formation (FAT-MASH) and also in a MASH model with atherosclerosis. The results showed that FASN inhibition alleviated established features of MASH. For mouse models, we used the FASN inhibitor, TVB-3664, as a surrogate for denifanstat in these experiments due to TVB-3664's pharmacokinetics in mice. TVB-3664 has a chemical structure highly related to denifanstat and has been shown to inhibit FASN with similar potency.

FASN inhibition ameliorated disease progression in diet-induced MASH mouse model (a therapeutic model). After 44 weeks on a high-fat/fructose/cholesterol diet, mice developed obesity, steatohepatitis and liver fibrosis before FASN inhibitor treatment was initiated for eight additional weeks, while the mice continued the same diet. After treatment with the FASN inhibitor, livers showed reduced steatosis and NAS score, despite being on a diet high in fat, fructose and cholesterol. FASN inhibition also improved biomarkers of liver inflammation, diminished liver triglyceride and cholesterol, and reduced expression of fibrosis biomarkers and fibrosis severity.

A combination of FASN inhibitor with resmetirom was tested in this diet-induced MASH model. After 38 weeks on a high-fat/fructose/cholesterol diet, mice developed obesity, steatohepatitis and liver fibrosis before drug treatment was initiated for up to 12 additional weeks, while the mice continued the same diet. The combination decreased liver fat dramatically within 6 weeks, to resemble that of mice on a normal chow diet, and to a greater extent than FASN inhibitor or resmetirom alone. The combination had a synergistic effect on important liver disease markers, including improvement of NAS (NAFLD Activity Score) by histologic analysis and more robust improvement in hepatic collagen content compared to the single agents. Synergistic activity of the combination was demonstrated in the rate of histological improvement (NAS ≥2 points). The FASN inhibitor monotherapy showed 33% improvement, resmetirom monotherapy showed 25% improvement, and the combination of the two showed an 80% improvement, a level of improvement that greatly exceeds a simple addition of the activity of the two drugs.

A combination of FASN inhibitor with semaglutide was also tested in this diet-induced MASH model. After 38 weeks on a high-fat/fructose/cholesterol diet, mice developed obesity, steatohepatitis and liver fibrosis before drug treatment was initiated for up to 12 additional weeks, while the mice continued the same diet. FASN inhibitor or semaglutide alone improved NAS and decreased several biomarkers associated with MASH. Only the FASN inhibitor, but not semaglutide, showed significant reduction of liver fibrosis by a digital AI pathology assessment. FASN inhibitor and semaglutide in combination showed further histological improvement of NAS and liver fibrosis compared to treatment with FASN inhibitor alone or semaglutide alone. Liver transcriptomic analysis indicated that the FASN inhibitor and semaglutide altered different gene expression pathways, with only FASN inhibitor modifying fibrosis pathways, while the combination had some unique effects on gene expression.

FASN inhibition had in vivo activity in the diet induced FAT-MASH model with established liver fibrosis and liver cancer (a therapeutic model). In a study performed by our collaborator Professor Scott Friedman at the Icahn School of Medicine at Mt. Sinai Hospital in New York, mice were fed a high-fat, high-sugar diet and given a once weekly injection of carbon tetrachloride, for six months. This toxic chemical causes liver fibrosis in rodent models of MASH. Mice received either placebo or FASN inhibitor for the last three months. After six months, mice in the placebo group had extensive fibrosis evidenced by scar tissue and collagen deposition in their livers as well as liver tumors. This was visualized by the picrosirius red staining of liver slices as shown below (left panel). In contrast, mice that received the FASN inhibitor (middle and right panels) for 12 weeks had significantly less scar tissue and collagen deposition in their livers and, in most cases, less than observed before the drug was started, indicating that FASN inhibition reversed fibrosis despite continued insult to the liver as shown in the figure below. Quantitation of collagen content by digital pathology showed that this decrease is statistically significant, as shown in the graph below. Additionally, animals receiving the FASN inhibitor had overall 85% fewer liver tumors than those receiving placebo and several drug-treated animals had no tumors in their livers at the end of the study. These results were consistent with the documented role of FASN and the DNL pathway in liver fat accumulation, inflammation and fibrogenesis.

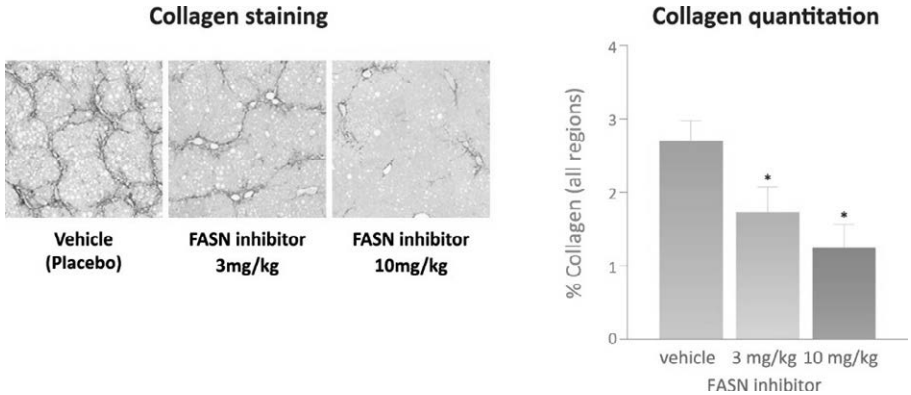


Figure 26. FASN inhibitor decreased liver fibrosis in mouse model of MASH. * $p<0.05$

FASN inhibition reduced atherosclerosis development in the LDL receptor knockout mouse model of diet-induced MASH with dyslipidemia (a therapeutic model). This MASH model incorporates features of human atherosclerosis. Mice were administered a fast-food diet for 18 weeks to allow development of dyslipidemia, atherosclerosis, and features of MASH including steatohepatitis and liver fibrosis, before FASN inhibitor treatment was initiated at that point in time for 10 additional weeks, while the mice continued the same diet. After treatment with the FASN inhibitor, a reduction in circulating cholesterol and triglycerides was apparent. Histology analysis showed that FASN inhibitor treatment reduced the total atherosclerotic lesion area per cross-section of aortic root. This was accompanied by reduction in several circulating inflammatory markers associated with atherosclerosis such as CCL4 and CXCL2. Liver histology steatosis inflammation and fibrosis also improved with FASN inhibitor treatment. These results show the potential cardiovascular and liver impacts of treatment with a FASN inhibitor, and are consistent with the decreased LDL cholesterol observed with denifanstat versus placebo in FASCINATE-1 and FASCINATE-2 clinical studies in MASH.

Combination of FASN inhibitor treatment with resmetirom treatment was also tested in this LDL receptor knockout model of diet induced MASH. The combination treatment normalized liver fat levels to that observed in mice on a normal chow diet and decreased both macrovesicular and microvesicular steatosis. The combination significantly decreased collagen production. In addition, the beneficial effect of FASN inhibition on markers of dyslipidemia described above as monotherapy was further improved by combination with resmetirom.

Precision medicine—enabling the right intervention for MASH patients

We have initiated a comprehensive biomarker program as part of our denifanstat development program. Biomarkers are indicators of the disease state and/or response to treatment, and typically measured using convenient, non-invasive approaches. In addition to disease-associated biomarkers, we are developing two types of biomarkers specific to denifanstat and FASN. We believe the identification of these biomarkers has the potential to prospectively identify appropriate patients that will respond to therapy with denifanstat alone or in combination, monitor treatment response to drive clinical outcomes for MASH patients, and help differentiate denifanstat as a potential therapy for MASH.

MASH, the hepatic manifestation of metabolic syndrome, is a complex, progressive disease, with few approved treatments for non-cirrhotic MASH (stages F1, F2 and F3 fibrosis) and no approved treatments for cirrhotic MASH (F4). With the large and growing global

MASH population, we believe that it would be beneficial to develop precision medicine approaches to confirm that the drug is having a positive impact based on biomarker assessments, and match MASH patients prior to initiation with the most appropriate treatment for their disease. These approaches potentially provide physicians with a helpful tool to better manage their patients, and increase the market opportunity for denifanstat and for combination treatments that include denifanstat.

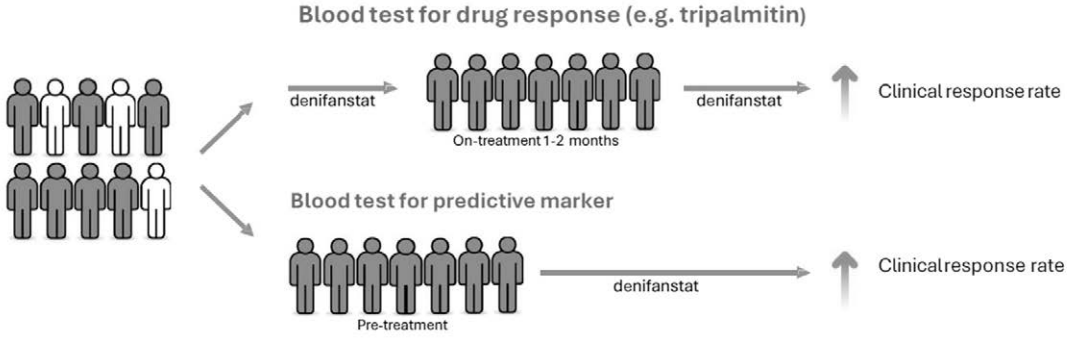


Figure 27. Precision medicine strategy

Drug response biomarkers

Pharmacodynamic (PD) biomarkers are drug response markers and provide evidence that a drug has modulated its target. This is important to test in clinical trials because lack of sufficient target modulation can cause lack of clinical activity. Over the past several years, we identified tripalmitin as a PD biomarker for FASN inhibition in several clinical trials and developed a reliable assay to measure serum tripalmitin in patients. Tripalmitin is a triglyceride with palmitate, a fatty acid produced by FASN, at each of the acyl moieties; therefore, a decrease of tripalmitin confirms FASN inhibition. In the Phase 2b FASCINATE-2 clinical trial, at 50mg denifanstat, tripalmitin showed an early and sustained reduction in de novo lipogenesis at 4-weeks (-2.4ug/mL with denifanstat vs. -0.4ug/mL placebo, p=0.001) and 13-weeks (-2.2ug/mL with denifanstat vs. -0.1ug/mL placebo, p=0.005) in the ITT population.

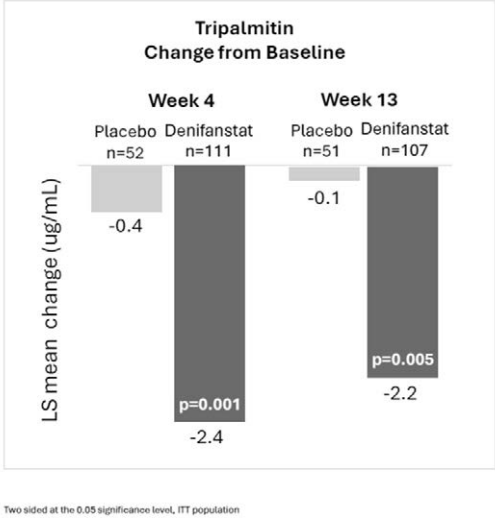


Figure 28. Tripalmitin levels at 4 and 13 weeks of dosing in Phase 2b FASCINATE-2

We anticipate that other biomarkers may be used in conjunction with PD biomarkers such as tripalmitin to refine and enhance the robustness of demonstrating drug response in treated patients. These markers may include ALT, AST or other parameters that change upon denifanstat treatment.

Predictive biomarkers

We also plan to develop a predictive test to select MASH patients most likely to have an efficacious clinical response.

This program includes two distinct technical approaches, both using blood samples to identify biomarkers or biomarker panels that may predict clinical response to denifanstat: metabolomic profiling to measure metabolic state, and SNP profiling to incorporate genetic markers associated with metabolic disease. From the FASCINATE-1 clinical trial, we identified a preliminary biomarker signature (termed Sig-A) that predicts liver fat response to denifanstat, based on the metabolomic profile of patient blood samples collected before treatment. We plan to conduct a similar process across clinical trials, including the FASCINATE-2 clinical trial, incorporating data from biomarkers panels with broad metabolomic and proteomic analyses of patient blood samples. Machine learning algorithms will be applied to identify biomarker panels of response.

Additional MASH indications

Non-cirrhotic MASH (F2-F3). According to a study published in 2018, the prevalence of MASH in the United States was estimated at 17.3 million in 2016 and expected to grow to 27.0 million by 2030. Of the MASH patients in the United States, 5.7 million had MASH with advanced fibrosis (F2-F3) in 2016. The number of MASH patients with advanced fibrosis (F2-F3) is expected to grow to 10.6 million in 2030. According to two studies published in 2021 and 2023, when left untreated, MASH can lead to liver cirrhosis, which is currently on par with alcohol as the leading indication for liver transplantation and is expected to surpass alcohol in the coming years. In January 2024, we announced that denifanstat had met both primary endpoints and multiple secondary endpoints in the Phase 2b FASCINATE-2 clinical trial evaluating denifanstat in 168 biopsy-confirmed MASH patients with stage F2 or F3 fibrosis compared to placebo at week 52. In October 2024, the FDA granted Breakthrough Therapy designation to denifanstat for the treatment of non-cirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). In October 2024, we completed successful end-of-Phase 2 interactions with the FDA.

Pediatric MASH. According to a study published in 2022, MASH is the most common form of liver disease in children; approximately 10% of children in the United States have MASLD, MASH was observed in 23% of children with MASLD, and 15% have F2-F3 fibrosis. We intend to submit plans to regulatory authorities for the development of denifanstat in pediatric MASH patients. We also plan to conduct toxicology studies in juvenile animals. The information provided could enable the design of a Phase 2 clinical trial in pediatric patients with MASH.

Acne: A highly prevalent skin condition

Acne is the most common skin condition in the United States, affecting up to 50 million Americans annually. Acne usually begins in puberty and affects many adolescents and young adults. Approximately 85% of people between the ages of 12 and 24 experience at least minor acne and the prevalence of severe acne may be as high as 20% of those affected by acne. FASN is responsible through lipid synthesis for the production of skin oils (sebum). More than 80% of key sebum lipids such as palmitate and sapienic acid are produced by DNL/FASN. In acne, excess sebum can lead to skin lesions and is a pro-inflammatory stimulus leading to exacerbation of those lesions, including development of nodules (nodular acne) and cysts (cystic acne). Studies in patients with acne vulgaris demonstrated that levels of sebum palmitate and sebum sapienate (a derivative of palmitate found in the skin) increased by 20% compared to healthy volunteers. Sebum reduction is one of the major mechanisms of isotretinoin (formerly branded as Accutane or Roaccutane), which is widely prescribed for cystic acne. However, isotretinoin has significant side effects including spontaneous abortion, birth defects and depression. Pfizer Inc. completed a Phase 1 clinical trial with a topical ACC inhibitor, which is another DNL inhibitor.

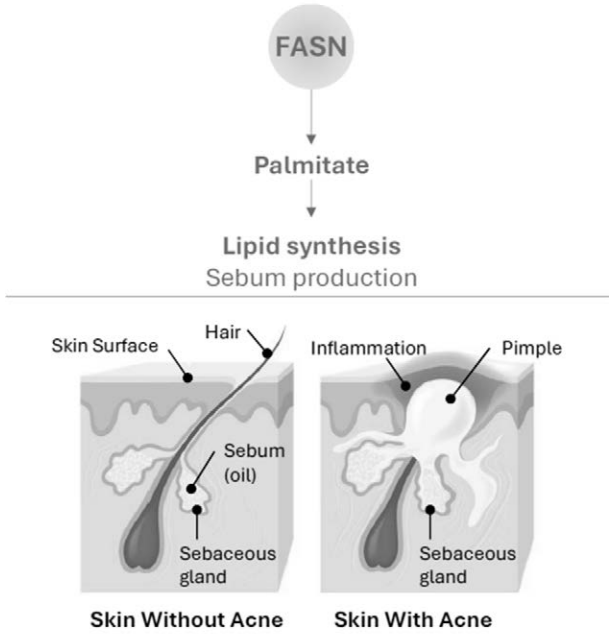


Figure 29. FASN role in acne

Acne clinical program

We have shown, in two separate Phase 1 clinical trials, that denifanstat can reduce the amount of sebum on patients' skin. Sebum samples were collected from patients in the Phase 1 DNL trial described above and in the Phase 1 oncology solid tumor trial described below. Sebum changes were exploratory lipidomic assessments incorporated into these trials to provide a potential non-invasive assessment of pharmacodynamic activity, and not prospectively powered for statistical significance. In the Phase 1 DNL trial, denifanstat reduced total lipid secretion in sebum in a dose-dependent manner by an average of 7% (50mg, n=6), 29% (100 mg, n=4) and 64% (150 mg, n=2) on day 10 of once daily treatment. In the Phase 1 oncology trial that tested higher denifanstat dose levels (typically 150 mg or 200 mg once daily), sebum total triacylglycerol levels decreased from pretreatment levels by an average of 28% on day 8 or 16 ($p \leq 0.05$ vs baseline) and by 69% on day 28 ($p \leq 0.05$ vs baseline). This included significant reductions in total sapienic acid, a sebum fatty acid produced only by de novo lipogenesis, confirming FASN inhibition. We believe these results provide mechanistic proof of concept for denifanstat in acne.

Phase 3 clinical trial of denifanstat in acne

In June 2025, our license partner for China, Ascletis, announced that denifanstat met all primary and secondary endpoints in its Phase 3 trial in moderate to severe acne vulgaris in China. The Phase 3 clinical trial was a randomized, double-blind, placebo-controlled, multicenter clinical trial of 480 enrolled patients randomized 1:1 to receive denifanstat 50mg or placebo, once daily for 12 weeks.

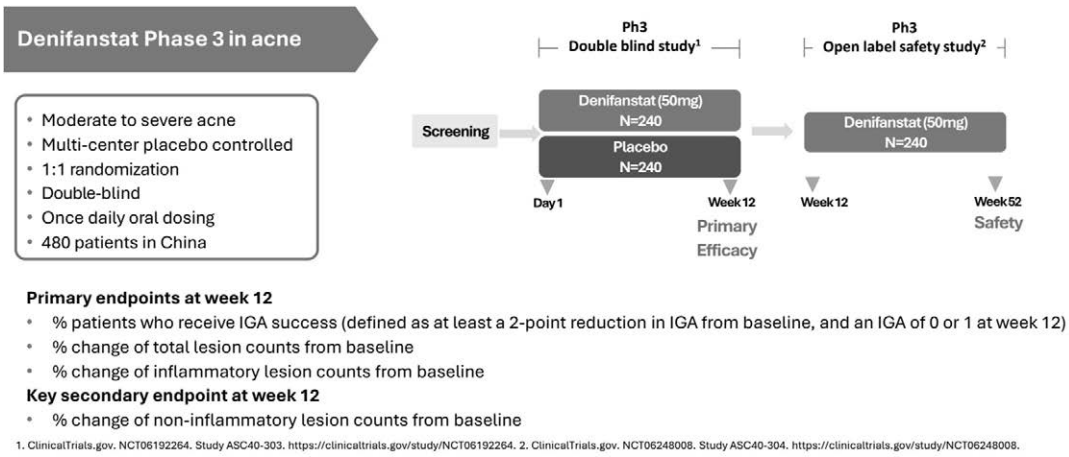


Figure 30. Ascletis acne Phase 3 clinical trial design

Ascletis reported the following efficacy data from the Phase 3 trial:

- All primary endpoints were met, including:
  - the percentage of treatment success (defined as an Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with at least a 2-point decrease from baseline) (denifanstat 33.2% vs. placebo 14.6%, p<0.0001).
  - the percentage change in total lesion count (denifanstat -57.4% vs. placebo -35.4%, p<0.0001).
  - the percentage change in inflammatory lesion count (denifanstat -63.5% vs. placebo -43.2%, p<0.0001).
- The secondary endpoint of change in non-inflammatory lesion count was also met (denifanstat -51.9% vs. placebo -28.9%, p<0.0001).

Ascletis reported that denifanstat was generally well-tolerated. Following 12 weeks of once-daily oral administration at 50 mg, the incidence rates of TEAE were comparable between denifanstat and placebo.

Baseline Characteristics	50mg denifanstat (n=240)	Placebo (n=240)		
Total lesion count	102.2	102.1		
Inflammatory lesion count	42.1	43.1		
IGA=3 (moderate), %	85.8	85.8		
IGA=4 (severe), %	14.2	14.2		
Efficacy endpoints [1]	**50mg denifanstat (n=240)**	**Placebo (n=240)**	**50mg denifanstat (placebo adjusted)**	**p value**
% Treatment success [IGA] [2] (primary endpoint)	33.2	14.6	18.6	<0.0001
% Change in total lesion count (primary endpoint)	-57.4	-35.4	-22.0	<0.0001
% Change in inflammatory lesion count (primary endpoint)	-63.5	-43.2	-20.3	<0.0001
% Change in non-inflammatory lesion count (key secondary endpoint)	-51.9	-28.9	-23.0	<0.0001
Absolute change in total lesion count (secondary endpoint)	-58.3	-36.2	-22.1	<0.0001
Absolute change in inflammatory lesion count (secondary endpoint)	-26.6	-18.4	-8.2	<0.0001

Baseline demographics and efficacy endpoints of 50 mg denifanstat oral, once daily for 12 weeks versus Placebo (Intent-to-treat, ITT analysis change from baseline).
1. The efficacy data are LSMEANs.
2. Treatment success is defined as an Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with at least a 2-point decrease from baseline.

Figure 31. Ascletis acne Phase 3 clinical trial: All primary and key secondary endpoints met

In January 2026, Ascletis reported positive topline results in the open-label Phase 3 trial evaluating the long-term safety of ASC40 (denifanstat) tablets in patients with moderate to severe acne in China. The Phase 3 multi-center open-label clinical trial ASC40-304 was designed to determine the long-term safety of denifanstat in patients with moderate to severe acne vulgaris who were previously enrolled in the double-blind, randomized, placebo-controlled 12-week Phase 3 ASC40-303 trial. All subjects in the open-label extension were administered oral denifanstat 50 mg once daily for up to 40 weeks. Subjects who were originally randomized to denifanstat in ASC40-303 study had a total of 52 weeks of denifanstat exposure.

Primary endpoints evaluated safety, and secondary endpoints evaluated efficacy, for up to 52 weeks of denifanstat treatment. Denifanstat was generally well tolerated, with the following:

- TEAEs: Only two categories of TEAEs had an incidence rate of 5% or more, with dry eye syndrome in 5.5% of denifanstat-treated subjects and dry skin reported in 5.2% of denifanstat-treated subjects.

- AEs: All denifanstat-related AEs were mild or moderate; no denifanstat-related grade 3 or 4 AEs; no AE-related permanent discontinuations; Grade 1 hair thinning in the study was experienced by only one denifanstat-treated patient (which resolved within 8 weeks while remaining in study without a change in dose); no deaths were reported.

- SAEs: No denifanstat-related SAEs; two non-denifanstat-related SAEs (one breast lump, one contusion), both resolved.

In December 2025, Ascletis announced that the China NMPA has accepted its NDA for denifanstat for the treatment of moderate to severe acne.

Phase 2 clinical trial of denifanstat in acne

In May 2023, Ascletis Pharma announced positive topline results with the achievement of primary and key secondary endpoints in a Phase 2 clinical trial in 179 patients with moderate to severe acne vulgaris in China. These patients were randomized and dosed with 25mg, 50mg or 75mg of denifanstat (ASC40) or placebo daily for 12 weeks. Ascletis Pharma reported that denifanstat met the primary endpoint of percentage change from baseline in total lesion count at week 12 with median reductions of 53.1% in the 25mg group ($p=0.006$, $n=45$), 61.3% in the 50mg group ($p=0.008$, $n=44$), and 53.1% in the 75mg group ($p=0.008$, $n=45$) versus a reduction of 34.2% with placebo ($n=45$). The incidence rates of treatment-related AEs were comparable among 25mg (grade 1=28.9%; grade 2=20.0%), 50mg (grade 1=36.4%; grade 2=11.4%), 75mg (grade 1=44.4%; grade 2=17.8%) denifanstat groups and the placebo group (grade 1=35.6%; grade 2=13.3%). The majority of treatment-related AEs were dry eye, and all dose levels had a rate of dry eye similar to placebo (grade 1=28.9%; grade 2=6.6%). There were no denifanstat-related grade 3 or 4 AEs, no treatment-related SAEs and no deaths reported.

Phase 1 clinical trial of TVB-3567 in acne

In June 2025, we initiated a first-in-human Phase 1 clinical trial of our potent and selective small molecule FASN inhibitor, TVB-3567, for development of an acne indication. The Phase 1 clinical trial is a randomized double-blind placebo-controlled trial designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of TVB-3567 in healthy participants with or without acne. The trial is comprised of several parts, including single ascending dose cohorts and multiple ascending dose cohorts in participants without acne, followed by testing in participants with acne including evaluation of pharmacodynamic biomarkers. Subject to consultation with regulatory authorities, and contingent on the results of the Phase 1 trial, we anticipate initiating the Phase 2 trial of TVB-3567 in 2026.

Oncology

Dysregulation of lipid metabolism is a hallmark of cancer. Increased expression of FASN has been associated with poor prognosis and reduced survival in several tumor cell types. While most normal cells get their palmitate from dietary sources, cancer cells have a high requirement of lipids for membrane synthesis and cell signaling to meet the demands of high proliferation. Some cancer cells become dependent upon the FASN pathway for proliferation to provide a reliable and self-sufficient source of fatty acids, referred to as onco-metabolism. This is the case for specific cancers driven by driver oncogenes such as mutant KRAS (KRASM), tyrosine kinase receptors and hormone receptors, such as the androgen receptor. The fatty acids made by FASN are saturated or monounsaturated and therefore relatively resistant to oxidative stress caused by driver oncogenes, which allows the highly proliferating cancer cells to avoid cell death. We believe that this dependence on FASN provides a vulnerability that can be attacked with FASN inhibitors.

FASN inhibition can also potentially address the enormous challenge of resistance to cancer therapies. Several cancer types have been shown to upregulate FASN to rewire lipid metabolism and change the nature of the tumor cell membrane making these cells resistant to traditional cancer drugs. Use of a FASN inhibitor to normalize metabolism and tumor cell membranes is an appealing strategy to confer susceptibility in combination with a second agent.

The following diagram depicts the role of FASN in the molecular mechanisms associated with cancer:

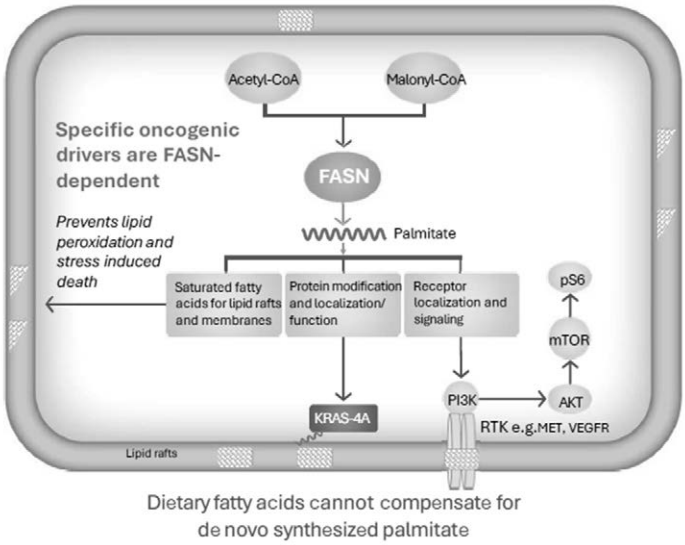


Figure 32. FASN role in molecular mechanisms associated with cancer.

FASN derived lipids play a structural role in membranes to avoid oxidative stress and create lipid rafts for oncogenic signaling (for example in KRASM or Androgen receptor signaling). This also contributes to resistance to targeted therapies. Palmitate itself (the immediate product of FASN) covalently modifies critical oncogenes to allow them to localize in membranes and function properly (for example KRAS4A). FASN derived lipids are important to create lipid rafts that anchor receptor tyrosine kinases appropriately in the plasma membrane for signaling, and the MET tyrosine kinase is one example of this class.

FASN inhibitors for oncology program

We are developing FASN inhibitors to treat specific subsets of solid tumors that are FASN-dependent in combination with other classes of oncology drugs. Our first-in-human Phase 1 clinical trial for denifanstat was conducted in patients with advanced solid tumors. The results provided a foundation and path for future clinical trials. The data from our preclinical, translational and clinical studies have identified three FASN-dependent tumor subtypes with potential clinical application, as described below.

Identification of FASN-dependent tumor types

(i) Non-small cell lung cancer (NSCLC) with KRAS mutations: KRAS mutations are among the most common mutant driver genes in NSCLC tumors and these patients have a poor prognosis. KRASM signaling depends on FASN and also depends on reactive oxygen species to maintain its pathogenic nature and high proliferation. Introduction of the KRAS mutation into a NSCLC adenocarcinoma induces the cancer cell to be highly dependent on FASN for proliferation and survival. We have generated preclinical and clinical results that demonstrate the potential of FASN inhibitors for the treatment of NSCLC KRASM, as follows:

- In preclinical screening of a large panel of cancer lines for drug sensitivity, we observed that treatment of NSCLC KRASM cells with FASN inhibitor resulted in cell death, whereas KRAS wild type (KRASWT) are less sensitive. Similar findings were made in mouse models.

- The mechanism that underpins FASN-dependence has recently been demonstrated in published studies using models of human cancer; KRASM tumors hijack the FASN pathway to make membrane lipids that are enriched for saturated or mono-unsaturated triglycerides. These membranes are more robust and resistant to oxygen free radicals that KRASM creates. FASN

inhibition disrupts this protective circuit meaning that cancer cells need to use poly unsaturated oxidation-prone fatty acids, which leads to stress induced cell death by ferroptosis.

- In our Phase 1 clinical trial in patients with solid tumors (described below), patients with NSCLC KRASM tumors treated with denifanstat exhibited stable disease significantly longer than NSCLC patients who did not have a KRAS mutation. The median time to disease progression was 22 weeks for KRASM versus five weeks for KRASWT ($p<0.02$, one sided ANOVA). We believe these clinical results with denifanstat validate the preclinical finding that KRASM is FASN-dependent.

- Preclinical combination studies of one of our FASN inhibitors plus a marketed KRASM G12C inhibitor, adagrasib, further decreased the growth of NSCLC KRASM tumors compared to either agent alone.

(ii) Hepatocellular carcinoma (HCC) FASN-dependent: We have generated preclinical results that demonstrate the potential of FASN inhibitors for the treatment of HCC, as follows:

- We have identified a subset of HCC tumors that are FASN-dependent, in a collaboration with Dr. Xin Chen at the University of California, San Francisco. This subset defined as MET-hi, PTEN-lo represents approximately 34% of human HCC, and is defined by high levels of the receptor tyrosine kinase MET and low levels of the tumor suppressor PTEN, which indicates high proliferation activity. Published clinical trials using mouse genetic HCC models support that these cancer pathways are FASN-dependent.

- Treatment of a mouse HCC MET-hi, PTEN-lo model with FASN inhibitor plus the standard of care kinase inhibitor cabozantinib triggered regression of HCC tumors. In addition, FASN inhibitor therapy combined with either cabozantinib or sorafenib, a second standard of care kinase inhibitor, improved the in vivo activity for c-MYC driven HCC.

- We have collaborated with Josep Llovet at Icahn School of Medicine at Mount Sinai, to profile FASN expression in samples from HCC patients. The results generated are consistent with the preclinical combination results with a kinase inhibitor.

- We have collaborated with Scott Friedman at Icahn School of Medicine at Mount Sinai on a preclinical mouse model of MASH with carbon tetrachloride induced fibrosis that develops HCC tumors. Treatment of mice with established liver fibrosis with FASN inhibitor significantly reduced the tumor burden compared to untreated mice. MASH-related HCC is an area that we will explore in bioinformatics analysis.

(iii) Metastatic castration resistant prostate cancer, FASN-dependent: Prostate cancer is a highly lipogenic tumor type. The androgen receptor (AR) is the main driver of disease progression in prostate cancer and upregulates levels of FASN to maintain membrane production and avoid oxidative stress. Several androgen receptor modulators are approved for treatment such as enzalutamide or abiraterone, but resistance emerges leading to relapse, often associated with new variants in AR such as Arv7.

- Preclinical results show that FASN inhibition can decrease the levels of resistance markers to androgen receptor modulators in prostate cancer preclinical models. Combination of FASN inhibitor with enzalutamide had a better anti-tumor effect than either agent alone. These results provided a strong mechanistic basis for conducting a clinical trial combining a FASN inhibitor with an AR inhibitor.

- We have collaborated with Massimo Loda and David Nanus at Weill Medical College of Cornell University on FASN in prostate cancer. Our collaborators at Weill Medical College are conducting an Investigator Sponsored Study in men with metastatic castration resistant prostate cancer to explore this combination. The results of this Phase 1 study are expected in the first half of 2027.

Phase 1 results in multiple solid tumors

We conducted a first-in-human Phase 1 clinical trial (which included dose escalation) of denifanstat in patients with advanced, heavily pretreated and mostly metastatic solid tumors. We hypothesized that the dose of denifanstat for clinical activity would be higher in cancer patients than in MASH patients, because the objective is to completely shut down FASN activity and cause cell death in cancer, rather than normalize FASN activity. In the Phase 1 clinical trial, 136 patients were treated with denifanstat, 76 treated with denifanstat only (monotherapy), and 60 treated in combination with a taxane, a commonly used class of anti-cancer drugs. The trial identified the maximum tolerable dose as 100mg per square meter of body surface area (100mg/m2), or approximately 150mg to 200mg daily, whether denifanstat was used alone or in combination. Denifanstat monotherapy treatment resulted in a disease control rate (DCR) of 42%.

Disease control was observed across multiple tumor types, including breast (100%), NSCLC (82%), and gynecological (ovarian and cervical) (53%). We believe these results are promising in these heavily pretreated, advanced stage patients.

In patients treated with denifanstat monotherapy, evaluation of time-to-progression (TTP) among patients with NSCLC revealed notably longer TTP for patients with a mutation in the KRAS gene (KRASM) (N=11) compared to those with a normal, or wild-type, KRAS gene (KRASWT) (N=6) (22 weeks versus five weeks; p<0·02).

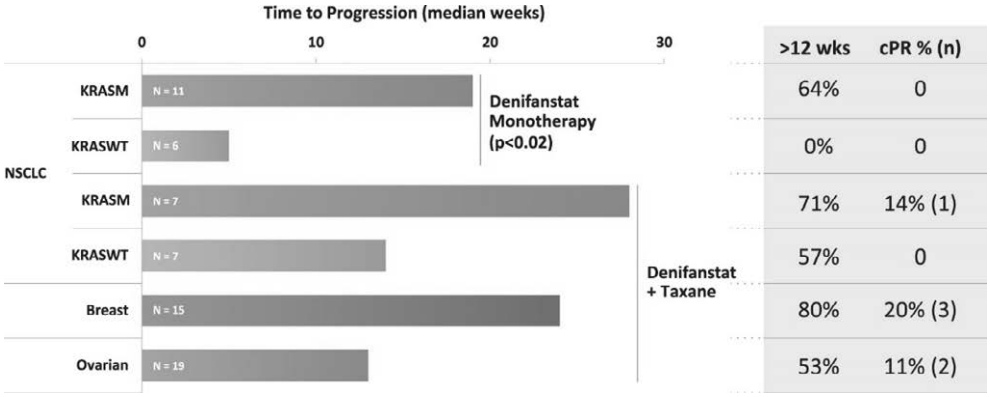


Figure 33. Time to progression in Phase 1 oncology trial

As anticipated, based on prior nonclinical toxicology clinical trial findings, the principal toxicities associated with denifanstat monotherapy were skin and ocular effects, with most being Grade 1 or 2. Common (i.e., incidence >10%) skin effects included alopecia (61%), PPE syndrome (46%), dry skin (22%), skin exfoliation (12%), and rash (11%). Ocular effects included dry eye (17%) and increased lacrimation (13%). Six episodes of serious pneumonitis were experienced by five patients receiving denifanstat and paclitaxel, one of which was fatal, all assessed by the investigator as at least possibly related to both denifanstat and paclitaxel. Pneumonitis was not observed in patients treated with denifanstat monotherapy. ECG and Holter monitoring data revealed no clinically relevant QTc prolongation with denifanstat.

This Phase 1 clinical trial successfully identified a recommended Phase 2 dose of 100mg/m2, which corresponds to 150mg or 200mg in most patients. It also identified several tumor types that may merit further development, including KRASM NSCLC, breast cancer, and ovarian cancer.

The next step would be to conduct additional clinical trials with a FASN inhibitor in tumor subtypes identified from preclinical, translational and the Phase 1 clinical study.

Glioblastoma

GBM is a disease of high unmet need. High FASN expression has been observed in glioblastoma tumors and may be associated with resistance to agents such as bevacizumab.

A Phase 2 investigator sponsored clinical trial was conducted in glioblastoma patients (Grade 4 astrocytoma) by Dr. Andrew Brenner from the University of Texas, San Antonio. In this trial, 25 bevacizumab naïve patients in their first relapse were treated with denifanstat (100mg/m2 once daily) plus bevacizumab (10mg/kg once every 2 weeks). The overall response rate was 56% (complete response 17%, partial response 39%) and six-month progression free survival was 31.4%. This represents a statistically significant improvement in six-month progression free survival over historical bevacizumab monotherapy such as the BELOB study 16% (p<0.01) and met the primary study endpoint. The observed six-month overall survival was 68%, with survival not reaching significance by log rank test (p=0.56). The most frequently reported AEs were PPE syndrome, hypertension, mucositis, dry eye, fatigue and skin infection. Most were Grade 1 or 2 in intensity. Based on these results, in early 2022, Ascletis Pharma initiated a Phase 3 registrational trial in China in patients with recurrent GBM. In September 2023, Ascletis Pharma announced the enrollment of 120 recurrent GBM patients. Ascletis announced cessation of its China GBM program in August 2025.

Discovery-FASN inhibitors

FASN plays a pathogenic role in several diseases beyond MASH. The overall strategy of our decade long research program followed four core steps: a) identify diseases where FASN contributes to the underlying pathology, b) generate proof of concept data to demonstrate the mechanism of action, c) use precision medicine to identify patient populations enriched for clinical response where feasible and, d) move promising drug candidates into clinical development.

We recognized that the over-activity of FASN may be involved in a number of different human diseases and have discovered and developed specific inhibitors of this enzyme. The goal of our program was to develop small molecule inhibitors of the enzyme that could be delivered orally for ease of use, required no more than two doses daily, and were highly selective for the FASN enzyme in order to avoid unexpected side effects. Early generation FASN inhibitors developed by others suffered poor potency, off target activity, or suboptimal physiochemical or pharmacokinetic properties; none of these entered clinical development. While early FASN inhibitors functioned as substrate competitors, our inhibitors are designed to target co-factor binding sites and avoid these liabilities.

Hundreds of molecules were ultimately designed, synthesized, and tested through iterative cycles, with several emerging as leading candidates based on their laboratory properties. A few were selected for further characterization leading to the identification of denifanstat as the leading candidate for human clinical trials. Our library of FASN inhibitors provides us with the possibility of selecting other compounds for additional indications. For example, we can select a compound from our library with preferred physio-chemical properties for a topical formulation that may be attractive for certain dermatology indications. We selected denifanstat and TVB-3567 out of more than 1,200 compounds within our library of FASN inhibitors.

Competition

MASH

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Accordingly, our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results than our drug candidates. For example, Madrigal Pharmaceuticals, Inc. (Madrigal) announced the approval of resmetirom (commercially available as Rezdiffra) for the treatment of MASH in patients with moderate to advanced liver fibrosis by the FDA in March 2024 and by the European Commission in August 2025. In August 2025, Novo Nordisk A/S announced the FDA approval of Wegovy (semaglutide) for the treatment of MASH in adult patients with moderate to advanced liver fibrosis. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies and universities and other research institutions, including Altimmune, Inc., AstraZeneca, Boehringer Ingelheim and Zealand Pharma, Eli Lilly and Company, Galmed Pharmaceuticals Ltd., Gilead Sciences, Inc., GSK plc (acquired Boston Pharmaceuticals in 2025), Inventiva S.A., Madrigal, Merck & Co., Inc., Novo Nordisk A/S (acquired Akero Therapeutics, Inc. in 2025), Pfizer Inc., Roche Holdings, Inc. (acquired 89bio, Inc. in 2025), Terns Pharmaceuticals, Inc., Viking Therapeutics, Inc., and Zydus Therapeutics Inc. Smaller or earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. We believe that the key competitive factors that will affect the development and commercial success of our drug candidates are efficacy, safety and tolerability profile, convenience of dosing, price, the level of generic competition and reimbursement.

Denifanstat could face competition from other classes individually or in combination, pursuing mechanisms including enzyme-specific inhibitors, gene expression activators, growth factor analogs, and anti-inflammation/anti-fibrotics. Given denifanstat's potential mechanism of action, and its potential complementary mechanism to other therapies, we believe that denifanstat can be used alone or in combination with some of these potential MASH products in development.

Acne

The acne therapeutics market is highly competitive and characterized by a wide range of prescription and over-the-counter products marketed by large pharmaceutical companies, specialty dermatology companies, generic drug manufacturers and consumer healthcare companies.

Current acne treatments include topical therapies, oral systemic therapies, and procedural or device-based approaches, and are prescribed based on disease severity, patient characteristics, physician judgment, and treatment guidelines. Topical therapies are commonly used as first-line treatment for mild to moderate acne and include topical retinoids, antibiotics, benzoyl peroxide, hormonal agents, and fixed-dose combination products. Many topical acne treatments are available as low-cost generics, and branded products compete primarily on formulation characteristics, tolerability, dosing convenience, and physician familiarity. Oral systemic therapies

are generally prescribed for moderate to severe acne or for patients who do not respond adequately to topical treatments. Oral therapies include antibiotics, hormonal agents, and oral isotretinoin. While oral isotretinoin is highly effective for cystic acne, its use is limited by significant safety considerations, monitoring requirements, and prescribing restrictions. Oral antibiotics are widely used but are generally recommended for limited duration due to concerns related to antibiotic resistance and adverse effects.

In addition, several companies are developing investigational acne therapies, including novel oral agents, new topical formulations, and reformulations or combinations of existing drugs. These product candidates are at varying stages of development and may compete with TVB-3567, if approved.

License agreement with Ascletis

In January 2019, we entered into a license agreement with Ascletis, a subsidiary of Ascletis Pharma, a biotechnology company incorporated in the Cayman Islands and headquartered in Hangzhou, China. The license agreement became effective in February 2019 in connection with the first closing of our Series E financing, which was led by Ascletis and its affiliates through a subsidiary. Under the license agreement, we granted Ascletis an exclusive, royalty-bearing, sub-licensable license under our know-how and patents to develop, manufacture, and commercialize denifanstat and products containing denifanstat-related compounds in the People's Republic of China, Hong Kong, Macau and Taiwan (referred to herein as Greater China or the Territory). We retained certain manufacturing rights in Greater China and the right to practice our intellectual property in Greater China as necessary to perform our obligations under the license agreement. Ascletis granted us a non-exclusive, sublicensable, royalty-free license under certain intellectual property of Ascletis to develop, manufacture, and commercialize denifanstat and products containing denifanstat-related compounds outside Greater China.

Under the license agreement, we conducted all development activities in connection with the Phase 2 FASCINATE-1 clinical trial in the United States and Greater China at our sole expense, except for certain in-kind contributions by Ascletis in Greater China. Ascletis is solely responsible at its sole expense for conducting development activities in connection with obtaining and maintaining regulatory approvals for denifanstat in Greater China. Ascletis will solely own all regulatory filings and approvals in Greater China other than those regulatory filings jointly applied for in connection with the Phase 2 FASCINATE-1 clinical trial. Further, during the term of the license agreement, Ascletis agreed not to develop, manufacture or commercialize any FASN inhibitors outside the scope of the license agreement in Greater China.

We are eligible to receive development and commercial milestone payments from Ascletis in aggregate of up to $122.0 million. In July 2023, we recognized $2.0 million of revenue related to a development milestone triggered by the initial dosing of a Phase 3 trial for recurrent GBM, of which $1.7 million was received from Ascletis in August 2023, net of applicable taxes, which were recorded in general and administrative expense in the statement of operations and comprehensive loss.

We are also eligible to receive tiered royalty payments from Ascletis ranging from high single digit to mid-teen percentages on annual net sales of denifanstat and other products containing licensed compounds in the Territory, subject to customary reductions. Ascletis' obligation to pay royalties expires on a product-by-product and region-by-region basis upon the earlier of the expiration of all valid claims covering a product in a region and 10 years following the first commercial sale of a product in a region.

Unless terminated earlier, the license agreement will continue until the expiration of the last to expire royalty payment obligation. Ascletis has the right to terminate the license agreement for any reason or no reason upon 90 days' written notice. In addition, either party may terminate the license agreement upon the other party's uncured material breach, insolvency, or bankruptcy. Termination of the license agreement does not terminate the non-exclusive license granted to us by Ascletis, however, in the event of early termination by Ascletis in the case of certain material breaches, we will pay Ascletis single digit royalties on net sales of products outside the territory covered by such non-exclusive license. In the event of early termination for any reason other than by Ascletis for our material breach, Ascletis will transfer all rights to us relating to the products, intellectual property, and regulatory approvals in Greater China, subject to our obligation to pay Ascletis royalties in the low single digit percentages on net sales of any reverted products in Greater China.

In October 2019, we entered into a Patent Assignment Agreement and Patent Re-Assignment Agreement with Gannex, an affiliate of Ascletis and subsidiary of Ascletis Pharma, whereby we assigned to Gannex all our rights, title, and interest in and to all patents and patent applications in China that we previously licensed to Ascletis pursuant to the license agreement. In July 2023, we amended and restated each of the Patent Assignment Agreement and Patent Re-Assignment Agreement to assign additional patents and patent applications to Gannex, effective as of October 2019, which additional patents and patent applications relate solely to licensed compounds under the license agreement, specifically, denifanstat and related compounds, and their use in the treatment of cancers, fatty liver diseases, inflammatory diseases, and diseases related thereto in Greater China. Also in July 2023, we entered into an Assignment

and Assumption Agreement with Ascletis and Gannex under which Ascletis, while remaining responsible for performance under the License Agreement, assigned all of its rights and obligations under the License Agreement to Gannex and Gannex assumed such rights and obligations, effective as of October 2019. The assignment of patents did not alter the economic terms under the license agreement with respect to the assigned patents and patent applications, and we retained such rights under the assigned patents and patent applications that we had previously retained under the license agreement. Upon early termination of the license agreement for any reason other than by Ascletis for our material breach, Gannex will reassign all assigned patents and patent applications in China back to us. Additionally, we retain control of the prosecution of the pending patent applications assigned to Gannex.

Sales and marketing

We are focused on the discovery and development of our drug candidates. We currently have no sales, marketing or distribution capabilities to commercialize any approved drug candidates. If our drug candidates are approved, we intend either to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize our products, or to outsource this function to a third party.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to rely, upon third-party CMOs for the manufacture of any drug candidates that we may develop for larger-scale preclinical and clinical testing, as well as for commercial quantities of any drug candidates that are approved. We currently rely on several manufacturers for the production of raw materials, APIs, and the finished products of denifanstat, TVB-3567 and resmetirom, and we believe that there are multiple sources for all raw materials employed in the manufacturing of our drug substances and drug products, and we believe that several CMOs are able to manufacture lots as needed.

Our contracted CMOs have manufactured multiple lots of denifanstat, each one yielding multiple kilograms of drug, and have manufactured the clinical trial supply in both capsule and tablet forms. To date, we have relied on four CMOs based in Europe, the United States and China, as well as our license partner, Ascletis, to produce drug substances and two CMOs in the United States and China, as well as our license partner, Ascletis, to produce drug products, across our programs. We will need to manufacture additional materials to support completion of mid- and late-stage studies such as Phase 2 and Phase 3 trials.

In December 2025, we entered into a license agreement with Assia Chemical Industries Ltd., doing business as TAPI Technology & API Services (TAPI), a subsidiary of Teva Pharmaceutical Industries Ltd. (the TAPI Agreement). Under the TAPI Agreement, TAPI granted us a global, exclusive license to certain intellectual property rights covering innovative forms of TAPI's resmetirom active pharmaceutical ingredient (API) for our technical evaluation and manufacture, and, if elected by us following an evaluation period, further development of a fixed-dose combination product containing denifanstat and resmetirom.

There are extensive regulations that govern the manufacturing of biopharmaceutical products, and the third-party manufacturing organizations we work with are required to adhere to these. Our CMOs are required to manufacture our drug candidates under cGMP requirements and applicable laws and regulations.

Intellectual property

We strive to protect the proprietary technologies that we believe are important to our business, including pursuing and maintaining patent protection intended to cover the composition of matter of our drug candidates, for example, denifanstat and TVB-3567, their methods of use, related technologies and other inventions that are important to our business. In addition to patent protection, we also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our commercial success depends in part upon our ability to obtain and maintain patent and other proprietary protection for our drug candidates and other commercially important technologies, inventions and know-how related to our business, defend and enforce our intellectual property rights, in particular, our patent rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others.

The patent positions for biotechnology and pharmaceutical companies like us are generally uncertain and can involve complex legal, scientific and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors.

In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any of our drug candidates will be protected or remain protectable by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented or invalidated by third parties. For more information regarding the risks related to our intellectual property see "Risk Factors—Risks related to our intellectual property."

As of December 31, 2025, we owned and/or had control of 12 U.S. patents, 151 issued foreign patents, which includes European patents that have been validated in various European countries, Hong Kong, and Macau, seven pending non-provisional U.S. patent applications, two pending U.S. provisional patent applications, three pending international PCT applications, and 40 pending foreign patent applications.

With regard to denifanstat, as of December 31, 2025, we owned one issued U.S. patent with composition of matter and pharmaceutical composition claims directed to denifanstat. The issued U.S. patent is expected to expire in 2032, without taking any potential patent term extension (PTE) into account. In addition, we owned and/or had control of patents that have been granted in various jurisdictions including Australia, Argentina, Brazil, countries across Europe, Canada, Eurasia, Hong Kong, Japan, China, South Korea, India, Israel, Macau, Mexico, New Zealand, Taiwan, and South Africa, which are expected to expire in 2032, without taking potential PTEs or other forms of extension into account. We also owned three issued U.S. patents with claims directed to methods of using denifanstat and combinations of denifanstat with additional agents. The issued U.S. patents are expected to expire in 2035 and 2036, without taking a potential PTE into account. Specifically, U.S. Patent No. 10,363,249, which is expected to expire in 2035, issued with claims directed to a method of treating a taxane-resistant tumor or cancer comprising administering a combination of denifanstat and a taxane. U.S. Patent No. 10,189,822, which is expected to expire in 2036, issued with claims directed to a method of treating various types of cancers (mantle cell lymphoma, chronic myelogenous leukemia, sarcoma; endometrial tumors, non-small cell lung carcinoma, gastric carcinomas, hepatocellular tumors, and head and neck cancer) comprising administering denifanstat, or a combination of denifanstat with additional agents. U.S. Patent No. 11,034,690, which is expected to expire in 2036, issued with claims directed to methods of treating MASH, formerly referred to as NASH, MASLD, formerly referred to as NAFLD, liver cirrhosis and liver fibrosis comprising administering denifanstat. In addition, we owned and/or had control of patents with claims directed to methods of using denifanstat, and/or methods of using combinations of denifanstat with additional agents, in Australia, China, Japan, various countries across Europe, South Korea, Israel, New Zealand, and Russia, which are expected to expire in 2035, 2036 and/or 2037. We also owned and/or had control of at least 12 pending applications in jurisdictions including the United States, Australia, China, Canada, Europe, Hong Kong, Japan, South Korea, Singapore, and South Africa, which, if issued, are expected to expire in 2036 and/or 2037, without taking potential PTEs into account. Additionally, we owned and/or had control of two pending U.S. applications and a pending international PCT application directed to a combination of denifanstat and THR-β agonists, including resmetirom, as well as methods of treating NASH/MASH using the same, which, if issued, are expected to expire in 2044, without taking potential PTEs into account. Further, the Company has a license from TAPI to certain innovative forms of resmetirom covered by pending patent applications in the United States, Canada and Europe; with respect to these patent applications, if issued, the patents are expected to expire in 2041, without taking potential PTEs into account.

We owned and/or had control of a pending international PCT application and a pending application in Tawain directed to a combination of denifanstat and GLP-1 agonists, including semaglutide for treating liver diseases, which, if issued, are expected to expire in 2044, without taking potential PTEs into account.

With regard to TVB-3567, as of December 31, 2025, we owned one issued U.S. patent with composition of matter claims, as well as claims directed to methods of using TVB-3567 to treat various types of cancer. The issued U.S. Patent No. 9,994,550 is expected to expire in 2035, without taking a potential PTE into account. In addition, we own and/or have control of patents that have been granted in Australia, Brazil, Canada, South Africa, Japan, South Korea, China, Hong Kong, Macau, Israel, India, Singapore, New Zealand, Russia, Mexico, and various countries across Europe, which are expected to expire in 2035, without taking potential term extensions into account. We also own and/or have control of granted patents in China, Israel, Japan, South Korea and New Zealand, which are expected to expire in 2037, without taking potential PTEs into account, and 12 pending patent applications in the United States, Australia, Canada, China, Europe, Hong Kong, Japan, South Korea, Singapore and South Africa with disclosures covering TVB-3567, which, if issued, are expected to expire in 2037 (2036 in the United States), without taking potential PTEs into account.

With respect to claims specifically directed to the treatment of MASH, formerly referred to as NASH, as of December 31, 2025, we owned U.S. Patent No. 11,034,690, which is expected to expire in 2036, without taking potential term extensions into account issued with claims directed to methods of treating MASH, formerly referred to as NASH, MASLD, formerly referred to as NAFLD, liver cirrhosis and liver fibrosis comprising administering denifanstat. In addition, we own and/or have control of patents that have been granted in Australia and South Korea (denifanstat), Israel, China, Japan and New Zealand (denifanstat and TVB-3567) which are

expected to expire in 2037, without taking potential term extensions into account. We also own and/or have control of 12 applications pending in the U.S., Australia, Canada, Europe, China, Hong Kong, Japan, South Korea, Singapore, and South Africa, that disclose chemical genera encompassing denifanstat and TVB-3567 for the treatment of MASH, formerly referred to as NASH. Any patents issuing from these applications are expected to expire in 2037 (2036 in the United States), without taking potential PTEs into account. Additionally, we owned and/or had control of a pending international PCT application directed to methods of using denifanstat to treat MASH patients with F2 and F3 fibrosis, which, if issued, are expected to expire in 2045, without taking potential PTEs into account.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application or international PCT application.

In the United States, the term of a patent covering an FDA-approved drug may, in certain cases, be eligible for a PTE under the Hatch-Waxman Act as compensation for the loss of patent term during the product development and the FDA regulatory review process. The period of extension may be up to five years, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering denifanstat and TVB-3567 may be entitled to PTE. If our drug candidates receive FDA approval, we intend to apply for PTE, if available, to extend the term of patents that cover the approved drug candidates. We also intend to seek PTE in any jurisdictions where they are available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we also rely on trade secret protection for our proprietary information that is not amenable to, or that we do not consider appropriate for, patent protection. However, trade secrets can be difficult to protect. Although we take steps to protect our proprietary information, including restricting access to our premises and our confidential information, as well as entering into agreements with our employees, consultants, advisors and potential collaborators, such individuals may breach such agreements and disclose our proprietary information including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. In addition, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. For more information regarding the risks related to our intellectual property, see "Risk Factors—Risks related to our intellectual property."

U.S. patent term restoration

Depending upon the timing, duration and specifics of the potential FDA approval of denifanstat and any future drug candidates, some of our U.S. patents may be eligible for limited PTE. The Hatch-Waxman Amendments permit a patent restoration term, often referred to as PTE, of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one half the time between the effective date of an IND and the submission date of an NDA plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug or biologic is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves or denies the application for any PTE or restoration. In the future, we intend to apply for extension of patent term for one of our patents covering denifanstat to add patent life beyond its current expected expiration date.

Government regulation and product approval

As a pharmaceutical company that operates in the United States, and in foreign countries, we are subject to extensive regulation. Government authorities in the United States (at the federal, state, and local level) and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of drug products such as those we are developing. Any drug candidates that we develop must be approved by the FDA before they may be legally marketed in the United States, and by the appropriate foreign regulatory authority before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in the European Union (EU) are addressed in a centralized way, but country-specific regulation remains essential in many respects.

U.S. drug development process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act (the FDCA) and implements regulations. Drugs are also subject to other federal, state, and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practices (GLP) regulations, and other applicable regulations;

- submission to the FDA of an IND, which must become effective before human clinical trials may begin and must be updated annually or when significant changes are made;

- approval by an IRB or ethics committee at each clinical site before each clinical trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with applicable regulations, including GCP regulations and other clinical-trial related regulations to establish the safety and efficacy of the proposed drug for its proposed indication;

- preparation and submission to the FDA of an NDA for a new drug after completion of all pivotal trials, which includes not only the results of the clinical trials, but also detailed information on the chemistry, manufacturing and controls for the drug candidate and proposed labeling;

- a determination by the FDA within 60 days of its receipt of an NDA to file the NDA for review;

- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality, and purity;

- potential FDA audit of the preclinical and/or clinical trial sites that generated the data in support of the NDA to assess compliance with GCP;

- satisfactory completion of an FDA advisory committee review, if applicable; and

- FDA review and approval of the NDA prior to any commercial marketing or sale of the drug in the United States.

Satisfaction of FDA pre-market approval requirements typically takes many years, and the actual time required may vary substantially based upon the type, complexity, and novelty of the proposed drug or disease. Even after obtaining initial marketing approval, a drug product and its manufacturer remain subject to extensive, continuing regulatory requirements, including with respect to manufacturing, quality control, adverse event reporting, advertising and promotion and periodic inspections by regulatory authorities.

U.S. preclinical and clinical development

Before testing any drug candidate in humans, the drug candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity, and formulation, as well as animal studies, to assess the potential safety and activity of the drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLPs. The sponsor must submit the results of the preclinical tests, together with chemistry, manufacturing and controls information, analytical data, any available clinical data or literature and a proposed clinical trial protocol to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product (i.e., the drug candidate) to humans.

An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions or places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns, non-compliance or other

issues affecting the integrity of the trial. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence and, once begun, issues may arise that could cause the trial to be suspended or terminated.

Clinical trials involve the administration of the drug candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an IRB or ethics committee at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers factors such as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or data monitoring committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. There are also requirements governing the registration of ongoing clinical trials and posting of completed clinical trial results to public registries.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA. The FDA may accept a well-designed and well-conducted foreign clinical study not conducted under an IND if the study was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1*. The drug candidate is initially introduced into a limited population of healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution, and excretion, and if possible, to gain early evidence of effectiveness. In the case of some drug candidates for severe or life-threatening diseases, especially when the candidate may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

- *Phase 2*. The drug candidate is evaluated in a limited patient population with the targeted disease or condition to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the drug candidate for the targeted disease or condition and to determine dosage tolerance, optimal dosage, and dosing schedule.

- *Phase 3*. The drug candidate is administered to an expanded patient population at geographically dispersed clinical trial sites, to provide substantial evidence of clinical efficacy and to further test for safety. These clinical trials are intended to establish the overall benefit/risk relationship of the drug candidate and provide adequate basis for the labeling of the drug candidate. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

In some cases, FDA may require, or sponsors may voluntarily pursue, post-approval studies, or Phase 4 clinical trials, that are conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, such as with drugs granted accelerated approval, FDA may mandate the performance of Phase 4 trials as a condition of approval of an NDA.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must develop methods for testing the identity, strength, quality, and purity of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

While the IND is active and before approval, progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators within fifteen days for serious and unexpected suspected AEs, findings from other studies suggesting a significant risk to humans exposed to the drug candidate and from animal or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a

serious suspected adverse reaction over that listed in the protocol or investigator brochure. Additionally, the sponsor must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of information. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

U.S. NDA review and approval processes

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug candidate, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the drug candidate. Data may come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the drug candidate to the satisfaction of the FDA. The submission of an NDA is subject to the payment of substantial application fees; a waiver of such fees may be obtained under certain limited circumstances. Sponsors of approved NDAs are also subject to an annual program fee. These fees are typically increased annually.

The FDA reviews all NDAs submitted before it accepts them for filing. As a result of such review, the FDA may refuse to file any NDA that it deems incomplete or not properly reviewable at the time of submission and may request additional information rather than accepting an NDA for filing. The FDA must make a decision on accepting an NDA for filing within 60 days of receipt of the application. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality, and purity. The FDA has a Prescription Drug User Fee Act (PDUFA) goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission, which means that review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after the application is submitted. The FDA does not always meet its PDUFA goal dates, and the review process is often significantly extended by FDA requests for additional information or clarification.

The FDA may refer applications for novel drug products or drug products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation, and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions and typically follows the advisory committee's recommendations.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical sites to assure compliance with GCP requirements. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates the application, manufacturing process, and manufacturing facilities, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The Complete Response Letter may require additional clinical data and/or (an) additional clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies, or manufacturing. If a Complete Response Letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, or precautions be included in the product labeling or may condition the approval of the NDA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. For example, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess a drug safety and effectiveness, and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized, and the FDA may limit further marketing of the product based on the results of these post-approval studies. The FDA may also determine that a Risk Evaluation and Mitigation Strategy (REMS) is necessary to ensure that the benefits of the drug outweigh the potential risks. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the NDA without an approved REMS, if required. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use (ETASU). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the product. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission to and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs. As with new NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

In addition, the Pediatric Research Equity Act (PREA) requires a sponsor to conduct pediatric clinical trials for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA may send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current, or submit a request for approval of a pediatric formulation.

Expedited development and review programs

The FDA offers a number of expedited development and review programs for qualifying drug candidates. For example, the Fast Track designation program is intended to expedite or facilitate the process for reviewing new drug candidates that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the drug candidate and the specific indication for which it is being studied. The sponsor of a Fast Track designated product has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the drug candidate may be eligible for priority review. A Fast Track designated drug candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A drug candidate intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A drug candidate can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the drug candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the Fast Track designation program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the drug candidate, including involvement of senior managers.

Any marketing application for a drug candidate submitted to the FDA for approval, including a drug candidate with a Fast Track designation and/or Breakthrough Therapy designation, may be eligible for rolling review, as well as other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A drug candidate is eligible

for priority review if it is designed to treat a serious or life-threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness compared to available alternatives for such disease or condition. For new molecular entity NDAs, priority review means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date.

Additionally, drug candidates studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the drug candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing confirmatory clinical studies which must be conducted with due diligence to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Under the Food and Drug Omnibus Report Act of 2022 (FDORA), the FDA may require that such confirmatory studies be underway prior to approval or within a specific time period after the date accelerated approval is granted. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the sponsor fails to conduct the required confirmatory studies in a timely manner, or if such post-approval studies fail to verify the predicted clinical benefit. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the agency, pre-approval of all advertising and promotional materials, which could adversely impact the timing of the commercial launch of the product. Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress.

Fast Track designation, Breakthrough Therapy designation, priority review, and accelerated approval do not change the standards for approval, but may expedite the development, review or approval process. Even if a drug candidate qualifies for one or more of these programs, the FDA may later decide that the drug candidate no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity could also block the approval of a drug candidate for seven years if a competitor obtains approval of the same drug as defined by the FDA.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Post-approval requirements

Any drug products manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, requirements related to manufacturing, record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and complying with FDA promotion and advertising requirements, which include, among

others, standards for direct-to-consumer advertising, restrictions on promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (off-label use), limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet.

The FDA closely regulates the marketing, labeling, advertising, and promotion of drug products. A company can make only those claims relating to safety and efficacy that are consistent with the FDA-approved labeling. The FDA and other agencies enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties. Physicians may prescribe, in their independent professional medical judgment, legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications regarding off-label use of their products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion of off-label use and has enjoined companies from engaging in off-label promotion. The FDA and other regulatory authorities have also required that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. However, companies may share truthful and non-misleading information that is otherwise consistent with a product's FDA-approved labelling.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval. We rely, and expect to continue to rely, on third parties for the production of clinical and, if approved, commercial quantities of our drug candidates in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP requirements. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. Drug manufacturers using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and notify the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

The FDA may withdraw product approvals or request product recalls if a company fails to maintain compliance with regulatory requirements and standards after the product reaches the market. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; requirements for post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product or complete withdrawal of the product from the market or product recalls;
- fines, FDA Form 483s warning letters, or untitled letters;
- clinical holds on clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;

- the issuance of safety alerts, Dear Healthcare Provider letters, press releases, and other communications containing warnings or other safety information about the product; or

- injunctions or the imposition of civil or criminal penalties.

U.S. marketing exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or accept for review an abbreviated new drug application (ANDA) or a Section 505(b)(2) NDA submitted by another company for another drug based on the same active moiety, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder.

The FDCA also provides three years of marketing exclusivity for an NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from accepting ANDAs or Section 505(b)(2) NDAs for drugs referencing the approved application for review.

Orphan drug exclusivity, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances. Pediatric exclusivity is another type of non-patent market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing regulatory exclusivity periods and, for drugs, patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

Regulation of companion diagnostics and complementary diagnostics

As a part of our later stage product development strategy, we may develop and commercialize one or more companion diagnostics or complementary diagnostics. Companion diagnostics and complementary diagnostics can identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics and complementary diagnostics are regulated as medical devices by the FDA. Such diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The two primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification, or 510(k), and approval of a premarket approval application (PMA). Beginning in February 2026, the FDA will evaluate PMA submissions against the harmonized Quality Management System Regulation (QMSR). For a novel therapeutic product for which a companion diagnostic device is essential for the safe and effective use of the product, the companion diagnostic device should be developed and approved or 510(k)-cleared contemporaneously with the therapeutic. The use of the companion diagnostic device will be stipulated in the labeling of the therapeutic product. A complementary diagnostic is not considered essential for the safe and effective use of the therapeutic product and does not need to be approved or cleared contemporaneously with the therapeutic.

After a companion diagnostic device is cleared or approved, it is subject to applicable post-marketing requirements including the FDA's QMSR, adverse event reporting, recalls and corrections, and product marketing requirements. Device manufacturers must register and list their devices with the FDA. Applicable portions of the QMSR may include the methods and documentation of the design, testing, production, processes, controls, quality assurance, labeling, packaging and shipping of medical devices. Companion and complementary diagnostic manufacturers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and the facilities for compliance with regulatory requirements. In January 2024, FDA announced its intention to initiate the reclassification process for most in vitro diagnostics. Further, FDA indicated that it will continue taking a risk-based approach in the initial classification of individual in vitro diagnostics to determine whether a new test may be classified into class II through the de novo classification process. In so doing, FDA indicated that it may regulate most future companion diagnostics as class II devices.

Disclosure of clinical trial information

Sponsors of applicable clinical trials of FDA regulated products are required to register their clinical trials within specific timeframes for publication on www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors and patients may use this publicly available information to gain knowledge regarding the progress of development programs. Failure to timely register a covered clinical study or to submit study results as provided for in the law could lead to consequences such as public notifications of noncompliance and civil monetary penalties.

Other U.S. healthcare laws and compliance requirements

Although we currently do not have any products on the market, we are and, upon approval and commercialization, will be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. In the United States, such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, price reporting, and healthcare provider sunshine laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting, or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing, or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor. Additionally, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

The federal False Claims Act prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-covered, uses. In addition, a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act.

The Health Insurance Portability and Accountability Act (HIPAA) also created federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items, or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Additionally, the U.S. Physician Payments Sunshine Act and its implementing regulations require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with certain exceptions) annually report information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, certain ownership and investment interests held by such physicians and their immediate family members.

In order to distribute products commercially, we must also comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers, and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, track, and report gifts, compensation and other remuneration made to physicians and other healthcare providers, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, significant civil, criminal and/or administrative penalties, damages, fines, disgorgement, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Pharmaceutical coverage, pricing and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug candidates for which we or our collaborators obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we or our collaborators receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such drug products.

In the United States, third-party payors include federal and state healthcare programs, government authorities, private managed care providers, private health insurers, and other organizations. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We or our collaborators may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Nonetheless, our drug candidates may not be considered medically necessary or cost-effective. Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

If we elect to participate in certain governmental programs, we may be required to participate in discount and rebate programs, which may result in prices for our future products that will likely be lower than the prices we might otherwise obtain. For example, drug manufacturers participating under the Medicaid Drug Rebate Program must pay rebates on prescription drugs to state Medicaid programs. Under the Veterans Health Care Act (VHCA) drug companies are required to offer certain drugs at a reduced price to a number of federal agencies, including the U.S. Department of Veterans Affairs and Department of Defense, the Public Health Service and certain private Public Health Service designated entities in order to participate in other federal funding programs, including Medicare and Medicaid. Discounted prices must also be offered for certain U.S. Department of Defense purchases for its TRICARE program via a rebate system. Participation under the VHCA also requires submission of pricing data and calculation of discounts and rebates pursuant to complex statutory formulas, as well as the entry into government procurement contracts governed by the Federal Acquisition Regulations. If our products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply.

Additionally, we may develop complementary diagnostic tests for use with our drug candidates. We, or our collaborators, may be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our drug candidates, once approved. While we have not yet developed any complementary diagnostic tests for our drug candidates, if we

do, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our drug candidates.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other Member States allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any drug candidates for which we or our collaborators receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we or our collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other healthcare funding and applying new payment methodologies. For example, in 2010, the Patient Protection and Affordable Care Act (the Affordable Care Act) was enacted, which affected existing government healthcare programs and resulted in the development of new programs.

Among the Affordable Care Act's provisions of importance to the pharmaceutical industry, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and a cap on the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price (AMP), which, effective January 1, 2024, was eliminated as a result of the American Rescue Plan Act of 2021;

- a Medicare Part D coverage gap discount program, later supplanted by the Medicare manufacturer discount program under the Inflation Reduction Act, in which manufacturers were required to agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals, including individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and

- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been executive, judicial and legislative challenges to certain aspects of the Affordable Care Act. It is unclear how any future litigation, and the healthcare reform measures of the current executive administration, will impact the Affordable Care Act.

Other legislative changes have also been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, the Budget Control Act of 2011 and subsequent legislation, among other things, created measures for spending reductions by Congress that include aggregate reductions of Medicare payments to providers of on average 2% per fiscal year, which remain in effect through 2032. Due to the Statutory Pay-As-You-Go Act of 2010, estimated budget deficit increases resulting from the American Rescue Plan Act of 2021, and subsequent legislation, Medicare payments to providers will be further reduced starting in 2025 absent further legislation. The U.S. American Taxpayer Relief Act of 2012 further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws and regulations may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our drug candidates for which we may obtain regulatory approval or the frequency with which any such drug candidate is prescribed or used.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, and review the relationship between pricing and manufacturer patient programs. The Inflation Reduction Act of 2022 (IRA), for example, includes several provisions that may impact our business to varying degrees, including provisions that reduce the out-of-pocket spending cap for Medicare Part D beneficiaries from $7,050 to $2,000 starting in 2025, thereby eliminating the so-called coverage gap; impose new manufacturer financial liability on certain drugs under Medicare Part D; allow the U.S. government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation; and delay until January 2032 the implementation of the HHS rebate rule that would have limited the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have approved indication(s) for the rare disease or condition(s) described in its orphan designation(s). The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA's Medicare drug price negotiation program. The effects of the IRA on our business and the healthcare industry in general is not yet known.

In addition, the One Big Beautiful Bill Act of 2025 (OBBBA) imposed significant reductions in Medicaid funding, additional work requirements for Medicaid recipients, and more frequent reenrollment requirements. These changes are expected to place substantial pressure on state Medicaid budgets, reduce enrollment, and limit covered services, which could decrease utilization of, and reimbursement for, our products, if approved.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. The Trump Administration has issued executive orders and supported proposed regulatory initiatives in 2025 that could have a significant impact on the prices that we, or any collaborators, may receive for any approved products.

On May 12, 2025, President Trump signed an executive order directing the Secretary of HHS to set and communicate most-favored-nation (MFN) price targets to manufacturers and propose a rulemaking plan to impose MFN pricing if "significant progress" is not made, and also directing the federal government to support regulatory paths to allow direct-to-patient sales for companies that meet these targets. The executive order further states that the Administration will take additional action (for example, examining whether marketing approvals should be modified or rescinded or considering individual drug importation waiver authorities) should manufacturers fail to offer American consumers the MFN lowest price. In July 2025, President Trump sent letters to certain pharmaceutical companies demanding that these companies extend MFN pricing to Medicaid and newly launched drugs as well as move to direct-to-consumer models priced at MFN pricing, and soliciting binding commitments by September 29, 2025. Since this time, multiple drug manufacturers have announced plans to, for certain of their drugs, lower prices to reflect similar pricing around the world, and to sell these reduced-price drugs on a direct-to-consumer purchasing platform developed by the federal government; however, it is not known what results will occur to the extent the recipients of these letters do not reduce their U.S. prices.

On December 19, 2025, CMS released two proposed rules that would incorporate MFN pricing principles into federal reimbursement for prescription drugs. The first proposal, the Global Benchmark for Efficient Drug Pricing Model (GLOBE) for Medicare Part B, would require manufacturers of specified single source drugs and sole source biologics to pay incremental rebates based on international benchmark prices, with participation triggered for products meeting CMS's spending and eligibility criteria. The second proposal, the Guarding U.S. Medicare Against Rising Drug Costs (GUARD) model for Medicare Part D, would similarly mandate manufacturer rebates for qualifying sole source drugs where the Medicare net price exceeds an MFN benchmark derived from international reference pricing methodologies. As proposed, GLOBE would begin a five-year performance period on October 1, 2026 and GUARD would begin its performance period in 2027. These proposals will likely be subject to legal challenges that could delay their implementation or modify their impact on manufacturer pricing and revenue. Additionally, in November 2025, CMS introduced the GENErating cost Reductions for U.S. Medicaid (GENEROUS) Model, a voluntary MFN framework for manufacturers participating in the Medicaid Drug Rebate Program. Although it is voluntary, the GENEROUS Model could also impact the drug pricing landscape for manufacturers.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

We expect that additional U.S. federal and state healthcare reform measures will be adopted in the future, any of which could limit the amounts that third-party payors or customers will pay for healthcare drugs and services, which could result in reduced demand for our drug candidates or additional pricing pressures

Data privacy and security laws

We may also be subject to federal, state, local, and foreign data privacy and security obligations such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security. In the United States, numerous federal, state, and local laws and regulations, including state data breach notification laws, state health information privacy laws, and federal, consumer protection laws and regulations (e.g., Section 5 of the FTC Act), and similar laws (e.g., wiretapping laws) govern the collection, use, disclosure, protection, and other processing of health-related and other personal data and may apply to our operations or the operations of our partners upon which we rely. For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and its implementing regulations, impose requirements relating to the privacy, security and transmission of individually identifiable health information on certain health care providers, health plans and health care clearinghouses, known as covered entities and their business associates that perform certain services that involve creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities as well as their covered subcontractors. Entities that are found to be in violation of HIPAA as the result of, for example, a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Further, entities that knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA may be subject to criminal penalties.

In addition, U.S. state laws govern the privacy and security of personal data, many of which differ from each other in significant ways and may be subject to different interpretations, thus complicating our compliance efforts. By way of example, the California Consumer Privacy Act (CCPA) applies to personal data of consumers, business representatives, and employees who are California residents, and requires businesses to provide specific disclosures in privacy notices and honor requests of such individuals. The CCPA provides for administrative fines of up to $7,500 per violation, as well as a private right of action for individuals affected by certain data breaches to recover significant statutory damages. In addition, the California Privacy Rights Act of 2020 (CPRA) expanded the CCPA's requirements, including by adding a new right for individuals to correct their personal data and establishing a new regulatory agency to implement and enforce the law. Numerous other states have also passed or proposed similarly comprehensive privacy laws. These state laws and the CCPA provide individuals with certain rights concerning their personal data, including the right to access, correct, or delete certain personal data, and opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. The exercise of these rights may impact our business and ability to provide our products and services. While these states, like

the CCPA, also exempt some data processed in the context of clinical trials, these developments may further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely. There are also states that are specifically regulating health information. For example, Washington's My Health My Data Act, which became effective on March 31, 2024, regulates the collection and sharing of health information and has a private right of action, which further increases the relevant compliance risk. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain specific types of information. For example, a small number of states have passed laws that regulate biometric data specifically.

These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. New privacy legislation will add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. In particular, the existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. State laws are changing rapidly and there is discussion in the U.S. Congress of a new comprehensive federal data privacy law to which we may likely become subject, if enacted.

Outside the United States, an increasing number of laws, regulations, and industry standards govern data privacy and security, including the European Union's General Data Protection Regulations (EU GDPR) and the United Kingdom's GDPR (UK GDPR, and together with the EU GDPR, referred to as GDPR). The GDPR applies to any company established in the European Economic Area (EEA) or United Kingdom as well as to those outside the EEA or United Kingdom if they collect and use personal data in connection with the offering of goods or services to individuals in the EEA or United Kingdom or the monitoring of their behavior.

The GDPR creates significant and complex compliance burdens for covered companies, including strict requirements for processing personal data. Companies violating the GDPR may face temporary or definitive bans on data processing and other corrective actions; fines of up to €20 million (£17.5 million) or 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. The processing of "special category personal data" (including health-related data) may also impose heightened compliance burdens under the GDPR and is a topic of active interest among relevant regulators.

Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the GDPR restricts the transfer of personal data from the EEA and United Kingdom to the United States and other countries whose privacy laws are believed to be inadequate. Although there are various mechanisms that may be used to transfer personal data from the EEA and the United Kingdom to the United States in compliance with law, such as the EEA and United Kingdom's standard contractual clauses, the UK's International Data Transfer Agreement / Addendum, and the EU-U.S. Data Privacy Framework and the UK extension thereto (which allows for transfers for relevant U.S.-based organizations who self-certify compliance and participate in the Framework), these mechanisms are subject to legal challenges and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer rules.

The EU GDPR also provides that EEA Member States may make their own laws and regulations to introduce specific requirements related to the processing of personal data and "special categories of personal data", which may lead to greater divergence on the law that applies to the processing of such data across Europe. Country-specific regulations could also limit our ability to collect, use and share European data, and/or could cause our compliance costs to increase, ultimately having an adverse impact on our business and harming our business and financial condition.

Our employees and personnel may use generative AI technologies to perform their work, and the disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and consumer lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages.

In addition to data privacy and security laws, we are or may become contractually subject to industry standards adopted by industry groups and may become subject to such obligations in the future. We are also bound by other contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. We publish privacy policies, marketing materials, and other statements, such as compliance with certain certifications or self-regulatory principles, regarding data privacy and

security. If these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators, or other adverse consequences.

Obligations related to data privacy and security are quickly changing, becoming increasingly stringent, and creating regulatory uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources and may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf.

The U.S. Foreign Corrupt Practices Act (FCPA)

The FCPA prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Europe / rest of world government regulation

In addition to regulations in the United States, we will also be subject to a variety of comparable regulatory requirements in other jurisdictions governing, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing, and export and import of drug products such as those we are developing. Whether or not we or our potential collaborators obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries.

Clinical trials in the EU

Similar to the United States, the various phases of preclinical and clinical research in the European Union (EU) are subject to significant regulatory controls.

In the EU, clinical trials are governed by the Clinical Trials Regulation (EU) No 536/2014 (CTR), which entered into application on January 31, 2022 repealing and replacing the former Clinical Trials Directive 2001/20/EC (CTD). As of January 31, 2025, all new clinical trial authorization applications in the EU must be made under the CTR.

The CTR is intended to harmonize and streamline clinical trial authorizations, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increase their transparency. Specifically, the CTR, which is directly applicable in all EU Member States, introduces a streamlined application procedure through a single-entry point, the Clinical Trials Information System (CTIS); a single set of documents to be prepared and submitted for the application; as well as simplified reporting procedures for clinical trial sponsors. A harmonized procedure for the assessment of applications for clinical trials has been introduced and is divided into two parts. Part I assessment is coordinated by the competent authority of a reporting EU Member State selected by the trial sponsor and relates to clinical trial aspects that are considered to be scientifically harmonized across EU Member States. This assessment is then submitted to the competent authorities of all concerned EU Member States in which the trial is to be conducted for their review. Part II is assessed separately by the competent authorities and ethics committees in each concerned EU Member State. Individual EU Member States retain the power to permit or refuse the conduct of clinical trials in their territory.

In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

EU review and approval process

In the EU, medicinal products can only be commercialized after a marketing authorization (MA), has been granted. To obtain an MA for a medicinal product, an applicant must submit a marketing authorization application (MAA) either under a centralized procedure administered by the EMA or one of the procedures administered by the competent authorities of EU Member States (decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to an applicant established in the EU.

The centralized procedure provides for the grant of a single MA by the European Commission that is valid throughout the EEA (which is comprised of the 27 Member States of the European Union plus Norway, Iceland and Liechtenstein). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for: (i) medicinal products derived from biotechnological processes, (ii) products designated as orphan medicinal products, (iii) advanced therapy medicinal products (ATMPs) (gene therapy, somatic-cell therapy and tissue engineered medicines), and (iv) products with a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of public health at the EU level, authorization through the centralized procedure is optional.

Under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use (CHMP), conducts the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA.

Under the centralized procedure, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanations are to be provided by the applicant in response to questions of the CHMP. Accelerated assessment may be granted by the CHMP in exceptional cases, when a medicinal product targeting an unmet medical need is expected to be of major interest from a public health perspective and, in particular, from the viewpoint of therapeutic innovation. If the CHMP accepts a request for accelerated assessment, the time limit of 210 days will be reduced to 150 days (excluding clock stops). The CHMP can, however, revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Unlike the centralized authorization procedure, the decentralized MA procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is substantially similar to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment report and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the Heads of Medicines Agencies' Coordination Group for Mutual Recognition and Decentralised Procedures—Human (CMDh), for review. If the CMDh cannot resolve the matter, the reference EU Member State may refer the matter to the CHMP for arbitration.

The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States. Like the decentralized procedure, the mutual recognition procedure is based on the acceptance by the competent authorities of the EU Member States of the MA of a medicinal product by the competent authorities of other EU Member States. The holder of a national MA may submit an application to the competent authority of an EU Member State requesting that this authority recognize the MA delivered by the competent authority of another EU Member State.

An MA in the EU has, in principle, an initial validity of five years. The MA may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or the competent authority of the EU Member State in which the original MA was granted. To support the application, the MA holder must provide the EMA or the competent authority with a consolidated version of the eCTD (Common Technical Document) providing up-to-date data concerning the quality, safety and efficacy of the product, including all variations introduced since the MA was granted, at least nine months before the MA ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide on justified grounds relating to pharmacovigilance to proceed with one further five-year renewal period for the MA. Once subsequently definitively renewed, the MA shall be valid for an unlimited period. Any authorization that is not followed by the actual placing of the medicinal product on the EU market (for a centralized MA) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIority MEdicines (PRIME) scheme, which provides incentives broadly similar to the Breakthrough Therapy designation in the U.S. PRIME is a voluntary scheme aimed at enhancing the EMA's support for the development of medicinal products that target unmet medical needs. Eligible products must target conditions for which there is an unmet medical need (there is no satisfactory method of diagnosis, prevention or treatment in the EU or, if there is, the new medicinal product will bring a major therapeutic advantage) and they must demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Benefits accrue to sponsors of drug candidates with PRIME

designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and potentially accelerated MAA assessment once a dossier has been submitted.

In the EU, a conditional MA may be granted in cases where all the required safety and efficacy data are not yet available. The European Commission may grant a conditional MA for a medicinal product if it is demonstrated that all of the following criteria are met: (i) the benefit-risk balance of the medicinal product is positive; (ii) it is likely that the applicant will be able to provide comprehensive data post-authorization; (iii) the medicinal product fulfils an unmet medical need; and (iv) the benefit of the immediate availability to patients of the medicinal product is greater than the risk inherent in the fact that additional data are still required. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and must be renewed annually until all related conditions have been fulfilled. Once such conditions have been fulfilled, the conditional MA may be converted into a standard MA. However, if the conditions are not fulfilled within the timeframe set by the EMA and approved by the European Commission, the MA will cease to be renewed.

An MA may also be granted "under exceptional circumstances" where the applicant can show that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. These circumstances may arise in particular when the intended indications are very rare and, in the state of scientific knowledge at that time, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. Like a conditional MA, an MA granted in exceptional circumstances is reserved for medicinal products intended for the treatment of rare diseases or unmet medical needs for which the applicant does not hold a complete data set that is required for the grant of a standard MA. However, unlike the conditional MA, an applicant for authorization in exceptional circumstances is not subsequently required to provide the missing data. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually, and the MA will be withdrawn if the risk-benefit ratio is no longer favorable.

Manufacturing regulation in the EU

Various requirements apply to the manufacturing and placing on the EU market of medicinal products. The manufacturing of medicinal products in the EU requires a manufacturing authorization, and the import of medicinal products into the EU requires a manufacturing authorization that permits importation. The manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including EU good manufacturing practice (GMP) standards. Similarly, the distribution of medicinal products within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate distribution authorizations granted by the competent authorities of EU Member States. MA holders, manufacturing and import authorization (MIA) holders and/or distribution authorization holders may be subject to civil, criminal or administrative sanctions, including suspension or revocation of any manufacturing authorization, in the event of non-compliance with the EU or EU Member States' requirements applicable to the manufacturing of medicinal products.

Post-approval requirements

Where an MA is granted in relation to a medicinal product in the EU, the holder of the MA is required to comply with a range of regulatory requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and/or the competent regulatory authorities of the individual EU Member States. The holder of an MA must establish and maintain a pharmacovigilance system and appoint a qualified person responsible for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (PSURs).

All new MAAs must include a risk management plan (RMP), describing the risk management system that we will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as conditions of the MA. Such risk-minimization measures or post-authorization obligations may include additional safety monitoring requirements, more frequent submission of PSURs, or the conduct of additional clinical trials or post-authorization safety studies.

In the EU, the advertising and promotion of medicinal products are subject to both EU and EU Member States' laws governing promotion of medicinal products, interactions with physicians and other healthcare professionals, misleading and comparative advertising and unfair commercial practices. Although general requirements for advertising and promotion of medicinal products are established under EU legislation, the details are governed by regulations in individual EU Member States and can differ from one country

to another. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics (SmPC), as approved by the competent authorities in connection with an MA. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU. Direct-to-consumer advertising of prescription medicinal products is also prohibited in the EU.

Data and marketing exclusivity

The EU also provides opportunities for regulatory data and market exclusivity. Upon receiving an MA in the EU, innovative medicinal products generally receive eight years of data exclusivity followed by an additional two years of market exclusivity. If granted, data exclusivity prevents generic or biosimilar applicants from referencing the innovator's preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA during a period of eight years from the date on which the reference product was first authorized in the EU. During the additional two-year period of market exclusivity, a generic or biosimilar MA can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity period. The overall ten-year period may be extended to a maximum of eleven years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to authorization, is considered to bring a significant clinical benefit in comparison with existing therapies.

In the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product. For such products, the results of appropriate preclinical or clinical trials must be provided in support of an application for MA. Guidelines from the EMA detail the type and quantity of supplementary data to be provided for different types of biological products.

Pediatric development

In the EU, Regulation (EC) No 1901/2006 provides that all marketing authorization applications for new medicinal products must include the results of trials conducted in the pediatric population, in compliance with a pediatric investigation plan (PIP), agreed with the EMA's Pediatric Committee (PDCO). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the medicinal product for which an MA is being sought. The PDCO may grant a deferral of the obligation to implement some or all of the measures provided in the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Furthermore, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once an MA is obtained and study results are included in the product information, even when negative, the product is eligible for a six-month extension to the Supplementary Protection Certificate (SPC), provided an application for such extension is made at the time of filing the SPC application for the product, or at any point up to two years before the SPC expires. The incentive in the case of orphan medicinal products is that a two-year extension of orphan market exclusivity may be available (but no extension to an SPC is available in the case of orphan medicinal products).

Orphan designation

In the EU, Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a medicinal product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish that: (i) the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition; (ii) either (a) such condition affects not more than 5 in 10,000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in developing the medicinal product; and (iii) there exists no satisfactory authorized method of diagnosis, prevention, or treatment of the condition that has been authorized in the EU, or even if such method exists, the product will be of significant benefit to those affected by that condition.

Regulation (EC) No 847/2000 sets out further provisions for the implementation of the criteria for designation of a medicinal product as an orphan medicinal product. An application for the designation of a medicinal product as an orphan medicinal product must be submitted at any stage of development of the medicinal product but before filing of an MAA. An MA for an orphan medicinal product may only include indications designated as orphan. For non-orphan indications treated with the same active pharmaceutical ingredient, a separate MA has to be sought.

Orphan medicinal product designation entitles an applicant to incentives such as fee reductions or fee waivers, protocol assistance, and access to the centralized marketing authorization procedure. Upon grant of a MA, orphan medicinal products are entitled to a ten-year period of market exclusivity for the approved therapeutic indication, which means that the EMA and national competent authorities cannot accept another MAA or an application to extend an MA, and the European Commission cannot grant an MA, in each case for a similar medicinal product for the same indication for such ten-year period. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed PIP. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan medicinal product designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The period of market exclusivity may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria on the basis of which it received orphan medicinal product designation, including where it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, an MA may be granted to a similar medicinal product with the same orphan indication during the ten-year exclusivity period if: (i) the MA holder for the authorized orphan product consents to a second medicinal product application, (ii) the manufacturer of the authorized orphan medicinal product is unable to supply sufficient quantities of the product; or (iii) the second applicant can establish that its product, although similar to an authorized orphan product, is safer, more effective or otherwise clinically superior to the authorized orphan medicinal product. A company may voluntarily remove a product from the register of orphan products.

Clinical trial data disclosure

Many jurisdictions have mandatory clinical trial information obligations incumbent on sponsors. In the EU, transparency requirements relating to clinical trial information are established in the CTR. The CTR establishes a general principle according to which information contained in CTIS shall be made publicly accessible unless confidentiality is justified on grounds of protecting personal data, or commercially confidential information, or is necessary to protect confidential communications between EU Member States in relation to the preparation of an assessment report, or to ensure effective supervision of the conduct of a clinical trial by EU Member States. This confidentiality exception may be overruled if there is an overriding public interest in disclosure. The publication of data and documents in relation to the conduct of a clinical trial will take place in accordance with specific timelines. The timelines are established by the EMA and are determined based on the documents and the categorization of the clinical trial.

In addition, Regulation (EC) No- 1049/2001 on access to documents, and the related EMA policy 0043 on access to documents, provide for a right for interested parties to submit an access to documents request to the EMA to access certain information held by the EMA. Certain limited categories of information are exempted from disclosure (i.e., commercially confidential information, which is construed increasingly narrowly and protected personal data). It is possible for competitors to access and use this data in their own research and development programs anywhere in the world, once these data are in the public domain.

Pricing, coverage and reimbursement

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Other countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies (so called health technology assessments) in order to obtain reimbursement or pricing approval. For example, some EU Member States may approve a specific price for a product, or they may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many EU Member States have increased the amount of discounts that pharmaceutical companies are required to offer. These efforts could continue as countries attempt to manage healthcare expenditures. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products onto national markets. Political, economic, and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various EU Member States, and parallel trade (arbitrage between low-priced and high-priced EU Member States), can further reduce prices.

In addition, some EU Member States may require the completion of additional studies that compare the cost-effectiveness of a particular medicinal drug candidate to currently available therapies. This Health Technology Assessment (HTA) process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding

specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The Regulation No 2021/2282 on Health Technology Assessment (HTA Regulation) was adopted in December 2021 and became applicable on January 12, 2025, with phased implementation. The HTA Regulation is intended to boost cooperation among EU Member States in assessing health technologies, including by introducing joint clinical assessments of new medicinal products. The new rules under the HTA Regulation will be introduced in stages, with joint clinical assessments initially applying to new cancer medicines or advanced therapy medicinal products, and ultimately being extended to all medicinal products authorized under the EU centralized procedure.

Regulation of Companion Diagnostics in the EU

In the EU, companion diagnostics are considered to be *in vitro* diagnostic medical devices (IVDs) and are governed by Regulation 2017/746 (IVDR), which entered into application in May 2022, repealing and replacing Directive 98/79/EC. The IVDR defines companion diagnostics as a device that is essential for the safe and effective use of a corresponding medicinal product to: (a) identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or (b) identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product.

The IVDR regulates the placing on the market, the general safety and performance requirements, the conformity assessment procedures, CE-marking and registration obligations for manufacturers and devices, as well as the vigilance and post-market surveillance requirements related to such products. IVDs, including companion diagnostics, must conform with the general safety and performance requirements (GSPR) of the IVDR. To demonstrate compliance with the GSPR laid down in Annex I to the IVDR, the manufacturer must conduct a conformity assessment procedure.

Companion diagnostics are specifically identified as falling within the scope of the IVDR. Prior to CE marking and marketing in the EU they must be the subject of a conformity assessment process that includes the intervention of a notified body. If the related medicinal product has been authorized, or is in the process of being authorized, through the centralized procedure for the authorization of medicinal products, the notified body will, before it can issue a CE Certificate of Conformity, be required to seek a scientific opinion from the EMA on the suitability of the companion diagnostic for use in relation to the medicinal product concerned. For medicinal products that have been or are in the process of authorization through any other route provided in EU legislation, the notified body must seek the opinion of the relevant national competent authority of an EU Member State.

All of the aforementioned EU rules are generally applicable in the EEA.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the EU for all medicines (including those for rare diseases and for children). In April 2024, European Parliament adopted its position on the legislative proposals and in June 2025, the Council of the European Union adopted its position. A common position on the text has been agreed upon December 11, 2025, in the context of subsequent inter-institutional trilogue negotiations. The proposed revisions remain to be adopted, and are not expected to become applicable before 2028.

Regulatory Framework in the United Kingdom

Following the end of the Brexit transition period on January 1, 2021 and the implementation of elements of the Windsor Framework from January 1, 2025, the United Kingdom, or UK, is not generally subject to EU laws in respect of medicines regulation. EU laws that have been transposed into UK law through secondary legislation remain applicable in the UK; however, new EU legislation such as the Clinical Trials Regulation (EU) No 536/2014 is not applicable in the UK. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or MHRA, is the UK's standalone medicines and medical devices regulator. As a result of the Northern Ireland Protocol, different rules applied in Northern Ireland than in England, Wales, and Scotland (together, "Great Britain," or GB) for a period following Brexit, with Northern Ireland continuing to follow certain aspects of the EU regulatory regime. However, on January 1, 2025 a new arrangement called the "Windsor Framework" came into effect and largely reintegrated Northern Ireland under the regulatory authority of the MHRA with respect to medicinal products placed on the UK market. The Windsor Framework removes EU licensing processes and certain EU labeling and serialization requirements in relation to medicinal products supplied to Northern Ireland under the UK-only scheme and introduces a UK-wide licensing process for medicines. In particular, the MHRA is responsible for approving medicinal products placed on the UK market (i.e., Great Britain and Northern Ireland), and the EMA no longer has a role in UK marketing authorizations. A single UK-wide MA may be granted by the MHRA for medicinal products to be sold in the UK, enabling

products to be sold in a single pack and under a single authorization throughout the UK. In addition, the new arrangements require, for certain packs placed on the UK market on or after January 1, 2025, a "UK Only" label, indicating they are not for sale in the EU. However, although separate authorization is now required to market medicinal products in the UK, since January 1, 2024, the MHRA may apply the International Recognition Procedure, or IRP, when reviewing certain types of MAAs. Pursuant to the IRP, the MHRA will take into account the expertise and decision-making of trusted regulatory partners (e.g. the medicines regulatory authorities in Australia, Canada, Switzerland, Singapore, Japan, the U.S.A. and the EMA in the EU) when assessing an application for a UK marketing authorization.

The MHRA has also been updating various aspects of the regulatory regime for medicinal products in the United Kingdom. These include: introducing the Innovative Licensing and Access Pathway to accelerate the time to market and facilitate patient access for innovative medicinal products; updates to the UK national approval procedure, introducing a 150-day target for assessing applications for MAs in the United Kingdom and a rolling review process for MA applications (rather than a consolidated full dossier submission).

Orphan designation in the United Kingdom is, unlike in the EU, not available prior to marketing authorization. Applications for orphan designation are made at the same time as an application for an MA. The criteria to be granted an orphan medicinal product designation are essentially identical to those in the EU but based on the prevalence of the condition in the United Kingdom.

The existing UK regulatory framework in relation to clinical trials is derived from the EU Clinical Trials Directive 2001/20/EC (as implemented into UK law, through secondary legislation). In April 2025, the UK government introduced the Medicines for Human Use (Clinical Trials) (Amendment) Regulations. Such legislation aims to provide a more flexible regime to make it easier to conduct clinical trials in the UK and increase the transparency of clinical trials conducted in the UK. This includes a notification scheme to enable lower-risk clinical trials to be automatically approved by the MHRA, where the risk is similar to that of standard medical care (although such trials would still require ethics committee approval). These changes will take full effect from April 2026 and aim to create a streamlined, risk-proportionate system that accelerates approvals while maintaining robust safety standards.

Ex-EU Regulatory Framework

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we or our potential collaborators fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Employees and human capital resources

As of December 31, 2025, we had a total of 16 full-time employees. Additionally, we utilize independent contractors and other third parties to assist with various aspects of our drug and product development as well as certain general and administrative functions. We are not a party to any collective bargaining agreements.

We recognize that our continued ability to attract, retain and motivate exceptional employees is vital to ensuring our long-term competitive advantage. Our employees are critical to our long-term success and are essential to helping us meet our goals. Among other things, we support and incentivize our employees in the following ways:

- Talent development, compensation and retention—We strive to provide our employees with a rewarding work environment, including the opportunity for success and a platform for personal and professional development. We provide a competitive benefits package designed to attract and retain a skilled and diverse workforce. We also offer employees a 401(k) plan.

- Health and safety—Employee health and safety in the workplace is one of our core values. One of the ways in which we support the health and safety of our employees includes a generous health insurance program.

- Inclusion and diversity—We are committed to efforts to increase diversity and foster an inclusive work environment that supports our workforce. We are an equal opportunity employer and strictly prohibit and do not tolerate discrimination against

employees, including based on race, creed, color, religion, national origin, citizenship status, age, gender, military and veteran status and sexual orientation. We also prohibit any form of harassment or abuse in the workplace.

Corporate Information

We were incorporated in Delaware in December 2006 under the name 3-V Biosciences, Inc., and changed our name to Sagimet Biosciences Inc. in August 2019. Our principal executive offices are located at 155 Bovet Road, Suite 303, San Mateo, California 94402, and our telephone number is (650) 561-8600.

Our website address is www.sagimet.com. On our Investor Relations website, ir.sagimet.com/investor-relations, we make available free of charge a variety of information for investors, including our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports, as soon as reasonably practicable after we electronically file that material with or furnish it to the Securities and Exchange Commission (the SEC). Information contained on, or that can be accessed through, our website is not incorporated by reference into this Annual Report or any other report we file with, or furnish to, the SEC, and the inclusion of our website address in this Annual Report is only an inactive textual reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Item 1A. Risk Factors

Investing in our Series A common stock involves a high degree of risk. You should consider and read carefully all of the risks and uncertainties described below, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes appearing elsewhere in this Annual Report and "Management's Discussion and Analysis of Financial Condition and Results of Operations". The following risks or additional risks and uncertainties not presently known to us or that we currently believe to be immaterial could materially and adversely affect our business, financial condition, results of operations and growth prospects.

This Annual Report on Form 10-K also contains forward-looking statements and estimates that involve risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. Our actual results could differ materially from those anticipated in our forward-looking statements as a result of specific factors, including the risks and uncertainties described below.

Risk Factors Summary

- We have incurred significant operating losses since our inception and we expect to incur significant operating losses for the foreseeable future. We may never become profitable or, if profitability is achieved, be able to sustain profitability.
- We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.
- Currently our business depends on the success of our lead drug candidate, denifanstat, which is still in clinical development. If we are unable to obtain regulatory approval for or successfully commercialize denifanstat, our business will be materially harmed.
- If we encounter difficulties enrolling patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. If clinical trials or regulatory approval processes for our drug candidates are prolonged, delayed or suspended, we may be unable to seek regulatory approval for and commercialize our drug candidates on a timely basis, which would require us to incur additional costs and substantially harm our business.
- We may not be successful in our efforts to expand our pipeline, including by identifying additional indications for which to investigate denifanstat or TVB-3567 in the future. We may expend our limited resources to pursue a particular indication or formulation for denifanstat or TVB-3567, or a combination with denifanstat or TVB-3567 and another molecule, and fail to capitalize on drug candidates, indications or formulations that may be more profitable or for which there is a greater likelihood of success.
- We have conducted, are currently conducting, and may in the future conduct clinical trials for our drug candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.
- Interim, top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- We intend to develop certain of our drug candidates in combination with other approved and investigational therapies, which exposes us to additional risks.
- If we or third parties are unable to successfully develop technologies or establish tests for biomarkers that enable patient selection or monitoring for drug responses, or if we experience significant delays in doing so, we may not realize the full commercial potential of our drug candidates.
- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.
- Obtaining and maintaining regulatory approval for a drug candidate in one jurisdiction does not mean that we will be successful in obtaining regulatory approval for that drug candidate in other jurisdictions.
- We may not be able to file INDs or IND amendments, or comparable foreign applications, to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or comparable foreign regulatory authorities may not permit us to proceed.
- Use of denifanstat, TVB-3567 or any future drug candidates, or the use of our drug candidates in combination with other molecules, could be associated with side effects, adverse events or other properties that could delay or prevent regulatory approval or result in significant negative consequences following marketing approval, if any.
- Although we have received Breakthrough Therapy designation for denifanstat for the treatment of non-cirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), this may not lead to a faster development,

regulatory review or approval process, and it does not increase the likelihood of receiving marketing approval in the United States.

- We have received Fast Track designation for denifanstat for F-2-F3 MASH and may seek such designation for our other drug candidates or for other indications, but we might not receive such designations, and even if we do, such designations may not actually lead to a faster development or regulatory review or approval process.
- Our drug candidates will remain subject to ongoing regulatory review even if they receive marketing approval, and if we fail to comply with continuing regulations, we could lose these approvals and the sale of any approved commercial products could be suspended.
- Our industry is highly competitive, and our drug candidates may become obsolete.
- We may attempt to seek approval from the FDA for one or more of our drug candidates through the use of the accelerated approval pathway. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw any accelerated approval we have obtained.
- Our employees, contractors and partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.
- If we fail to develop and commercialize other drug candidates, we may be unable to grow our business.
- If we are unable to successfully validate, develop and obtain regulatory approval for diagnostic tests for certain of our drug candidates that would commercially benefit from such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these drug candidates.
- We may engage in strategic transactions that could increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, subject us to other risks, adversely affect our liquidity, increase our expenses and present significant distractions to our management.
- If we are unable to obtain, maintain and enforce sufficient patent protection for our drug candidates, or if the scope of the patent protection is not sufficiently broad, third parties, including our competitors, could develop and commercialize products similar or identical to ours, and our ability to commercialize our drug candidates successfully may be adversely affected.
- We may not be able to enforce our intellectual property rights throughout the world.
- We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.
- We have licensed rights to denifanstat to Ascletis, for a territory that we refer to as "Greater China" throughout this Annual Report. Under the license agreement, Ascletis controls certain product development efforts in its territory, including conduct of clinical trials, which could have an impact on our clinical development programs.
- We rely on third parties to conduct our clinical trials of our drug candidates and expect to rely on third parties to conduct future clinical trials, as well as investigator-sponsored clinical trials of our drug candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.
- We have relied on, and we expect to continue to rely on, third-party manufacturers to produce our drug candidates. Our manufacturers may experience manufacturing difficulties due to the ongoing effects of inflationary pressures, resource constraints, labor disputes or unstable political environments, which could delay the completion of our clinical trials, increase the costs associated with maintaining clinical trial programs and, significantly impact our ability to develop, obtain regulatory approval for, or market denifanstat, TVB-3567 and any future drug candidates, or any combinations of our drug candidates and any other molecule.
- We currently have no marketing and sales organization and have no organizational experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell denifanstat, TVB-3567 and any future drug candidates, we may not be able to generate product revenues.
- A drug candidate may not achieve adequate market acceptance among physicians, patients, third-party payors and others in the medical community necessary for commercial success.
- Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.
- Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.
- Unfavorable global political or economic conditions could adversely affect our business, financial condition or results of operations.

Risks related to our business

We have incurred significant operating losses since our inception, and we expect to incur significant operating losses for the foreseeable future. We may never become profitable or, if profitability is achieved, be able to sustain profitability.

We have incurred significant operating losses since our inception, and we expect to incur significant operating losses for the foreseeable future as we continue our clinical trials and development programs for denifanstat, TVB-3567 and other future drug candidates. Our net losses were $51.0 million and $45.6 million for the years ended December 31, 2025 and 2024, respectively. We had cash, cash equivalents and marketable securities of $113.1 million and $158.7 million as of December 31, 2025, and 2024, respectively. In the future, we intend to continue to conduct research and development, preclinical and clinical testing, regulatory compliance and, if denifanstat, TVB-3567 or other future drug candidates or combination therapies are approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in the incurrence of further significant operating losses for the foreseeable future.

As an organization, we have not yet demonstrated an ability to successfully complete clinical development, obtain regulatory approvals, manufacture a commercial-scale product, or conduct sales and marketing activities necessary for successful commercialization. We have no products approved for commercial sale and have not generated any commercial revenue to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred significant net losses since our inception. We may never be able to commercialize denifanstat, TVB-3567 or other future drug candidates or combination therapies.

We may not be profitable even if we or any of our future development partners succeed in commercializing any of our drug candidates. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our preclinical and clinical development of, and seek regulatory approvals for, denifanstat, TVB-3567 and any future drug candidates or combination therapies. We may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior net losses and expected future net losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Because of the numerous risks and uncertainties associated with drug development, we are unable to accurately predict the timing or amount of increased expenses, or when, if at all, we will be able to achieve profitability.

We will require substantial additional capital to finance our operations. If we are unable to raise such capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate one or more of our research and drug development programs or future commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. Our operations have consumed substantial amounts of cash since our inception. We expect to continue to spend substantial amounts to continue the preclinical and clinical development of, and seek regulatory approval for, denifanstat and any future drug candidates.

Because the design and outcome of our planned and anticipated preclinical studies and clinical trials are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of denifanstat, TVB-3567, or any other drug candidate or combination therapy we develop. If we are required by the FDA, or any comparable foreign regulatory authority to perform clinical trials or preclinical studies in addition to those that we currently anticipate, our expenses could increase. In addition, if we obtain regulatory approval to market denifanstat, TVB-3567, or any other drug candidates or combination therapies, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Other unanticipated costs may also arise.

Since our initial public offering (IPO) of Series A common stock in July 2023, we also have incurred, and expect to continue to incur, additional costs associated with operating as a public company. Accordingly, we will continue to need to obtain substantial additional funding in order to maintain our continuing operations.

To date, we have financed our operations primarily through public and private equity and debt financings, including our IPO of Series A common stock in July 2023 and our follow-on offering in January 2024, from which we received aggregate net proceeds of $190.9 million.

We currently have no outstanding debt obligations. We have incurred net losses and negative cash flows from operations since inception, including net losses of $51.0 million and $45.6 million for the years ended December 31, 2025 and 2024, respectively. For the years ended December 31, 2025, and 2024, we had negative cash flows from operations of $45.7 million and $42.4 million, respectively. We had cash, cash equivalents and marketable securities of $113.1 million and $158.7 million as of December 31, 2025 and 2024, respectively. We expect to incur additional losses and negative cash flows from operations for at least the next 12 months. Based on our current operating plan, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2025, will be sufficient for us to fund our operating expenses for at least the next 12 months from the issuance of this Annual Report.

Our estimate as to how long we expect our current cash, cash equivalents and marketable securities to be able to continue to fund our operating expenses and capital expenditures requirements is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Moreover, it is particularly difficult to estimate with certainty our future expenses given the dynamic nature of our business, global economic conditions and volatility in the credit and financial markets, inflationary pressures, the Russian invasion of Ukraine, the conflict in Israel and other geopolitical conditions. Our current cash, cash equivalents and marketable securities will not be sufficient to fund all of the activities that are necessary to complete the development and commercialization of our drug candidates.

Until we can generate significant revenue from sales of our drug candidates, if ever, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources, which may dilute our stockholders or restrict our operating activities. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research-stage programs, clinical trials or future commercialization efforts.

Currently our business depends on the success of our lead drug candidate, denifanstat, which is still in clinical development. If we are unable to obtain regulatory approval for or successfully commercialize denifanstat, our business will be materially harmed.

Currently, our product development is primarily focused on our lead drug candidate, denifanstat, for the potential treatment of MASH, formerly known as NASH. Successful continued development and ultimate regulatory approval of denifanstat for MASH, or other indications that we may pursue, is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in the preclinical and clinical development of denifanstat. We will need to raise sufficient funds to successfully complete the development program for denifanstat. The future regulatory and commercial success of denifanstat is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for denifanstat, including registrational clinical trials to obtain regulatory approval;
- the mechanism of action of denifanstat is complex and we do not know the degree to which it will translate into a therapeutic benefit, if any, in MASH or any other indication or to which it may contribute to long term safety issues or AEs, if any, when denifanstat is taken for prolonged periods such as in the treatment of MASH, or any other indication;
- patients in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to denifanstat, and there may be more uncertainty regarding relatedness to denifanstat if we pursue clinical trials of denifanstat in combination with other drugs or drug candidates, and this uncertainty could delay or prevent further clinical development;
- we may not be able to obtain adequate evidence from clinical trials of efficacy and safety for denifanstat, or denifanstat in combination with another molecule, in MASH, or any other indication;
- in our clinical programs for denifanstat, we may experience variability in patients, adjustments to clinical trial procedures and the need for additional clinical trial sites, which could delay our clinical trial progress;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for marketing approval;
- the standards implemented by clinical or regulatory authorities may change at any time;

- the FDA or comparable foreign regulatory authority may require efficacy endpoints for rials for the treatment of MASH, or any other indication, that differ from the endpoints of our current or future trials, which may require us to conduct additional clinical trials;

- we do not know the degree to which denifanstat, or any combination therapy including denifanstat, will be accepted as a therapy by physicians, patients and third-party payors, even if approved;

- if approved for MASH, denifanstat will likely compete with the off-label use of any marketed drugs and other therapies in development that may reach approval for MASH prior to denifanstat; and

- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights in a manner that prevents our competitors from developing and commercializing products similar or identical to denifanstat or that otherwise compete with denifanstat.

Of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a new drug application (NDA) to the FDA and even fewer are approved for commercialization. Furthermore, even if we receive regulatory approval to market denifanstat, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the drug. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development program for denifanstat, we may be unable to successfully develop or commercialize denifanstat. If we or any of our future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize denifanstat, we may not be able to generate sufficient revenue to continue our business.

If we encounter difficulties enrolling patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trials until their conclusion. We may not be able to initiate, continue, or complete clinical trials that may be required by the FDA or comparable foreign regulatory authorities to obtain regulatory approval for denifanstat or any other future drug candidates if we are unable to locate, enroll and retain a sufficient number of eligible patients to participate in these clinical trials. Patient enrollment, a significant factor in the timing to conduct and complete clinical trials, is affected by many factors, including:

- the size and nature of the patient population;

- the severity of the disease under investigation;

- eligibility criteria for the trial;

- the proximity of patients to clinical sites;

- the number and location of clinical sites we activate;

- the design of the clinical protocol;

- the ability to obtain and maintain patient consents;

- the ability to recruit clinical trial investigators with the appropriate competencies and experience;

- the risk that patients enrolled in clinical trials will drop out of the trials before the administration of our drug candidates or trial completion;

- the availability of competing clinical trials;

- the availability of new drugs approved for the indication the clinical trial is investigating;

- clinicians' and patients' awareness of the clinical trials and perceptions as to the potential advantages of the drug being studied in relation to other available therapies; and

- other factors outside of our control, such as the effects of any future pandemics, global economic conditions and volatility in the credit and financial markets, inflationary pressures, and geopolitical conflicts.

In certain of our proposed MASH clinical trials, patient willingness to undergo a liver biopsy, particularly for trials of a longer duration, may also impact patient enrollment and retention. Potential patients for denifanstat, TVB-3567 or any other future drug candidates or any combination treatment may not be adequately diagnosed or identified with the indications that we are targeting or may not meet the entry criteria for our trials.

We also may encounter difficulties in identifying and enrolling MASH patients with a stage of disease appropriate for ongoing or future clinical trials. In addition, the process of finding and diagnosing patients may prove costly. Other pharmaceutical companies with more resources and greater experience in drug development and commercialization are targeting treatments for MASH, and this competition reduces the number and types of patients available to us, as some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Because the number of qualified clinical investigators and clinical trial sites is also limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial sites, and may delay or make it more difficult to fully enroll our clinical trials. We also rely on contract research organizations (CROs) and clinical trial sites to enroll subjects in our clinical trials and, while we have agreements governing their services, we will have limited influence over their actual performance.

These factors may make it difficult for us to enroll enough patients to complete our clinical trials in a timely and cost-effective manner. Delays in the completion of any clinical trials of our drug candidates will increase our costs, slow down our drug candidate development and approval process and delay or potentially jeopardize our ability to commence product sales and generate revenue. In addition, some of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our drug candidates.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. If clinical trials or regulatory approval processes for our drug candidates are prolonged, delayed or suspended, we may be unable to seek regulatory approval for and commercialize our drug candidates on a timely basis, which would require us to incur additional costs and substantially harm our business.

Drug development has inherent risk. We will be required to demonstrate through adequate and well-controlled clinical trials that our drug candidates are safe and effective for use in their target indications before we can seek regulatory approvals for their commercial sale. Clinical studies are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. Delay or failure can occur at any stage of development, including after commencement of any of our clinical trials. In addition, success in early clinical trials does not mean that later clinical trials will be successful, because later-stage clinical trials may be conducted in broader patient populations and involve different study designs. For instance, the results from our Phase 1 PK trial of a combination of denifanstat and THR-β agonist, resmetirom may not be predictive of the results from our planned Phase 2 combination proof-of-concept efficacy trial for patients living with MASH with F4 fibrosis or any potential future Phase 3 clinical trials. Furthermore, our future trials will need to demonstrate sufficient safety and efficacy in larger patient populations for approval by regulatory authorities. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In addition, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

We cannot predict whether we will encounter problems with any completed, ongoing or planned clinical trials that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation or continuation of clinical trials. For example, carcinogenicity and reproductive toxicology studies may be required to support late-stage clinical trials and/or approval;

- reaching a consensus with regulatory authorities on study design or implementation of the clinical trials;

- difficulties obtaining regulatory authorization to commence a clinical trial or complying with conditions imposed by a regulatory authority regarding the scope or term of a clinical trial;
- reaching or failing to reach agreement on acceptable terms with prospective CROs, contract manufacturing organizations (CMOs), and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly;
- identifying, recruiting and training suitable clinical investigators;
- insufficient or inadequate supply or quality of our drug candidates or other materials necessary to conduct and complete our clinical trials, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- manufacturing, testing, releasing, validating or importing/exporting sufficient stable quantities of our drug candidates for use in clinical trials;
- difficulties obtaining institutional review board (IRB) approval or positive ethics committee opinions to conduct a clinical trial at a prospective site;
- recruiting, screening and enrolling patients and delays caused by patients withdrawing from clinical trials or failing to return for post-treatment follow-up;
- changes to the clinical trial protocols;
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines;
- serious and unexpected side effects related to the drug candidate being tested;
- lack of adequate funding to continue the clinical trial;
- severe adverse effects in clinical trials of the same class of agents conducted by other companies;
- changes in the standard of care on which a clinical development plan was based, which may require new or additional trials;
- selection of clinical endpoints that require prolonged periods of observation or analyses of resulting data;
- failure of our third-party vendors to perform manufacturing and distribution services in a timely manner or to sufficient quality standards;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practice (GCP), or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; and
- failure of our third-party contractors, such as CROs and CMOs, or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner.

We cannot be certain whether our clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, if at all. Delays in the initiation, enrollment, or completion of our clinical trials will result in increased development costs for our drug candidates, and our financial resources may be insufficient to fund any incremental costs. If our clinical trials are delayed, our competitors may be able to bring products to market before we do and the commercial viability of our drug candidates could be limited.

Additionally, our clinical trials have used and our planned clinical trials may utilize an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates when studied in a controlled environment with a placebo or active control.

In addition, disruptions caused by any future pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting, or completing our planned and ongoing clinical trials. For example, we previously experienced delays in enrollment and temporary closures of clinical trial sites due to COVID-19. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs or relevant ethics committees of the institutions in which such trials are being conducted or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols or informed consents, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs, relevant ethics committees or competent authorities for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

Further, conducting clinical trials in foreign countries, as our licensee, Ascletis, and its affiliate Gannex Pharma Co., Ltd. (Gannex), to whom Ascletis has assigned the license, are doing for denifanstat in China, and as we may continue to do in the future for our drug candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory frameworks, as well as political and economic risks relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve and have served as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the results from the trial. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of our drug candidates.

We may not be successful in our efforts to expand our pipeline, including by identifying additional indications for which to investigate denifanstat or TVB-3567 in the future. We may expend our limited resources to pursue a particular indication or formulation for denifanstat or TVB-3567, or a combination with denifanstat or TVB-3567 and another molecule, and fail to capitalize on other drug candidates, indications or formulations that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we are currently focused on developing denifanstat for MASH and TVB-3567 in acne. We have also identified other potential indications where fatty acid synthase (FASN) inhibition could have clinical benefit, including oncology. However, we may fail to generate additional clinical development opportunities for denifanstat, TVB-3567 or the other molecules in our catalog of FASN inhibitors for a number of reasons, including because denifanstat or TVB-3567 may in certain indications, or on further study, be shown to have harmful side effects, limited to no efficacy, or other characteristics that decrease the product candidate's likelihood to receive marketing approval and achieve market acceptance in such additional indications.

We plan to conduct several clinical trials for denifanstat and TVB-3567 in parallel over the next several years. If we make incorrect determinations regarding the viability or market potential of denifanstat, TVB-3567 or any of our other drug candidates or combination therapies or misread trends in MASH, acne or in the pharmaceutical, biopharmaceutical or biotechnology industry, our business, financial condition and results of operations could be materially adversely affected. As a result, we may forgo or delay pursuit of

opportunities with other indications that could have had greater commercial potential or likelihood of success. For example, we may focus on or pursue one or more of our target indications over other potential indications and such development efforts may not be successful, which would cause us to delay the clinical development and approval of denifanstat. Furthermore, research programs to identify additional indications for denifanstat and TVB-3567 require substantial technical, financial, and human resources. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for specific indications may not yield any commercially viable products.

We have conducted, are currently conducting, and may in the future conduct clinical trials for our drug candidates outside the United States, and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We have conducted and may in the future conduct one or more clinical trials of our current or future drug candidates outside the United States. For example, we conducted a cohort of our FASCINATE-1 clinical trial in China and are conducting a portion of our Phase 1 clinical trial of TVB-3567 in Australia. The acceptance of study data from clinical trials conducted outside the United States or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical power, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the United States or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, we would need to conduct additional trials, which could be costly and time-consuming.

Interim, top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also may make assumptions, estimations, calculations and conclusions as part of our analyses of preliminary or topline data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our Series A common stock.

Others, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure. If the interim, top-line, or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our drug candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

We intend to develop certain of our drug candidates in combination with other approved and investigational therapies, which exposes us to additional risks.

We intend to develop certain of our drug candidates in combination with one or more other approved therapies. For example, we conducted a Phase 1 PK clinical trial of a combination of denifanstat and a thyroid hormone receptor beta (THR-β) agonist, resmetirom, for development in MASH.

Our ability to develop and ultimately commercialize our drug candidates in combination with other therapies will depend on our ability to access such therapies on commercially reasonable terms for the clinical trials and their availability for use with our drug candidate. We cannot be certain that current or potential future commercial relationships will provide us with a steady supply of such therapies on commercially reasonable terms or at all.

Any failure to maintain or enter into new successful commercial relationships or the expense of purchasing these therapies may delay our development timelines, increase our costs and jeopardize our ability to develop our current drug candidates. If any of these circumstances occur, our business, financial condition, operating results, stock price and prospects may be materially harmed.

Moreover, the development of drug candidates for use in combination with another therapy may present challenges that are not faced for single agent drug candidates. The FDA or comparable foreign regulatory authorities may require us to use more complex clinical trial designs in order to evaluate the contribution of each drug candidate or therapy to any observed effects. It is possible that the results of such trials could show that any positive trial results are attributable to the other therapy and not our current drug candidates.

Even if any drug candidate we develop were to receive regulatory approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or comparable foreign regulatory authorities outside of the United States could revoke or amend approval of the therapy used in combination with our product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies we use in combination with our drug candidates are replaced as the standard of care for the indications we choose for any of our drug candidates, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

We also may choose to evaluate our current drug candidates and any other future drug candidates in combination with one or more therapies that have not yet been approved for marketing by the FDA or comparable foreign regulatory authorities. We will not be able to market and sell our current drug candidates or any future drug candidates we develop in combination with any unapproved therapies for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved therapies face the same risks described with respect to our drug candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

If the FDA or comparable foreign regulatory authorities do not approve these other products or revoke or amend their approval, or if safety, efficacy, quality, manufacturing or supply issues arise with the products we choose to evaluate in combination with our drug candidate, we may be unable to obtain approval of or market such combination therapy.

If we or third parties are unable to successfully develop technologies or establish tests for biomarkers that enable patient selection or monitoring for drug responses, or if we experience significant delays in doing so, we may not realize the full commercial potential of our drug candidates.

A key component of our strategy includes the use of biomarkers to inform patient selection for and/or to confirm responses to our drug candidates. In some cases, third parties provide this technology. It is not always the case, however, that the biomarker we have identified is on a standard panel offered by testing providers. If not already commercially available, we may collaborate with testing providers for the development of biomarker tests associated with our drug candidates. We may have difficulty in establishing or maintaining such development relationships, and we will face competition from other companies in establishing these collaborations.

There are also several risks associated with biomarker identification and validation. We, in collaboration with any testing providers, may not be able to identify predictive biomarkers or pharmacodynamic biomarkers for one or more of our programs. We may not be able to validate potential biomarkers or their functional relevance preclinically in relevant *in vitro* or *in vivo* models. Data analytics and information from databases that we rely on for identifying or validating some of our biomarker-target relationships may not accurately reflect potential patient populations. Potential biomarkers, even if validated preclinically, may not be functionally effective or validated in human clinical trials.

If testing providers experience any delays including the biomarkers we have identified for patient selection and/or drug response monitoring on their panels or tests, or if they do not include those biomarkers on their panels or tests, our clinical trials may be delayed

or may not identify sufficient patients to complete the trial, and our drug candidates may not advance to approval or realize their full commercial potential.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our drug candidates, our business will be substantially harmed.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a drug candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any of our drug candidates, and it is possible that any drug candidates we may seek to develop in the future will never obtain regulatory approval. Neither we nor any future collaborator is permitted to market any of our drug candidates in the United States until we receive regulatory approval of an NDA from the FDA. The FDA and other regulatory authorities may delay, limit or deny approval of our drug candidates for many reasons, including:

- we may not be able to demonstrate to the satisfaction of the FDA or other regulatory authorities that denifanstat, TVB-3567 or any of our other future drug candidates are safe and effective for any indication or for combination therapies;
- the results of clinical trials may not meet the level of statistical significance or clinical significance required by the FDA or other regulatory authorities for approval;
- the FDA or other regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials;
- the FDA or other regulatory authorities may not find the data from preclinical studies and clinical trials sufficient to demonstrate that the benefits of denifanstat, TVB-3567 or any of our other future drug candidates outweigh their safety risks;
- the FDA or other regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials, or may not accept data generated at our clinical trial sites;
- the data collected from preclinical studies and clinical trials of denifanstat, TVB-3567 or any of our other future drug candidates or combination therapies may not be sufficient to support the submission of an NDA or other application for regulatory approval;
- the FDA may have difficulties scheduling an advisory committee meeting in a timely manner, or the advisory committee may recommend against approval of our application or may recommend that the FDA require as a condition of approval, additional preclinical studies or clinical trials, limitations on approved labeling, or distribution and use restrictions;
- the FDA or other regulatory authorities may require development of a risk evaluation and mitigation strategy (REMS), or risk management plan (RMP), as a condition of approval;
- the FDA or other regulatory authorities may identify deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we enter into agreements for clinical and commercial supplies;
- the FDA or other regulatory authorities may change their approval policies or adopt new regulations; and
- the FDA or other regulatory authorities may require simultaneous approval for both adults and for children and adolescents, which may delay approval, or we may have successful clinical trial results for adults but not children and adolescents, or vice versa.

In addition, any of these regulatory authorities may change requirements for the approval of a drug candidate even after reviewing and providing comments or advice on a protocol for a clinical trial. The FDA or other regulatory authorities may require that we conduct additional clinical, preclinical, manufacturing validation or drug product quality studies and submit those data before considering or reconsidering the application. Depending on the extent of these or any other studies, approval of any applications that we submit may

be delayed by several years or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA or other regulatory authorities for obtaining approval.

In addition, the FDA or other regulatory authorities may approve a drug candidate for fewer or more limited indications than we request, may impose significant limitations related to use restrictions for certain age groups, warnings, precautions or contraindications or may grant approval contingent on the performance of costly post-marketing clinical trials or risk mitigation requirements, such as the implementation of a REMS or comparable foreign risk management approaches. The FDA or other regulatory authorities may not accept the labeling claims that we believe would be necessary or desirable for the successful commercialization of our drug candidates.

Obtaining and maintaining regulatory approval for a drug candidate in one jurisdiction does not mean that we will be successful in obtaining regulatory approval for that drug candidate in other jurisdictions.

Obtaining and maintaining regulatory approval for a drug candidate in one jurisdiction does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval for a drug candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the drug candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical trials conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a drug candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for denifanstat or any of our other future drug candidates is also subject to approval.

Regulatory authorities in jurisdictions outside of the United States and the European Union also have requirements for approval for drug candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of denifanstat or any of our other future drug candidates in certain countries. If we fail to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of denifanstat or any of our other future drug candidates will be harmed, which would adversely affect our business, prospects, financial condition, and results of operations.

We may not be able to file INDs or IND amendments, or comparable foreign applications, to commence additional clinical trials on the timelines we expect, and even if we are able to, the FDA or comparable foreign regulatory authorities may not permit us to proceed.

We may not be able to file Investigational New Drug applications (INDs), or comparable foreign applications, for our drug candidates on the timelines we expect. For example, we may experience manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND, or comparable foreign applications, will result in the FDA or other regulatory authorities allowing clinical trials to begin, or that, once begun, issues will not arise that result in the suspension, termination, or clinical hold of the clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND, or comparable foreign applications, we cannot guarantee that such regulatory authorities will not change their requirements in the future. These considerations also apply to new clinical trials we may submit as amendments to existing INDs or to a new IND or comparable foreign applications. Any failure to file INDs, or comparable foreign applications, or submit our clinical trial protocols to regulatory authorities for review on the timelines we expect may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

Use of denifanstat, TVB-3567 or any future drug candidates, or the use of our drug candidates in combination with other molecules, could be associated with side effects, adverse events or other properties that could delay or prevent regulatory approval or result in significant negative consequences following marketing approval, if any.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and AEs associated with the use of denifanstat, TVB-3567 or any future drug candidates or combination therapies. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. For example, in our oncology Phase 1 clinical trial, six episodes of serious pneumonitis were experienced by five patients, one of which was fatal, assessed by the investigator as at least possibly related to both denifanstat and paclitaxel. No SAEs assessed as drug-related have been reported in our MASH trials to date. Undesirable side effects caused by denifanstat, TVB-3567 and any future drug candidates could cause us or regulatory authorities to

interrupt, delay or halt clinical trials, including issuing a clinical hold, and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. If drug-related SAEs are observed, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval for denifanstat, TVB-3567 or any of our other future drug candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition, and prospects significantly.

Over 1,200 subjects have been treated with denifanstat in our clinical trials to date. It is possible that as we test our drug candidates in larger, longer and more extensive clinical trials, illnesses, injuries, discomforts and other AEs that were observed in previous trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by patients. In many cases, side effects are only detectable after investigational products are tested in large-scale clinical trials or, in some cases, after they are made available to patients on a commercial scale following approval.

Additionally, if denifanstat, TVB-3567 or any future candidate or combination therapy receives marketing approval, and we or others later identify undesirable side effects caused by such drug candidates, a number of potentially significant negative consequences could result, including:

- we may be forced to suspend marketing of that product, or decide to remove the product from the marketplace;
- regulatory authorities may withdraw approvals or change their approvals of such product, or seek an injunction against its manufacture or distribution;
- regulatory authorities may require additional warnings on the label, including boxed warnings, issue safety alerts or press releases, or limit access to that product;
- we may be required to create a REMS, which could include a medication guide outlining the risks of such side effects for distribution to patients and other elements to assure safe use, or comparable foreign risk management approaches;
- we may be required to change the way the product is administered;
- we could be subject to fines, injunctions, or the imposition of criminal or civil penalties, or be sued and held liable for harm caused to subjects or patients; and
- the product may become less competitive, and our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of denifanstat, TVB-3567 or any future drug candidates or combination therapies, if approved, and could significantly harm our business, results of operations, and prospects.

Although we have received Breakthrough Therapy designation for denifanstat for the treatment of non-cirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis), this may not lead to a faster development, regulatory review or approval process, and it does not increase the likelihood of receiving marketing approval in the United States.

In October 2024, the FDA granted Breakthrough Therapy designation to denifanstat for the treatment of non-cirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis). A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, interactions and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies designated as breakthrough therapies by the FDA may also be eligible for rolling review, priority review and accelerated approval.

The Breakthrough Therapy designation we have obtained for denifanstat may not result in faster development processes, reviews or approvals compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, the FDA may later decide that our denifanstat development program no longer meets the criteria for the designation and may rescind the designation.

We have received Fast Track designation for denifanstat for F2-F3 MASH and may seek such designation for our other drug candidates or for other indications, but we might not receive such designations, and even if we do, such designations may not actually lead to a faster development or regulatory review or approval process.

If a drug candidate is intended for the treatment of a serious or life-threatening condition and preclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a product sponsor may apply for FDA Fast Track designation. The sponsor of a Fast Track drug candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the drug candidate may be eligible for priority review if the relevant criteria are met. A fast track drug candidate may also be eligible for rolling review, where the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. In March 2021, we received Fast Track designation for denifanstat for the treatment of MASH and we may seek Fast Track designation for certain other indications for denifanstat or any future drug candidates we may develop, but we might not receive such designations from the FDA. However, even if we receive Fast Track designation, Fast Track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with Fast Track designation compared to conventional FDA procedures. In addition, the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast Track designation alone does not guarantee qualification for the FDA's priority review procedures. The European Medicines Agency (EMA) has a similar program called the PRIority MEdicines (PRIME) scheme. The purpose of this program is to enhance support for the development of medicinal products that target an unmet medical need. PRIME provides enhanced interaction and early dialogue between the EMA and developers of promising medicinal products to optimize generation of robust data on the benefits and risks of a medicinal product and may enable accelerated assessment of marketing authorization applications. Participation in PRIME does not, however, limit the obligations that must be fulfilled for the grant of a related marketing authorization. We may seek PRIME designation for one or more of our drug candidates, but might not receive such designations. Even if we receive PRIME designation, there is no guarantee of grant of marketing authorization at all or within any specific timeframe.

Our drug candidates will remain subject to ongoing regulatory review even if they receive marketing approval, and if we fail to comply with continuing regulations, we could lose these approvals and the sale of any approved commercial products could be suspended.

Any regulatory approvals that we may receive for our drug candidates will require the submission of reports to regulatory authorities and surveillance to monitor the safety and efficacy of the drug candidate, may contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, and may include burdensome post-approval study or risk management requirements. For example, the FDA may require a REMS in order to approve our drug candidates, which could entail requirements for a medication guide, physician training and communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA or foreign regulatory authorities approve our drug candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export, sampling and recordkeeping for our drug candidates will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, on-going compliance with GCP for any clinical trials that we conduct post-approval, and product tracking and tracing requirements.

Further, the FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for their approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on companies' communications regarding off-label use, and if we market our products for uses beyond their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDCA relating to the promotion of prescription drugs may lead to FDA enforcement actions and investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other domestic and foreign regulatory authorities for compliance with current good manufacturing practice (cGMP), regulations and standards. If we or a regulatory authority discover previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facilities where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with the regulatory requirements of the FDA and other applicable domestic and foreign regulatory authorities, or if previously unknown problems with any approved product, manufacturer, or manufacturing process are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on the marketing or manufacturing of our products;
- revisions to the labeling, including limitation on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings;
- imposition of a REMS, or comparable foreign risk management approaches, which may include distribution or use restrictions;
- requirements to conduct additional post-marketing clinical trials to assess the safety of the product;
- civil or criminal penalties;
- fines, warning letters or holds on clinical trials;
- injunctions;
- product seizures or detentions;
- product recalls;
- suspension, modification or withdrawal of regulatory approvals; and
- refusal by the FDA or other domestic or foreign regulatory authorities to approve pending applications for marketing approval of new products or supplements to approved applications.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our drug candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad, and compliance with such regulation may be expensive and consume substantial financial and management resources. If we or any future marketing collaborators or CMOs are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies or are not able to maintain regulatory compliance, it could delay or prevent the promotion, marketing or sale of our products, which would adversely affect our business and results of operations.

Changes in the manufacturing process or formulation may result in additional costs or delay.

As drug candidates progress through preclinical studies and clinical trials to marketing approval and commercialization, it is common that various aspects of the manufacturing program, such as methods and formulation, are altered along the way in an effort to optimize yield and manufacturing batch size, minimize costs and achieve consistent quality and results. Such changes carry the risk that they will not achieve these intended objectives. Any such changes could cause our drug candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials, and limit our ability to rely on data from clinical trials conducted with an earlier version of our drug candidate. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our drug candidates and jeopardize our ability to commercialize our drug candidates, if approved, and generate revenue. If we or our CMOs are not able to successfully manufacture our drug candidates in sufficient quality and quantity, clinical development and timelines for our drug candidates and subsequent approval could be adversely impacted.

Changes in funding for the FDA and other domestic and foreign government authorities could hinder their ability to hire and retain key leadership and other personnel, or otherwise prevent new products and services from being developed or commercialized in a timely manner, which could negatively impact our business.

The ability of the FDA and other domestic and foreign government authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel, accept the payment of user fees, and statutory, regulatory, leadership and policy changes. Average review times at the agency have fluctuated recently. In addition, government funding of other government authorities that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other domestic and foreign authorities may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government authorities, which would adversely affect our business. For example, the U.S. government has shut down several times and certain regulatory authorities, such as the FDA, have had to furlough critical FDA employees and stop critical activities. Our business depends upon the ability of the FDA to accept and review our potential regulatory filings. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our ability to advance clinical development of our drug candidates. Further, future shutdowns of other government authorities, such as the U.S. Securities and Exchange Commission (SEC), may also impact our business through review of our public filings and our ability to access the public markets.

Our industry is highly competitive, and our drug candidates may become obsolete.

We are engaged in a rapidly evolving field. Competition from other pharmaceutical companies, biotechnology companies and research and academic institutions is intense and likely to increase. Many of those companies and institutions have substantially greater financial, technical and human resources than we have. Those companies and institutions also have substantially greater experience in developing products, conducting clinical trials, obtaining regulatory approval and in manufacturing and marketing pharmaceutical products. Our competitors may succeed in obtaining regulatory approval for their products more rapidly than we do. Competitors have developed or are in the process of developing technologies that are, or in the future may be, the basis for competitive products. Some of these competitive products may have an entirely different approach or means of accomplishing the desired therapeutic effect than products being developed by us. Our competitors may succeed in developing products that are more effective and/or cost competitive than those we are developing, or that would render our drug candidates less competitive or even obsolete.

In addition, one or more of our competitors may achieve product commercialization or patent protection earlier than us, which could materially adversely affect our business. For example, Madrigal Pharmaceuticals, Inc. (Madrigal) announced the approval of Rezdiffra (resmetirom) for the treatment of MASH in patients with moderate to advanced liver fibrosis by the FDA in March 2024 and the European Commission in August 2025. In August 2025, Novo Nordisk A/S announced the FDA approved Wegovy (semaglutide) for the treatment of MASH in adult patients with moderate to advanced liver fibrosis.

If denifanstat is approved for the treatment of MASH, future competition could also arise from products currently in development with multinational pharmaceutical companies, specialized biotechnology companies and universities and other research institutions, including Altimmune, Inc., AstraZeneca, Boehringer Ingelheim and Zealand Pharma, Eli Lilly and Company, Galmed Pharmaceuticals Ltd., Gilead Sciences, Inc., GSK plc (acquired Boston Pharmaceuticals in 2025), Inventiva S.A., Madrigal, Merck & Co., Inc., Novo Nordisk A/S (acquired Akero Therapeutics, Inc. in 2025), Pfizer Inc., Roche Holdings, Inc. (acquired 89bio, Inc. in 2025), Terns Pharmaceuticals, Inc., Viking Therapeutics, Inc., and Zydus Therapeutics Inc. Smaller or earlier- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. It is also probable that the number of companies seeking to develop drugs and therapies for the treatment of serious metabolic diseases, such as MASH, will increase.

We also face significant competition in the acne therapeutics market, which is highly competitive and characterized by a wide range of prescription and over-the-counter products. Current acne treatments include topical therapies, oral systemic therapies and procedural or device-based approaches, and are prescribed based on disease severity, patient characteristics, physician judgment and treatment guidelines. Topical therapies are commonly used as first-line treatment for mild to moderate acne and include topical retinoids, antibiotics, benzoyl peroxide, hormonal agents and fixed-dose combination products. Many topical acne treatments are available as low-cost generics, and branded products compete primarily on formulation characteristics, tolerability, dosing convenience and physician familiarity. Oral systemic therapies are generally prescribed for moderate to severe acne or for patients who do not respond adequately to topical treatments. Oral therapies include antibiotics, hormonal agents and oral isotretinoin. While oral isotretinoin is highly effective for cystic acne, its use is limited by significant safety considerations, monitoring requirements and prescribing restrictions. Oral

antibiotics are widely used but are generally recommended for limited duration due to concerns related to antibiotic resistance and adverse effects.

In addition, several companies are developing investigational acne therapies, including novel oral agents, new topical formulations and reformulations or combinations of existing drugs. These product candidates are at varying stages of development and may compete with our acne product candidate, including TVB-3567, if approved. The availability of numerous established, lower-cost generic therapies and evolving standards of care in dermatology may make it more difficult for us to differentiate our product candidates, achieve market acceptance, obtain favorable pricing or secure adequate reimbursement. If we are unable to compete effectively in the acne market, whether due to safety, efficacy, cost, convenience, physician prescribing patterns or other factors, our business, financial condition and results of operations could be materially adversely affected.

Recently enacted legislation, future legislation and healthcare reform measures may increase the difficulty and cost for us to obtain marketing approval for and commercialize denifanstat and any future drug candidates and may affect the prices we may set.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any drug candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of legislative and executive initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For a detailed discussion, see the section of this report titled, "Business—Government regulation and product approval—Healthcare reform."

For example, the Inflation Reduction Act's (IRA's) drug price negotiation provisions, inflation rebates, and Medicare Part D discount requirements, along with recently proposed most-favored-nation pricing models issued by the Centers for Medicare and Medicaid Services, could significantly impact our ability to obtain adequate pricing for our product candidates. Although the IRA exempts orphan drugs from drug price negotiation provisions, we do not know if additional drug pricing reforms could eliminate or narrow this exemption. These provisions are subject to ongoing legal challenges, and their ultimate implementation and impact remain uncertain. Additionally, the One Big Beautiful Bill Act's reductions in Medicaid funding, work requirements, and reenrollment requirements could decrease utilization of, and reimbursement for, our products, if approved.

We cannot predict the likelihood, nature, or extent of healthcare reform initiatives that may arise from future legislation or administrative action. We expect that healthcare reform measures, including those that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from third-party payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize denifanstat or our other drug candidates, if approved.

We may attempt to seek approval from the FDA for one or more of our drug candidates through the use of the accelerated approval pathway. If we are unable to obtain such approval, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals. Even if we receive accelerated approval from the FDA, if our confirmatory trials do not verify clinical benefit, or if we do not comply with rigorous post-marketing requirements, the FDA may seek to withdraw any accelerated approval we have obtained.

We may in the future seek an accelerated approval for one or more of our drug candidates. Under the accelerated approval pathway, the FDA may grant accelerated approval to a drug candidate designed to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies, upon a determination that the drug candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective.

If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit and, under the Food and Drug Omnibus Reform Act of 2022 (FDORA), the FDA is permitted to require, that such studies be underway prior to approval or within a specified time period after the date accelerated approval is granted. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. In addition, FDORA gives the FDA increased authority to withdraw accelerated approval on an expedited basis if, for example, the sponsor fails to conduct such studies in a timely manner, such studies fail to confirm the drug's clinical benefit, or the sponsor fails to send the necessary updates to the FDA. The FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. In addition, the FDA generally requires, unless otherwise informed by the agency, pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product.

Prior to seeking accelerated approval for any of our drug candidates, we intend to seek feedback from the FDA and will otherwise evaluate our ability to seek and receive accelerated approval. There can be no assurance that after our evaluation of the feedback and other factors we will decide to pursue or submit an NDA seeking accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that after subsequent FDA feedback we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or receive an expedited regulatory designation (e.g., Fast Track designation) for our drug candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. The FDA or other comparable foreign regulatory authorities could also require us to conduct further studies prior to considering our application or granting approval of any type. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our drug candidates would result in a longer time period to commercialization of such drug candidate, if any, could increase the cost of development of such drug candidate, and could harm our competitive position in the marketplace.

In addition, the policies of the FDA and other comparable regulatory authorities with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the European Union has evolved. The EU Clinical Trials Regulation (CTR), which was adopted in April 2014 and repealed the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR allows sponsors to make a single submission through the centralized EU portal (the Clinical Trials Information System) to apply for authorization of the clinical trial in all applicable EU Member States. The assessment procedure for the authorization of clinical trials has been harmonized as well, including a joint assessment by all EU Member States concerned, and a separate assessment by each EU Member State with respect to specific requirements related to its own territory, including ethics rules. Each EU Member State's decision is communicated to the sponsor via the centralized EU portal. Once the clinical trial has been approved, clinical study development may proceed. All new applications for clinical trial authorization in the EU must be made under the CTR and, as of January 31, 2025, all ongoing trials previously authorized under the EU Clinical Trials Directive became subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our development plans.

The existing UK regulatory framework in relation to clinical trials is derived from the EU Clinical Trials Directive. However, on December 12, 2024, the UK government introduced a legislative proposal - the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2024 - that, if implemented, will replace the current regulatory framework for clinical trials in the UK. The legislative proposal aims to provide a more flexible regime to make it easier to conduct clinical trials in the UK and increase the transparency of clinical trials conducted in the UK. This includes a notification scheme to enable lower-risk clinical trials to be automatically approved by the MHRA, where the risk is similar to that of standard medical care (although such trials would still require ethics committee approval). Such Regulations are expected to come into force in early 2026. Compliance with new regulations for clinical trials in the UK could impact our development plans or have an effect on the cost of any trials we intend to conduct in the UK.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

If any product liability lawsuits are brought against us or any of our collaborative partners, we may incur substantial liabilities and may be required to limit commercialization of our drug candidates.

We face an inherent risk of product liability lawsuits related to the testing of our drug candidates in seriously ill patients and will face an even greater risk if drug candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us or our partners by participants enrolled in our clinical trials, patients, healthcare providers or others using,

administering or selling any of our future approved products. If we cannot successfully defend against any such claims, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any of our future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs;
- substantial monetary awards to or costly settlements with patients or other claimants;
- product recalls or a change in the indications for which products may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our drug candidates.

If any of our drug candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of our company and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to patients. In addition, because of our dependence upon consumer perceptions, any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our results of operations.

We do not currently hold commercial product liability insurance coverage. Prior to commercialization of our drug candidates, we will need to purchase insurance coverage. As a result, we may be unable to maintain or obtain sufficient insurance at a reasonable cost to protect us against losses that could have a material adverse effect on our business. These liabilities could prevent or interfere with our product development and commercialization efforts. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our available insurance coverage, could decrease our cash resources and adversely affect our business, financial condition and results of operations.

Our employees, contractors and partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud or other misconduct by our employees, contractors or partners. Misconduct by these parties could include failures to comply with FDA regulations or comparable foreign regulations, to provide accurate information to the FDA or comparable foreign authorities, to comply with federal, state or foreign healthcare fraud and abuse laws and regulations, to report financial information or data timely, completely or accurately, or to disclose unauthorized activities to us, or failure to comply with comparable foreign requirements. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Third-party misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us resulting from this misconduct and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement,

imprisonment, FDA debarment, exclusion from government funded healthcare programs, such as Medicare and Medicaid or comparable foreign equivalents, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our potential sublicensees' exercise of rights under the agreement. With respect to our commercial agreements, we indemnify our vendors from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we were denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage, and if the collaborator does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

If we fail to develop and commercialize other drug candidates, we may be unable to grow our business.

Although the development and commercialization of denifanstat is our primary focus, as part of our longer-term growth strategy, we plan to evaluate the development and commercialization of other therapies related to MASH, FASN inhibition, and other diseases mediated by overproduction of palmitate, including acne and some forms of cancer. We will evaluate internal opportunities from our compound libraries, and also may choose to in-license or acquire other drug candidates as well as commercial products to treat patients suffering from MASH or other disorders with high unmet medical needs and limited treatment options. These other drug candidates may require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All drug candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the drug candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot be certain that any such products that are approved will be manufactured or produced economically, be successfully commercialized, be widely accepted in the marketplace, or be more effective than other commercially available alternatives.

If we are unable to successfully validate, develop and obtain regulatory approval for diagnostic tests for certain of our drug candidates that would commercially benefit from such tests, or experience significant delays in doing so, we may not realize the full commercial potential of these drug candidates.

In connection with the clinical development of certain of our drug candidates for certain indications, we may engage third parties to develop or otherwise obtain access to in vitro complementary diagnostic tests to identify patients within a disease category who may derive meaningful benefit from our drug candidates. Such complementary diagnostics may be used during our clinical trials as well as in connection with the commercialization of our products that receive regulatory approval. To be successful, we or our collaborators will need to address a number of scientific, technical, regulatory and logistical challenges. The FDA and comparable foreign regulatory authorities regulate in vitro complementary diagnostics as medical devices and, under that regulatory framework, will likely require the conduct of clinical trials to demonstrate the safety and effectiveness of any diagnostics we or third parties may develop, which we expect will require separate regulatory clearance or approval prior to commercialization of such diagnostics.

We intend to rely on third parties for the design, development and manufacture of such complementary diagnostic tests for our drug candidates. If we enter into such collaborative agreements, we will be dependent on the sustained cooperation and effort of our future collaborators in developing and obtaining approval for these complementary diagnostics. It may be necessary to resolve issues such as selectivity/specificity, analytical validation, reproducibility, or clinical validation of complementary diagnostics during the development and regulatory approval processes. Moreover, even if data from preclinical studies and early clinical trials appear to support development of a complementary diagnostic for a drug candidate, data generated in later clinical trials may fail to support the analytical and clinical validation of the complementary diagnostic. We and our future collaborators may encounter difficulties in developing, obtaining regulatory clearance or approval for, manufacturing and commercializing complementary diagnostics similar to those we face

with respect to our drug candidates themselves, including issues with achieving regulatory clearance or approval, production of sufficient quantities at commercial scale and with appropriate quality standards, and in gaining market acceptance. If we are unable to successfully develop complementary diagnostics for these drug candidates, or experience delays in doing so, the development and commercialization of these drug candidates may be adversely affected, these drug candidates may not obtain regulatory approval, and we may not realize the full commercial potential of any of these products that obtain regulatory approval. As a result, our business, results of operations and financial condition could be materially harmed. In addition, a diagnostic company with whom we contract may decide to discontinue selling or manufacturing the complementary diagnostic test that we anticipate using in connection with development and commercialization of our drug candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our drug candidates or do so on commercially reasonable terms.

We may engage in strategic transactions that could increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities, subject us to other risks, adversely affect our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as mergers, acquisitions, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. We may not be able to find suitable partners or acquisition candidates, and we may not be able to complete such transactions on favorable terms, if at all. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our Series A common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of our management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the full benefits. Furthermore, we may experience losses related to investments in other companies, including as a result of failure to realize expected benefits or the materialization of unexpected liabilities or risks, which could have a material negative effect on our results of operations and financial condition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

Any pandemic, epidemic, or outbreak of an infectious disease may materially and adversely affect our business and our financial results and could cause a disruption to the development of our drug candidates.

Public health crises, such as pandemics or similar outbreaks, could adversely impact our business. For example, the impact of the COVID-19 pandemic resulted in disruptions to the global economy, as well as businesses and capital markets around the world. We experienced modest delays in our development activities as a result of the COVID-19 pandemic, primarily due to temporary closures of certain clinical sites that delayed patient enrollment in our FASCINATE-2 trial. Any future pandemic, epidemic or outbreak of an infectious disease could have similar effects. Furthermore, economic recessions, increased inflation and/or interest rates, and any disruptions to our operations or workforce availability may have a negative effect on our operating results. The foregoing and other disruptions to our business as a result of a public health crisis could result in an adverse effect on our business, results of operations, financial condition and cash flows.

Risks related to intellectual property

If we are unable to obtain, maintain and enforce sufficient patent protection for our drug candidates, or if the scope of the patent protection is not sufficiently broad, third parties, including our competitors, could develop and commercialize products similar or identical to ours, and our ability to commercialize our drug candidates successfully may be adversely affected.

Our success depends in large part on our ability to protect our proprietary technologies that we believe are important to our business, including pursuing and maintaining patent protection intended to cover the composition of matter of our drug candidates, including denifanstat, their methods of use, related technologies and other inventions that are important to our business. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our technologies and drug candidates that are important to our business. In addition to patent protection, we also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection, including our proprietary platform of selective FASN

inhibitors. If we do not adequately obtain, maintain, protect or enforce our intellectual property, third parties, including our competitors, may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability.

The patent application and approval process is expensive, time-consuming and complex. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. The standards applied by the United States Patent and Trademark Office (the USPTO) and foreign patent offices in granting patents are not always applied uniformly or predictably. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Thus, we cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents, whether any issued patents will be found invalid and unenforceable or will be threatened by third parties or whether any issued patents will effectively prevent others from commercializing competing technologies and drug candidates.

Our pending patent applications may not result in issued patents if other parties invented or filed patent applications on the same technology prior to our invention or filing of patent applications on our technology.

Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. Because patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to our drug candidates. Further, in cases where a particular compound of interest is in the public domain, third parties may be able to obtain patents on improvements or other inventions relating to such compound if they were to discover the same patentable inventions relating to such compounds after us but manage to file a patent application before we do. In addition, we may enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development output, including any polymorphs and variants, such as our employees, collaborators, consultants, advisors and other third parties; however, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to obtain patent protection. Furthermore, if third parties have filed patent applications related to our drug candidates or technology, an interference proceeding in the United States can be initiated by the USPTO or a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

We cannot ensure that patent rights relating to inventions described and claimed in our pending patent applications will issue, or that our issued patents or patents that issue in the future will not be challenged and rendered invalid and/or unenforceable.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our drug candidates by obtaining and defending patents. We have pending and issued U.S. and foreign patents and patent applications in our portfolio; however, we cannot predict:

- if and when patents may issue based on our patent applications;
- the scope of protection of any patent issuing based on our patent applications;
- whether the claims of any issued patent will provide protection against competitors;
- whether or not third parties will find ways to invalidate or circumvent our patent rights;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications;
- whether we will need to initiate litigation or administrative proceedings to enforce and/or defend our patent rights which will be costly whether we win or lose; and/or

- whether the patent applications will result in issued patents with claims that cover each of our drug candidates or uses thereof in the United States or in other foreign countries.

We may be subject to a third-party pre-issuance submission of prior art to the USPTO or become involved in post-grant review procedures, oppositions, derivations, revocation, reexaminations, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such challenge may result in loss of exclusivity or in our patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products or limit the duration of the patent protection of our technology and products. Such challenges also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations, and prospects. Furthermore, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates.

We may rely on more than one patent to provide multiple layers of patent protection for our drug candidates. If the latest-expiring patent is invalidated or held unenforceable, in whole or in part, the overall protection for the drug candidate may be adversely affected. For example, if the latest-expiring patent is invalidated, the overall patent term for our drug candidate, denifanstat, could be adversely affected.

Our pending and future patent applications may not result in patents being issued that protect our drug candidates, in whole or in part, or which effectively prevent others from commercializing competitive products.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, our patents protecting such drug candidates might expire before or shortly after such drug candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Our competitors and other third parties may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors or other third parties may seek to market generic or biosimilar versions of any approved products and in so doing, claim that patents owned by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or may find that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

Moreover, some of our patents may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co-owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

Our patents may be subject to a reservation of rights by one or more third parties.

If any of our technologies are developed in the future with government funding, the government may obtain certain rights in any resulting patents, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf. If the U.S. government then decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. These rights may also permit the government to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use our licensed technology. The government may also exercise its march-in rights if it determines that action is necessary because we failed to achieve practical application of the government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such government-funded inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any exercise by the government of aforementioned proprietary rights could harm our competitive position, business, financial condition, results of operations, and prospects.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. Recent patent reform legislation in the United States and other countries, including the Leahy-Smith America Invents Act (Leahy-Smith Act), signed into law in September 2011, could increase those uncertainties and costs and it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and increase the uncertainties and costs surrounding the prosecution of our or our collaboration partners' patent applications and the enforcement or defense of our or our collaboration partners' issued patents, all of which could harm our business, results of operations, financial condition and prospects.

The U.S. Supreme Court and the Court of Appeals for the Federal Circuit (the Federal Circuit) have ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. For example, with respect to patent term adjustment, the Federal Circuit's recent holding in *In re Cellect, LLC,* 81 F.4th 1216 (Fed. Cir. 2023), that obviousness-type double patenting analysis for a patent that has received patent term adjustment must be based on the expiration date of the patent after the patent term adjustment has been added, which may negatively impact the term of certain U.S. patents. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For a description of the intellectual property regulatory framework, see "Business—Intellectual property."

We may become involved in lawsuits or administrative disputes to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents, trademarks, copyrights, trade secrets or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents or their intellectual property, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from manufacturing and selling the competing product at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover said product. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our Series A common stock.

Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Furthermore, third parties may also raise invalidity or unenforceability claims before administrative bodies in the United States or comparable foreign authorities, even outside the context of litigation. Such mechanisms include re-examination, *inter partes* review, post-grant review, interference proceedings, derivation proceedings and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation, cancellation or amendment to our patents in such a way that they no longer cover and protect our drug candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our licensors, our patent counsel and the patent examiner were unaware during prosecution. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our drug candidates. Any such loss of patent protection could have a material adverse impact on our business, financial condition, results of operations and prospects.

We may not be able to enforce our intellectual property rights throughout the world.

Filing, prosecuting and defending patents with respect to our drug candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. The requirements for patentability may differ in certain countries, particularly in developing countries. Consequently, competitors and other third parties may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we may obtain patent protection, but where patent enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued or licensed patents or where any future patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing with us.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and several developing countries, do not favor the enforcement of patents and other intellectual property rights, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement, misappropriation or other violation of our patents or other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. In addition, many countries limit the enforceability of patents against government authorities or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

We may not identify relevant third-party patents or may incorrectly interpret the relevance, scope or expiration of a third-party patent, which might adversely affect our ability to develop and market our products.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our drug candidates in any jurisdiction.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect. For example, we may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third-party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States

or abroad that we consider relevant may be incorrect. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

If we are sued for infringing, misappropriating or otherwise violating intellectual property rights of third parties, such litigation or disputes could be costly and time consuming and could prevent or delay us from developing or commercializing our drug candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our drug candidates without infringing, misappropriating or otherwise violating the intellectual property and other proprietary rights of third parties. If any third-party patents or patent applications are found to cover our drug candidates or their methods of use or manufacturing, we may be required to pay damages, which could be substantial, and we would not be free to manufacture or market our drug candidates without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our drug candidates. Third parties may assert infringement, misappropriation or other claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation and other disputes is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of using or manufacturing products. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our drug candidates, products or methods of use, manufacturing or other applicable activities either do not infringe the patent claims of the asserted patent or that the patent claims are invalid or unenforceable, and we may not be successful in doing so. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity that applies to all issued patents. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, or enforceability. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe, misappropriate or otherwise violate a third party's intellectual property rights and we are unsuccessful in demonstrating that such intellectual property rights are invalid or unenforceable, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing drug candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing drug candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our drug candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties, particularly from our competitors currently developing products for the treatment of MASH, could have a similar negative impact on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees or consultants or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property, or we may need to bring similar claims against third parties.

Some of our employees and consultants are currently or have been previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. These employees and consultants may have executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such other current or previous employment. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of third parties. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be

a distraction to our management. Any of the foregoing would have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. In addition, such agreements may not be self-executing such that the intellectual property subject to such agreements may not be assigned to us without additional assignments being executed, and we may fail to obtain such assignments. In addition, such agreements may be breached. Accordingly, we may be forced to bring claims against third parties, or defend claims that they may bring against us, related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our collaborators may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing our drug candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of our patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our drug candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

The term of our patents may be inadequate to protect our competitive position on our products.

Patent rights are of limited duration. In the United States, if all maintenance fees are paid timely, the natural expiration of a patent is generally 20 years after its first effective filing date. Upon issuance in the United States, the term of a patent can be increased by patent term adjustment, which is based on certain delays caused by the USPTO, but this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. The term of a United States patent may also be shortened if the patent is terminally disclaimed over an earlier-filed patent. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Depending upon the timing, duration and other factors relating to any FDA marketing approval we receive for any of our drug candidates, one or more of our U.S. patents may be eligible for limited patent term extension (PTE), under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments). We plan to seek PTE in the United States, however, only a single patent can be extended for each marketing approval, and any patent can be extended only once, for a single product. Moreover, the scope of protection during the period of the PTE does not extend to the full scope of the claim, but instead only to the scope of the product as approved. We also plan to see analogous forms of PTE in other countries where we are prosecuting patents. However, the laws governing analogous PTEs in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Additionally, we may not receive an extension if we fail to exercise due diligence during the testing phase or regulatory review process. If we are unable to obtain PTE or the term of any such extension is less than we request, our competitors and other third parties may be able to obtain approval of competing products following our patent expiration and take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Any of the foregoing would have a material adverse effect on our business, financial condition, results of operations and prospects. For more information about obtaining extensions, see “Business—Intellectual property.”

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent offices, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of the patent. The USPTO and patent offices in foreign countries require compliance with a number of procedural, documentary, fee payment and other requirements during the patent application process. While an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result

in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors and other third parties might be able to enter the market with similar or identical products of technology, which would have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our trade secrets and proprietary know-how, the value of our technology could be materially adversely affected, and our business would be harmed.

While we have obtained composition of matter patents with respect to certain of our drug candidates, including denifanstat, we also rely on proprietary know-how and trade secret protection and confidentiality agreements to protect proprietary know-how or trade secrets that are not patentable or that we elect not to patent. For example, we may elect to not patent some composition matter from our proprietary library of selective FASN inhibitors and therefore rely on protecting the proprietary aspects of our platform as a trade secret. We seek to protect our trade secrets and proprietary know-how in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, advisors, CMOs, suppliers, collaborators and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. However, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our trade secrets or proprietary know-how. Additionally, our confidentiality agreements and other contractual protections may not be adequate to protect our intellectual property from unauthorized disclosure, third-party infringement or misappropriation. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. Courts outside the United States are sometimes less willing to protect proprietary information, technology and know-how. Further, we may need to share our trade secrets and confidential know-how with current or future business partners, collaborators, contractors and others located in countries at heightened risk of theft of trade secrets, including through direct intrusion by private parties or foreign actors, and those affiliated with or controlled by state actors. In addition, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets, including with respect to our proprietary platform of selective FASN inhibitors, were to be disclosed to or independently developed by a competitor or other third party, our business, financial condition, results of operations and prospects our business and competitive position could be materially harmed.

If we fail to comply with our obligations under any license, collaboration or other agreement, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our drug candidates.

We rely, in part, on license, collaboration and other agreements, including our license agreement with Ascletis. We may need to obtain additional licenses from others to advance our research or allow commercialization of our drug candidates and it is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

In addition, our present and future licenses, collaborations and other intellectual property related agreements, currently impose, and are likely to further impose development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement or other obligations on us. If we breach any of these obligations, or use any future intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and our licensors may have the right to terminate the license. If any future license or other intellectual property related agreements are terminated, we may be required to cease developing and commercializing drug candidates that are covered by the licensed intellectual property. Disputes may arise regarding intellectual property subject to a licensing, collaboration or other agreement, including:

- the scope of rights granted under the agreement and other interpretation related issues;

- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the agreement;

- the sublicensing of patent and other rights under our collaborative development relationships;

- our diligence obligations under the agreement and what activities satisfy those diligence obligations;

- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our collaborators; and

- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology to third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering the technology that we have licensed or assigned to third parties. Therefore, we cannot be certain that these patents and applications will be prosecuted, maintained and enforced in a manner consistent with the best interests of our business. If our licensees or assignees fail to obtain or maintain such intellectual property, or lose rights to such intellectual property, our right to develop and commercialize any of our products that are subject to such licensed rights could be adversely affected.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or drug candidate and our business, financial condition, results of operations and prospects could suffer.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products similar to any drug candidates we may develop or utilize similarly related technologies that are not covered by the claims of the patents that we license or may own in the future;

- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we license or may own in the future;

- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;

- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing, misappropriating or otherwise violating any of our owned or licensed intellectual property rights;

- it is possible that our pending licensed patent applications or those that we may own in the future will not lead to issued patents;

- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors or other third parties;

- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;

- we may not develop additional proprietary technologies that are patentable;

- the patents of others may harm our business;
- we may choose not to file a patent in order to maintain certain trade secrets or proprietary know- how, and a third party may subsequently file a patent covering such intellectual property; and
- our trade secrets or proprietary know-how may be unlawfully disclosed, thereby losing their trade secret or proprietary status.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our current or future trademarks or trade names may be challenged, infringed, circumvented or declared generic or descriptive or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable authorities in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively, and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Although these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names.

Moreover, any proprietary name we have proposed to use with our drug candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed proprietary product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Risks related to third parties

We have licensed rights to denifanstat to Ascletis for Greater China. Under the license agreement, Ascletis controls certain product development efforts in its territory, including conduct of clinical trials, which could have an impact on our clinical development programs.

Under our license agreement with Ascletis, Ascletis is responsible for the design and conduct of certain clinical trials for the licensed drug candidate, denifanstat, which is referred to as ASC40 in the People's Republic of China, Hong Kong, Macau and Taiwan (referred to collectively as Greater China). As a result, these clinical trials may not be conducted in the manner or on the timeline we desire or may not be designed in a manner that will demonstrate a statistically significant result, any of which may negatively impact our development efforts outside of Greater China. We do not have any right to control those trial designs nor control their interactions with respect to obtaining and maintaining regulatory approvals in Greater China. In addition, if Ascletis elects not to continue development of ASC40 or abandons clinical trials, it could have a negative effect on our business and our drug candidate development efforts outside of Greater China. Our lack of control over aspects of drug candidate development in our agreement with Ascletis, or any

other future license partner, could cause delays or other difficulties in the development and commercialization of our drug candidates, which could harm our business and prospects.

We may be exposed to reputational risk as a result of certain allegations against our license partners, which may require the attention of their management. For example, Ascletis, its affiliate Gannex, and certain of its other affiliates, are the subject of legal complaints filed by another biopharmaceutical company in the U.S. District Court in the Southern District of California and the U.S. International Trade Commission with respect to intellectual property matters. We are not the subject of or party to such complaints, nor are they directed at the intellectual property under our license agreement with Ascletis. We do not believe that Ascletis' legal proceedings will have a material impact on our business, operations or financial condition.

We rely on third parties to conduct our clinical trials of our drug candidates and expect to rely on third parties to conduct future clinical trials, as well as investigator-sponsored clinical trials of our drug candidates. If these third parties do not successfully carry out their contractual duties, comply with regulatory requirements or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our drug candidates and our business could be substantially harmed.

We currently rely on, and intend to continue relying on third parties, including independent clinical investigators and third-party CROs, to conduct certain aspects of our preclinical studies and clinical trials for denifanstat, TVB-3567 and any other future drug candidates or combination therapies. While we have agreements governing their activities, we have limited influence over their actual performance and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our clinical trials is conducted in accordance with applicable protocol, legal, regulatory, and scientific standards, and our reliance on our CROs does not relieve us of our regulatory responsibilities.

We, our investigators and CROs are required to comply with GCP, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for drug candidates in clinical development. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these CROs fail to comply with applicable GCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing products. Upon inspection, such regulatory authorities may determine that our clinical trials do not comply with the GCP regulations. In addition, our clinical trials must be conducted with drug product produced under cGMP regulations and will require a large number of test subjects. Our failure or any failure by our investigators or CROs to comply with these regulations or to recruit a sufficient number of eligible patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of our investigators or CROs violate federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws and foreign equivalents.

Our investigators and CROs are not our employees, and, except for remedies available to us under our agreements with such investigators and CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical, clinical and nonclinical programs. These investigators and CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could affect their performance on our behalf. If our investigators and CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, contractual obligations, or regulatory requirements or for other reasons, our clinical trials may be extended, delayed, or terminated and we may not be able to complete development of, obtain regulatory approval for or successfully commercialize denifanstat or any other future drug candidates. As a result, our financial results and the commercial prospects for denifanstat, TVB-3567 and any future drug candidates could be harmed, our costs could increase and our ability to generate revenues could be delayed.

Our investigators and CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our investigators and CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Switching or adding investigators or CROs involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new investigator or CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Although we carefully manage our relationships with our investigators and CROs, we may encounter challenges or delays in the future and these delays or challenges may have a material adverse impact on our business, prospects, financial condition, and results of operations.

We may also rely on individual investigators or academic and non-academic institutions to conduct investigator-sponsored clinical trials relating to our drug candidates. We will not control the design or conduct of these investigator-sponsored trials, and it is possible that the FDA or comparable foreign regulatory authorities will not view these investigator-sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results. Such arrangements will likely provide us certain information rights with respect to the investigator-sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we would not have control over the timing and reporting of the data from investigator-sponsored trials, nor would we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our drug candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our drug candidates, or if the data proves to be inadequate compared to the first-hand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected. For any violations of laws and regulations during the conduct of our preclinical or clinical trials, we could be subject to FDA Form 483s, warning letters, untitled letters, or enforcement action that may include civil penalties up to and including criminal prosecution.

We have relied on, and we expect to continue to rely on, third-party manufacturers to produce our drug candidates. Our manufacturers may experience manufacturing difficulties due to the ongoing effects of inflationary pressures, resource constraints, labor disputes or unstable political environments, which could delay the completion of our clinical trials, increase the costs associated with maintaining clinical trial programs and, significantly impact our ability to develop, obtain regulatory approval for, or market denifanstat, TVB-3567 and any future drug candidates, or any combinations of our drug candidates and any other molecule.

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our drug candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely, and expect to rely for the foreseeable future, on third-party manufacturers to supply our drug candidates. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured our drug candidates ourselves, including:

- the failure of the third-party to manufacture our drug candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our drug candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the reduction or termination of production or deliveries by suppliers, or the raising of prices or renegotiation of terms;
- the breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the failure of the third-party to manufacture our drug candidates according to our specifications;
- the mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or study drug or placebo not being properly identified;
- clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales;
- the misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or non-renewal of manufacturing agreements by third parties, at a time that is costly or inconvenient to us.

If we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities, which could delay or impair our ability to obtain regulatory approval for our drug candidates and substantially increase our costs or deplete profit margins, if any. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us. In some cases, the technical skills required to manufacture our drug candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate manufacturer, or we may be unable to transfer such skills at all. In

addition, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and all applicable regulations, and there could be a substantial delay before new facilities could be qualified and registered with the FDA and other foreign regulatory authorities. We will also need to verify, such as through a comparability study, that any new manufacturer or new manufacturing process will produce our drug candidate according to the specifications previously submitted to the FDA or another domestic or foreign regulatory authority. The delays associated with the verification of a new manufacturer and demonstrating comparability of clinical trial drug product could negatively affect our ability to develop drug candidates or commercialize our products in a timely manner or within budget. To date, we have relied on four CMOs based in Europe, the United States and China, as well as our license partner, Ascletis, to produce drug substances and two CMOs in the United States and China, as well as our license partner, Ascletis, to produce drug products, across our programs. We will need to manufacture additional materials to support completion of mid- and late-stage studies such as Phase 2 and Phase 3 trials.

We currently rely on several manufacturers for the production of raw materials, APIs, and the finished products of denifanstat and TVB-3567. Our reliance on third-party suppliers and CMOs could harm our ability to develop denifanstat, TVB-3567 and any future drug candidates or combinations or to commercialize any drug candidates that are approved. Further, any delay in identifying and qualifying a manufacturer for commercial production could delay the potential commercialization of denifanstat, TVB-3567 and any future drug candidates or combinations, and, in the event that we do not have sufficient product to complete our clinical trials, it could delay such trials.

The FDA and other foreign regulatory authorities require manufacturers to register their manufacturing facilities. The FDA and corresponding foreign regulators also inspect these facilities to confirm compliance with cGMP and other applicable laws. We, our CMOs, any future collaborators and their CMOs could be subject to periodic unannounced inspections by the FDA or other comparable foreign regulatory authorities, to monitor and ensure compliance with cGMP. CMOs may face manufacturing or quality control problems causing production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Despite our efforts to audit and verify regulatory compliance, one or more of our CMOs or third-party vendors may be found on regulatory inspection by the FDA or other comparable foreign regulatory authorities to be noncompliant with cGMP regulations. Any failure to comply with cGMP requirements or other FDA and foreign regulatory authority requirements may result in shutdown of the CMO or third-party vendor or invalidation of drug product lots or processes and could adversely affect our clinical research activities and our ability to develop our drug candidates and market our products following approval, if obtained. In some cases, a product recall may be warranted or required, which would materially affect our ability to supply and market our drug products, if approved.

We currently do not control the manufacturing process of denifanstat or TVB-3567 and are completely dependent on our CMOs for complying with the FDA's cGMP requirements for manufacture of both the active drug substances and finished drug product. If our CMOs cannot successfully manufacture material that conforms to our specifications and the FDA and comparable foreign regulatory authorities' strict regulatory requirements, we will not be able to secure or maintain FDA or comparable foreign regulatory approval for our drug candidates. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel.

If the FDA or any other applicable regulatory authority does not approve these facilities for the manufacture of denifanstat, TVB-3567 or any future drug candidates or combinations, or if it withdraws any such approval in the future, or if our suppliers or CMOs decide they no longer want to supply or manufacture for us, we may need to find alternative manufacturing facilities, in which case we might not be able to identify manufacturers for clinical or commercial supply on acceptable terms, or at all, which would significantly impact our ability to develop, obtain regulatory approval for, or market denifanstat, TVB-3567 and any future drug candidates or combinations.

The manufacture of pharmaceutical products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, particularly in scaling up and validating initial production and absence of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error, shortages of qualified personnel, as well as compliance with strictly enforced federal, state, and foreign regulations. Furthermore, if contaminants are discovered in our supply of denifanstat, TVB-3567 or any future drug candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. Any stability or other issues relating to the manufacture of denifanstat, TVB-3567 or any future drug candidates or combinations may occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to inflationary pressures, resource constraints, labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to provide our drug candidate to patients in clinical trials would

be jeopardized. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

In addition, legislative proposals are pending that, if enacted, could negatively impact U.S. funding for certain biotechnology providers having relationships with foreign adversaries or which pose a threat to national security. The potential downstream adverse impacts on entities having commercial relationships with any impacted biotechnology providers is unknown but may include supply chain disruptions or delays. Our current and anticipated future dependence upon others for the manufacture of our drug candidates may adversely affect our future profit margins and our ability to develop our drug candidates and commercialize any products that receive regulatory approval on a timely basis.

Disputes under key agreements or conflicts of interest with our scientific advisors or clinical investigators could delay or prevent development or commercialization of our drug candidates.

Any agreements we have or may enter into with third parties, such as collaboration, license, formulation supplier, manufacturing, clinical research organization or clinical trial agreements, including our license agreement with Ascletis, may give rise to disputes regarding the rights and obligations of the parties. Disagreements could develop over contract interpretation, rights to ownership or use of intellectual property, the scope and direction of research and development, rights to receive milestones, royalties or other payments, the approach for regulatory approvals or commercialization strategy. Any disputes, delays or commercial conflicts could lead to the termination of agreements, delay progress of our product development programs, compromise our ability to renew agreements or obtain future agreements, lead to the loss of intellectual property rights, result in increased financial obligations for us or result in costly litigation.

We currently have no marketing and sales organization and have no organizational experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell denifanstat, TVB-3567 and any future drug candidates, we may not be able to generate product revenues.

We currently do not have a commercial organization for the marketing, sales, and distribution of pharmaceutical products. To commercialize denifanstat, TVB-3567 and any future drug candidates, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services.

The establishment and development of our own sales force or the establishment of a contract sales force to market denifanstat, TVB-3567 and any future drug candidates, if approved, will be expensive and time-consuming and could delay any commercial launch. Moreover, we may not be able to successfully develop this capability. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train, and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of denifanstat, TVB-3567 or any of our other future drug candidates. To the extent we rely on third parties to commercialize denifanstat, TVB-3567 or any of our other future drug candidates, if approved, we may have little or no control over the marketing and sales efforts of such third parties and our revenues from product sales may be lower than if we had commercialized denifanstat, TVB-3567 or any future drug candidates ourselves. In the event we are unable to develop our own marketing and sales force or collaborate with a third-party marketing and sales organization, we would not be able to commercialize denifanstat, TVB-3567 or any future drug candidates.

Risks related to our industry and the regulatory environment in which we operate

A drug candidate may not achieve adequate market acceptance among physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Even if a drug candidate receives regulatory approval, it may not gain adequate market acceptance among physicians, patients, third-party payors, pharmaceutical companies and others in the medical community. Demonstrating the safety and efficacy of a drug candidate and obtaining regulatory approvals will not guarantee future revenue.

Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government authorities or private third-party payors will determine that our products

are safe, therapeutically effective and cost effective as compared with competing treatments. If any drug candidate is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that drug candidate and may not become or remain profitable.

Our ability to commercialize any products successfully will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations.

Our commercial success depends on obtaining and maintaining coverage and adequate reimbursement of a drug candidate by third-party payors, including government payors, which may be difficult or time-consuming to obtain, may be limited in scope and may not be obtained in all jurisdictions in which we may seek to market our products. In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. For a detailed discussion, see the section of this report titled, "Pharmaceutical coverage, pricing and reimbursement."

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we or our partners commercialize or, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any drug candidate for which we or our partners obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we and our partners may not be able to successfully commercialize any drug candidate for which marketing approval is obtained.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or third-party payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Additionally, we may develop complementary diagnostic tests for use with our drug candidates. We, or our collaborators, may be required to obtain coverage and reimbursement for these tests separate and apart from the coverage and reimbursement we seek for our drug candidates, once approved. While we have not yet developed any complementary diagnostic tests for our drug candidates, if we do, there is significant uncertainty regarding our ability to obtain coverage and adequate reimbursement for the same reasons applicable to our drug candidates.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval.

The regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted.

In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. In many regions, including Europe, Japan and Canada, where we may market a product, either directly or with a collaborator, the pricing of prescription drugs is controlled by the government or regulatory authorities. Regulatory authorities in these countries could determine that the pricing for a product should be based on prices of other commercially available drugs for the same disease, rather than allowing us to market a drug at a premium as new drugs. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay or limit our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenue we generate from the sale of the product in that particular country.

Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.

Many EU Member States periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. We expect that legislators, policymakers and healthcare insurance funds in the EU Member States will continue to propose and implement cost-containing measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative to branded products, and/or branded products available through parallel import to keep healthcare costs down. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. Health Technology Assessment (HTA), of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States.

In December 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted in the European Union. This Regulation, which entered into force in January 2022 and have applied as of January 2025, is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at European Union level for joint clinical assessments in these areas. The Regulation foresees a three-year transitional period and will permit EU Member States to use common HTA tools, methodologies, and procedures across the European Union, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. If we are unable to maintain favorable pricing and reimbursement status in EU Member States for drug candidates that we may successfully develop and for which we may obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the European Union could be negatively affected.

Legislators, policymakers and healthcare insurance funds in the European Union may continue to propose and implement cost-containing measures to keep healthcare costs down. These measures could include limitations on the prices we would be able to charge for drug candidates that we may successfully develop and for which we may obtain regulatory approval or the level of reimbursement available for these products from governmental authorities or third-party payors. Further, an increasing number of European Union and other foreign countries use prices for medicinal products established in other countries as "reference prices" to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere.

Our relationships with customers, healthcare providers, and third-party payors may be subject, directly or indirectly, to federal, state and foreign healthcare fraud and abuse laws, transparency laws, and other healthcare laws and regulations, including analogous foreign laws. If we or our employees, independent contractors, consultants, commercial partners, or vendors violate these laws, we could face substantial penalties.

Our relationships with customers, healthcare providers, and third-party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, transparency laws with respect to drug pricing and payments and other transfers of value made to physicians and other healthcare providers, and other healthcare laws and regulations. These laws may impact, among other things, our clinical research program, as well as our proposed and future sales, marketing, and education programs. In particular, the promotion, sales and marketing of healthcare items and services is subject to extensive laws and regulations designed to prevent fraud, kickbacks, self-dealing, and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting,

marketing and promotion, sales commission, customer incentive, and other business arrangements. For a detailed discussion, see the section of this report titled, "Business—Government regulation and product approval—Other U.S. healthcare laws and compliance requirements."

In addition, we may be subject to federal or comparable foreign consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers, as well as state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope. For example, we may be subject to the following: state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental, third-party payors, including private insurers, or that apply regardless of payor; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures, or drug pricing; and state and local laws requiring the registration of pharmaceutical sales and medical representatives.

Outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities, or our arrangements with physicians, some of whom have been granted stock options, could be subject to challenge under one or more of such laws. It is not always possible to identify and deter employee misconduct or business noncompliance, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If we or our employees, independent contractors, consultants, commercial partners and vendors violate these laws, we may be subject to investigations, enforcement actions and/or significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs or similar foreign programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of denifanstat or any of our future drug candidates outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Our internal computer systems, or those used by our CROs or other contractors or consultants, may fail or suffer cybersecurity incidents or breaches and we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits, loss of customers or sales, and other adverse consequences.

We and the third parties upon which we rely face a variety of evolving threats, which could cause cybersecurity incidents or breaches, such as cyber-attacks, malicious internet-based activity, online and offline fraud, and other similar activities. Such threats are prevalent and continue to rise, are increasingly difficult to detect, and come from a variety of sources.

Despite the implementation of security and back-up measures designed to protect against cybersecurity incidents and breaches, our internal computer, server, and other information technology systems as well as those of our third-party collaborators, consultants, contractors, suppliers, and service providers upon which we rely, may be vulnerable to various threats including, but not limited to, damage from physical or electronic break-ins, computer viruses, malware, ransomware, personnel misconduct or error, supply chain attacks, natural disasters, terrorism, war, telecommunication and electrical failure, denial of service, attacks enhanced or facilitated by artificial intelligence (AI), and other cyberattacks or disruptive incidents that could result in unauthorized access to, use or disclosure of, corruption of, or loss of sensitive, and/or proprietary data, including personal data, and health-related information, and could subject us to significant liabilities and regulatory and enforcement actions, and reputational damage. In particular, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions in our operations.

For example, the loss of clinical trial data from completed or ongoing clinical trials could result in delays in any regulatory approval or clearance efforts and significantly increase our costs to recover or reproduce the data, and subsequently commercialize the product. Additionally, theft of our intellectual property or proprietary business information could require substantial expenditures to remedy. Such theft could also lead to loss of intellectual property rights through disclosure of our proprietary business information, and such loss may not be capable of remedying.

In addition, our reliance on third-party partners could introduce new cybersecurity risks and vulnerabilities. If we or our third-party collaborators, consultants, contractors, suppliers, or service providers upon which we rely were to suffer a cyber-attack, cybersecurity incident or breach, for example, that resulted in the unauthorized access to or use or disclosure of personal data, we may have to notify consumers, partners, collaborators, government authorities, other stakeholders and the media, and may be subject to investigations, civil penalties, administrative and enforcement actions, and litigation, any of which could harm our business and reputation. Any such disclosures may involve inconsistent requirements and are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences. Likewise, we rely on third parties to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. While we may be entitled to damages if these providers fail to satisfy their data privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

Our reliance on internet technology and the number of our employees, and those of our CROs, who continue to work remotely may create additional opportunities for cybercriminals to exploit vulnerabilities, as this has caused an increased usage of computers operated on home networks, while in transit, or in public locations. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience cybersecurity incidents or breaches that may remain undetected for an extended period.

We take steps to detect and remediate vulnerabilities, but we may not be able to detect and remediate all vulnerabilities because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated in nature. Therefore, such vulnerabilities could be exploited but may not be detected until after a security incident has occurred. Un-remediated high risk or critical vulnerabilities pose material risks to our business.

Like other companies in our industry, we have experienced threats and cybersecurity incidents relating to our information technology systems and infrastructure, and we expect to continue to experience them. To the extent that any disruption or cybersecurity incident or breach were to result in a loss of, or damage to, our data or systems, or inappropriate or unauthorized access to or disclosure or use of confidential, proprietary, and/or sensitive data, we could incur liability and suffer reputational harm, and the development and commercialization of denifanstat, or future drug candidates could be delayed.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be sure that any insurance coverage that we do or will obtain will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

In addition to experiencing a cybersecurity incident, third parties may gather, collect, or infer sensitive information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Furthermore, our sensitive information could be leaked, disclosed or revealed as a result of or in connection with our employees', personnel's or vendors' use of generative AI technologies.

Failure to comply with data privacy and security laws, regulations and other obligations could lead to government enforcement actions (which could include civil or criminal penalties), private litigation, negative publicity, and/or other adverse consequences that could negatively affect our operating results and business.

We and our partners may be subject to federal, state, and foreign data protection laws and regulations (i.e., laws and regulations that address privacy and data security). In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations that govern the collection, use, disclosure, and protection of health-related and other personal data could apply to our operations or the operations of our partners. In addition, we may obtain health information from third parties (including research institutions from which we obtain

clinical trial data) that are subject to privacy and security requirements under the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Depending on the facts and circumstances, we could be subject to penalties if we violate HIPAA.

Even when HIPAA does not apply, according to the Federal Trade Commission (FTC), failing to take appropriate steps to keep consumers' personal data secure may constitute unfair acts or practices in or affecting commerce in violation of the Federal Trade Commission Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, certain state laws govern the privacy and security of health-related and other personal data in certain circumstances, some of which may be more stringent, broader in scope or offer greater individual rights with respect to protected health information than HIPAA, many of which may differ from each other, thus, complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, the California Consumer Privacy Act, as amended by the California Privacy Rights Act (collectively, the CCPA), grants individual privacy rights for California consumers, business representatives, and employees who are California residents, including the right to access, correct, or delete certain personal data, and opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. The CCPA provides for administrative fines of up to $7,500 per violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA increases compliance costs and potential liability with respect to other personal data we maintain about California residents. The CCPA also created a new California data protection agency authorized to implement and enforce the law. Additional compliance investment and potential business process changes may be required.

The CCPA marked the beginning of a trend toward more stringent privacy legislation in the United States, which could increase our potential liability and adversely affect our business. For example, consumer privacy laws similar to the CCPA have been passed or proposed in numerous other states, including Connecticut, Colorado, Virginia and Utah, and other states, such as Washington, have enacted privacy laws specifically regulating health information. Additionally, a small number of states have implemented privacy laws which regulate other specific types of information, such as biometric data. Such legislation may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies.

All of these evolving compliance and operational requirements impose significant costs, such as costs related to organizational changes, implementing additional protection technologies, training employees and engaging consultants and legal advisors, which are likely to increase over time. The existence of comprehensive privacy laws in different states in the country could also make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. In addition, such requirements may require us to modify our data processing practices and policies, utilize management's time and/or divert resources from other initiatives and projects. Any failure or perceived failure by us to comply with any applicable federal, state or foreign laws and regulations relating to data privacy and security could result in damage to our reputation, as well as proceedings or litigation by governmental agencies or other third parties, including class action privacy litigation in certain jurisdictions, which would subject us to significant fines, sanctions, awards, injunctions, penalties or judgments. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

For additional information, see "Business—Government regulation and product approval—Data privacy and security laws."

The use of new and evolving technologies, such as AI, in our business may result in spending material resources and presents risks and challenges that can impact our business including by posing security and other risks to our confidential and/or proprietary information, including personal information, and as a result we may be exposed to reputational harm and liability.

We have used and may continue to use and integrate AI into our business processes, and this innovation presents risks and challenges that could affect its adoption, and therefore our business. For example, we have used, and intend to continue to use AI-based digital pathology to evaluate denifanstat in our clinical trials. Additionally, our employees and personnel may use generative AI technologies to perform their work, and the disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. The use of certain AI technology can give rise to intellectual property risks, including compromises to proprietary intellectual property and intellectual property infringement. Governments have also passed and are likely to pass additional laws regulating generative AI. For example, the EU's Artificial Intelligence Act (the AI Act) — the world's first comprehensive AI law — was entered into force on August 1, 2024 and most provisions will become effective on August 2, 2026. This legislation imposes

significant obligations on providers and deployers of high risk AI systems, and encourages providers and deployers of AI systems to account for EU ethical principles in their development and use of these systems. The rapid evolution of AI intelligence will require the application of significant resources to design, develop, test and maintain our products and services to help ensure that AI is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and consumer lawsuits. If we enable or offer solutions that draw controversy due to perceived or actual negative societal impact, we may experience brand or reputational harm, competitive harm or legal liability.

Our vendors may also incorporate AI tools into their offerings, and the providers of these AI tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of AI, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages.

Foreign data protection laws, including the European Union's General Data Protection Regulation (the EU GDPR), and the UK equivalent of the same (the UK GDPR, together with the EU GDPR, the GDPR) may also apply to our processing of health-related and other personal data regardless of where the processing in question is carried out.

The GDPR imposes stringent requirements for controllers and processors of personal data of individuals within the EEA, or the United Kingdom. The GDPR applies to any company established in the EEA or United Kingdom as well as to those outside the EEA or United Kingdom if they collect and use personal data in connection with the offering of goods or services to individuals in the EEA or United Kingdom or the monitoring of their behavior. The GDPR, together with national legislation, regulations and guidelines of the EEA Member States and the United Kingdom governing the processing of personal data, impose strict obligations and restrictions on the ability to collect, analyze and transfer personal data, including health data from clinical trials and adverse event reporting. In particular, these obligations and restrictions concern the consent of the individuals to whom the personal data relates, the information provided to the individuals, the transfer of personal data out of the EEA or the United Kingdom, security breach notifications, security and confidentiality of the personal data and imposition of substantial potential fines for breaches of the data protection obligations. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million (£17.5 million) or 4% of the annual global revenues of the noncompliant company, whichever is greater. The EU GDPR also confers a private right of action on data subjects to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the EU GDPR. The UK Government introduced a Data Protection and Digital Information Bill which failed in the UK legislative process. A new Data (Use and Access) Bill (UK Bill) has now been introduced into parliament. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime. Further, this may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU's and UK's GDPR may further diverge in the future and create additional regulatory challenges and uncertainties. In addition, EU Member States have adopted implementing national laws to implement the GDPR which may partially deviate from the GDPR and the competent authorities in the EU Member States may interpret GDPR obligations slightly differently from country to country, so that we do not expect to operate in a uniform legal landscape in the EU.

The EU GDPR prohibits the transfer of personal data from the EEA to third countries that are not considered to provide adequate protections for personal data, including the U.S. With regard to transfers of personal data from the EEA, transfers to third countries that have not been approved as "adequate" are prohibited unless an appropriate safeguard specified by the EU GDPR is implemented, such as the Standard Contractual Clauses (SCCs) approved by the European Commission, certification to the EU-U.S. Data Privacy Framework (which allows for transfers for relevant U.S.-based organizations who self-certify compliance and participate in the framework), binding corporate rules, or a derogation applies. Where relying on the SCCs for data transfers, we may also be required to carry out transfer impact assessments to assess whether the recipient is subject to local laws which allow public authority access to personal data. Like the EU GDPR, the UK GDPR restricts personal data transfers outside the UK to countries not regarded by the UK as providing adequate protection. The UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The Information Commissioner's Office has introduced mechanisms for international transfers of personal data originating from the UK (an International Data Transfer Agreement along with a separate addendum to the EU SCCs). The UK and U.S. have also agreed an extension to the EU-US Data Privacy Framework to cover transfers of personal data from the UK to the U.S. These mechanisms are subject to legal challenges, and therefore the circumstances where we can rely on these measures may change with time, such that there is no assurance that we can continue to satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the United Kingdom, or other jurisdictions to the United States, or if the requirements for a legally-compliant transfer are too onerous, we could face significant adverse consequences,

including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and United Kingdom to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activities groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data out of Europe for allegedly violating the GDPR's cross-border data transfer rules.

Implementing mechanisms to endeavor to ensure compliance with the GDPR and relevant local legislation in EEA Member States and the United Kingdom may be onerous and may interrupt or delay our development activities, and adversely affect our business, financial condition, results of operations, and prospects. In addition to the foregoing, a breach of the GDPR or other applicable privacy and data protection laws and regulations could result in regulatory investigations, reputational damage, and orders to cease/ change our use of data or enforcement notices. While we have taken steps to comply with the GDPR where applicable, our efforts to achieve and remain in compliance may not be fully successful.

Compliance with U.S. and foreign privacy and security laws, rules and regulations could require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Each of these constantly evolving laws can be subject to varying interpretations. Failure (or perceived failure) to comply with U.S. and foreign data protection laws and regulations could result in government investigations and enforcement actions which could include civil or criminal penalties (e.g., fines, penalties, audits, additional reporting requirements and/or oversight, bans on processing personal data, and orders to destroy or not use personal data), private litigation (including class-action claims) and mass arbitration demands, and/or adverse publicity and could negatively affect our operating results and business. Moreover, patients about whom we or our partners obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws, or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

In particular, plaintiffs have become increasingly more active in bringing privacy-related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for significant statutory damages, depending on the volume of data and the number of violations. Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; inability to process personal data or to operate in certain jurisdictions (including in relation to clinical trials); limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations.

For additional information, see "Business—Government regulation and product approval—Data privacy and security laws."

Our ability to use our net operating loss carryforwards and certain other tax attributes to offset future taxable income or taxes may be limited.

We have incurred substantial losses during our history and do not expect to become profitable in the near future, and we may never achieve profitability. Our ability to use our U.S. federal and state net operating loss carryforwards (NOLs) and other tax attributes to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of our NOLs, or other tax attributes. Unused U.S. federal NOLs arising in taxable years beginning before January 1, 2018, may be carried forward to the earlier of the next subsequent twenty tax years to offset future taxable income, if any. Under current federal tax law, U.S. federal NOLs incurred in taxable years beginning after December 31, 2017, can be carried forward indefinitely, but the ability to use such U.S. federal NOLs to offset taxable income in taxable years beginning after December 31, 2017, is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to current U.S. federal tax law.

As of December 31, 2025, we had U.S. federal NOLs of approximately $213.6 million which may be available to offset future U.S. federal income. Our U.S. federal NOLs incurred in taxable years beginning prior to January 1, 2018 of approximately $91.0 million expire beginning in 2029 while U.S. federal NOLs incurred in taxable years beginning after December 31, 2017 of approximately $122.6 million will have an indefinite carryforward period, subject to annual limitations. As of December 31, 2025, we also had state NOL carryforwards of approximately $26.3 million which may be available to offset future state income and expire at various years beginning with 2028. Our NOL carryforwards are subject to review and possible adjustment by the U.S. federal and state tax authorities.

As of December 31, 2025, we had U.S. federal research and development tax credit carryforwards of approximately $8.5 million available to reduce future tax liabilities which expire at various years beginning with 2028. As of December 31, 2025, we had state credit carryforwards of approximately $3.2 million available to reduce future tax liabilities which do not expire.

Our NOL carryforwards and research and development (R&D) credits are subject to review and possible adjustment by the U.S. federal and state tax authorities.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (Code), and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage point change (by value) in its equity ownership by "5% shareholders" over a rolling three-year period, the corporation's ability to use its pre-change NOLs, R&D credits and certain other tax attributes to offset its post-change income or taxes may be limited. This could limit the amount of NOLs, R&D credit carryforwards or other applicable tax attributes that we can utilize annually to offset future taxable income or tax liabilities. Subsequent ownership changes and changes to the U.S. tax rules in respect of the utilization of NOLs, R&D credits and other applicable tax attributes carried forward may further affect the limitation in future years. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our NOL carryforwards and other tax attributes, which could adversely affect our future cash flows.

Changes in tax law may adversely affect us or our investors.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service (IRS) and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our Series A common stock. In recent years, many such changes have been made, and changes are likely to continue to occur in the future. It cannot be predicted whether, when, in what form or with what effective dates tax laws, regulations and rulings may be enacted, promulgated or issued, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law.

We have incurred, and will continue to incur, significant increased costs as a result of operating as a public company, and our management is devoting substantial time and resources to compliance initiatives.

As a public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (Exchange Act), the Sarbanes-Oxley Act of 2002 (Sarbanes-Oxley Act), the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Market and other applicable securities rules and regulations. Complying with these rules and regulations has increased, and will continue to increase, our legal and financial compliance costs and may make some activities more difficult, time consuming or costly and increase demand on our systems and resources. The Exchange Act requires, among other things, that we file annual, quarterly and current reports with respect to our business and operating results. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are required to disclose changes made in our internal control and procedures on a quarterly basis. In order to maintain and, if required, improve our disclosure controls and procedures and internal control over financial reporting to meet this standard, significant resources and management oversight may be required. As a result, management's attention may be diverted from other business concerns, which could significantly harm our business, financial condition, results of operations and prospects. We have a very small team with only 16 full-time employees as of December 31, 2025.

In addition, changing laws, regulations and standards relating to corporate governance and public disclosure are creating uncertainty for public companies, increasing legal and financial compliance costs and making some activities more time consuming. These laws, regulations and standards are subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If our efforts to comply with new laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to their application and practice, regulatory authorities may initiate legal proceedings against us and our business, financial condition, results of operations and prospects may be significantly harmed.

As a public company, we are obligated to maintain proper and effective internal controls over financial reporting and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our Series A common stock.

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act to furnish a report by management on, among other things, the effectiveness of our internal controls over financial reporting. This assessment includes disclosure of any material weaknesses identified by our management in our internal controls over financial reporting. We are also required to disclose changes made to our internal controls and procedures on a quarterly basis. However, we expect that our independent registered public accounting firm will not be required to report on the effectiveness of our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act until the date we are no longer an "emerging growth company" as defined in the JOBS Act, if we take advantage of the exemptions contained in the JOBS Act. At such time, our independent registered public accounting firm may issue a report that is adverse if it is not satisfied with the level at which our controls are documented, designed, or operating.

Additionally, the existence of any material weakness or significant deficiency would require management to devote significant time and incur significant expense to remediate any such material weaknesses or significant deficiencies and management may not be able to remediate any such material weaknesses or significant deficiencies in a timely manner. The existence of any material weakness in our internal control over financial reporting could also result in errors in our financial statements that could require us to restate our financial statements, cause us to fail to meet our reporting obligations, and cause stockholders to lose confidence in our reported financial information, all of which could materially and adversely affect our business and the price of our Series A common stock.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. The loss of the services of any of our executive officers, other key employees and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development and harm our business. We are highly dependent on the management, research and development, clinical, financial, and business development expertise of David Happel, our Chief Executive Officer, Thierry Chauche, our Chief Financial Officer,

Dr. Eduardo Martins, our Chief Medical Officer, Elizabeth Rozek, our Chief Legal and Administrative Officer and Marie O'Farrell, our Chief Scientific Officer. We do not currently maintain "key person" insurance for any of our executives or employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our product pipeline toward scaling up for commercialization, manufacturing and sales and marketing personnel, will also be critical to our success. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. If we fail to manage these transitions successfully, we could experience significant delays or difficulty in the achievement of our product development and our business, financial condition and results of operations could be materially and adversely affected. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

Risks related to our Series A common stock

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, many of which are beyond our control, including without limitation:

- variations in the level of expense related to the ongoing development of our drug candidates or future development programs;
- results of clinical trials, or the addition or termination of clinical trials or funding support by us or potential future partners;
- our execution of any collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under potential future arrangements or the termination or modification of any such potential future arrangements;
- any intellectual property infringement, misappropriation or violation lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our drug candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such drug candidates;
- regulatory developments affecting our drug candidates or those of our competitors; and
- changes in general market and economic conditions.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our Series A common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Our stock price has been and may continue to be volatile, and purchasers of our Series A common stock could incur substantial losses.

Our stock price has been and is likely to continue to be volatile. The market price for our Series A common stock may be influenced by various factors, many of which are beyond our control, including the other risks described in this "Risk Factors" section and many others, such as but not limited to:

- our ability to advance denifanstat or potential future drug candidates;
- results of preclinical studies and clinical trials of denifanstat or potential future drug candidates, or those of our competitors or potential collaborative partners;
- regulatory or legal developments in the United States and other countries, especially changes in laws or regulations applicable to our drug candidates;
- the success of competitive products;
- introductions and announcements of new products by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory authorities with respect to our drug candidates, potential products, clinical trials, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, products or drug candidates;
- developments concerning any future collaborations, including, but not limited to, those with our sources of manufacturing supply and our commercialization partners;
- market conditions in the biopharmaceutical and biotechnology sectors;
- manufacturing, supply or distribution delays or shortages;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, financing efforts or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in securities analyst recommendations regarding our Series A common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;

- speculation in the press or investment community;
- trading volume of our Series A common stock;
- sales of our Series A common stock by us or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- macroeconomic conditions, including volatility in the credit and financial markets and inflationary pressures;
- terrorist acts, acts of war or periods of widespread civil unrest, including Russia's invasion of Ukraine and the conflict in Israel;
- natural disasters, including earthquakes, and other calamities; and
- general economic, industry and market conditions.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that has been often unrelated to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our Series A common stock, regardless of our operating performance.

The dual series structure of our common stock may limit our Series A common stockholders' ability to influence corporate matters and may limit visibility with respect to certain transactions.

The dual series structure of our common stock may limit our Series A common stockholders' ability to influence corporate matters. Holders of our Series A common stock are entitled to one vote per share, while our Series B common stock is non-voting. Nonetheless, each share of our Series B common stock may be converted at any time into one share of our Series A common stock at the option of the holder by providing written notice to us, subject to the limitations provided for in our amended and restated certificate of incorporation. Consequently, if the holder of our Series B common stock exercises its option to make this conversion, this will have the effect of increasing the relative voting power of the holder of our Series B common stock, and correspondingly decreasing the voting power of the holders of our Series A common stock, which may limit our stockholders' ability to influence corporate matters. Additionally, stockholders who hold, in the aggregate, more than 10% of our Series A common stock and Series B common stock, but 10% or less of our Series A common stock, and are not otherwise an insider, may not be required to report changes in their ownership due to transactions in our Series B common stock pursuant to Section 16(a) of the Exchange Act, and may not be subject to the short-swing profit provisions of Section 16(b) of the Exchange Act.

Future sales and issuances of our Series A common stock, or rights to purchase our Series A common stock, could result in dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital may be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating as a public company. To the extent that additional capital is raised through the issuance of shares of Series A common stock or other securities convertible into shares of Series A common stock, our stockholders will be diluted. Future issuances of our Series A common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our Series A common stock and impair our ability to raise capital through future offerings of shares or equity securities. In August 2025, we entered into a Sales Agreement with Leerink Partners LLC to establish an at-the-market offering (2025 ATM Offering) through which we may sell, from time to time at our sole discretion, up to $75.0 million shares of our Series A common stock. There were no sales under the 2025 ATM Offering during the year ended December 31, 2025. No prediction can be made as to the effect, if any, that future sales of Series A common stock or other equity securities or the availability of Series A common stock for future sales will have on the trading price of our Series A common stock.

We are an "emerging growth company" and a "smaller reporting company" and our election of reduced reporting requirements applicable to emerging growth companies and smaller reporting companies may make our Series A common stock less attractive to investors

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act (JOBS Act). For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act (Section 404), reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements.

We will remain an emerging growth company until the earliest to occur of: (i) the last day of the fiscal year in which we have more than $1.235 billion in annual revenue; (ii) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; (iii) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period; and (iv) December 31, 2028. Even after we no longer qualify as an emerging growth company, we could still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our Series A common stock less attractive because we may rely on these exemptions.

In addition, the JOBS Act provides that an emerging growth company can also take advantage of an extended transition period for complying with new or revised accounting standards until such time as those standards apply to private companies. We have elected to avail ourselves of this exemption from new or revised accounting standards, and therefore we will not be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies.

We are also a "smaller reporting company" as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our Series A common stock will be the sole source of gain for our stockholders in the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. Any return to stockholders will therefore be limited to the appreciation of their stock. There is no guarantee our Series A common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

We may incur significant costs from class action litigation due to our expected stock volatility.

Our stock price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts for our discovery platform and our drug candidates, the development efforts of future partners or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of biopharmaceutical and biotechnology companies. This risk is especially relevant to us because biopharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. When the market price of a stock has been volatile as our stock price may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may delay or prevent an acquisition of our company or a change in our management. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

- a prohibition on actions by our stockholders by written consent;
- a requirement that special meetings of stockholders be called only by our board of directors;
- advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings;
- division of our board of directors into three classes, serving staggered terms of three years each; and
- the authority of the board of directors to issue preferred stock with such terms as the board of directors may determine.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, as amended, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions would apply even if the proposed merger or acquisition could be considered beneficial by some stockholders.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware and, to the extent enforceable, the federal district courts of the United States of America will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative claim or cause of action brought on our behalf;
- any claim or cause of action for a breach of fiduciary duty owed by any of our current or former directors, officers, or other employees to us or our stockholders;
- any claim or cause of action against us or any of our current or former directors, officers or other employees arising out of or pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation, or our bylaws (as each may be amended from time to time);
- any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws (as each may be amended from time to time, including any right, obligation, or remedy thereunder);
- any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction to the Court of Chancery of the State of Delaware; and
- any claim or cause of action against us or any of our current or former directors, officers, or other employees governed by the internal-affairs doctrine.

However, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all claims brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. Consequently, this provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction. Moreover, Section 22 of the Securities Act of 1933, as amended (the Securities Act), creates concurrent jurisdiction for federal and state courts over all claims brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder.

In addition, our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the federal district courts of the United States of America shall be the exclusive forum for the resolution of any complaint asserting a cause or causes of action arising under the Securities Act, including all causes of action asserted against any defendant to such complaint. For the avoidance of doubt, this provision is intended to benefit and may be enforced by us, our officers and directors, the underwriters to any offering giving rise to such complaint, and any other professional entity whose profession gives authority to a statement made by that person or entity and who has prepared or certified any part of the documents underlying such offering.

While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions, and there can be no assurance that such provisions will be enforced by a court in those other jurisdictions. We note that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder.

Additionally, our amended and restated bylaws provide that any person or entity holding, owning or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to these provisions.

General risk factors

Our operations are vulnerable to interruption by earthquake, fire, power loss, telecommunications failure, terrorist activity and other events beyond our control, which could harm our business.

Our facility is located in a seismically active region. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major earthquake, fire, power loss, terrorist activity or other disasters and do not have a complete recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business.

If securities or industry analysts issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our Series A common stock depends in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property rights or our Series A common stock performance, or if our target studies and operating results fail to meet the expectations of the analysts, our stock price could decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Unfavorable global political or economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The global credit and financial markets have experienced severe volatility and disruptions in the past several years. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A weak or declining economy could also result in supply chain disruptions. In addition, the ongoing military conflict between Russia and Ukraine and in Israel could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have been or may in the future be initiated by nations including the United States, the European Union or Russia, which could adversely affect our business and/or our supply chain, our CROs, CMOs and other third parties with whom we conduct business. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

Adverse developments affecting the financial services industry, such as actual events or concerns involving liquidity, defaults or non-performance by financial institutions or transactional counterparties, could adversely affect our current and projected business operations and financial condition and results of operations.

Events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions, transactional counterparties or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds or other similar risks, have in the past and may in the future lead to market-wide liquidity problems. Even though we assess our banking relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that affect us, the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry. In addition, investor concerns regarding the U.S. or international financial systems could result in less favorable commercial financing terms, including higher interest rates or costs and tighter financial and operating covenants, or systemic limitations on access to credit and liquidity sources, thereby making it more difficult for us to acquire financing on acceptable terms or at all. Any decline in available funding or access to our cash and liquidity resources could, among other risks, adversely impact our ability to meet our operating expenses, financial obligations or fulfill our other obligations, result in breaches of our contractual obligations or result in violations of federal or state wage and hour laws. Any of these impacts, or any other impacts resulting from the factors described above or other related or similar factors not described above, could have material adverse impacts on our liquidity and our business, financial condition or results of operations.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended (FCPA), the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell our products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Cyber Risk Management and Strategy

We have developed and implemented a cybersecurity risk management program designed to protect the confidentiality, integrity, and availability of our critical systems and information. Our cybersecurity risk management program is integrated into our broader information security policy, which is informed by industry standards such as the National Institute of Standards and Technology (NIST) Cybersecurity Framework and Center for Internet Security (CIS) benchmarks.

Our approach to cybersecurity risk management includes, but is not limited to, the following elements:

- Security incident management processes designed to oversee, identify and manage security events and incidents, including a cybersecurity incident response plan and a managed 24/7 security operation center, which monitors all security events from endpoints and cloud services.

- System lifecycle and management processes designed to oversee and manage systems and services used by Sagimet, including system assessments and the management of vulnerabilities.

- System protections including firewalls, endpoint protection, access controls and cloud-based security systems.

- Annual cloud system assessments designed to help identify material cybersecurity risks to our critical systems, information and our broader enterprise Information Technology (IT) environment.

- Cybersecurity awareness training for all users with access to our systems including employees, consultants and senior management, with timely relevant security topics, which include social engineering, phishing, password protection, protecting personal data and appropriate use of assets.

We have leveraged the support of a third-party data privacy organization to perform a risk assessment designed to identify, assess, and manage data privacy risks. Further, we follow a formal, documented process to assess the data protection practices of certain third-party vendors that handle sensitive information on our behalf. This process includes a risk assessment process which is designed to oversee, identify and manage material cybersecurity and data privacy risks associated with systems, services and third parties.

To date, we have not experienced any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition; however, like other companies in our industry, we have, from time to time, experienced threats and security incidents relating to our and our third-party vendors' information technology systems and infrastructure. For more information, please see the section entitled "Risk Factors" in this Annual Report on Form 10-K.

Governance Related to Cybersecurity Risks

Our Senior Director of IT is responsible for the strategic leadership and direction of our cybersecurity program. The Senior Director of IT has over 16 years of experience as an information technology professional.

Our Board of Directors has delegated oversight of our cybersecurity risk management program to our audit committee, per the audit committee charter. Our audit committee has oversight over cybersecurity risks. Our management provides periodic presentations to the audit committee on our cybersecurity program, including updates on cybersecurity risks and related cybersecurity strategy, as applicable. In addition, management alerts the audit committee of any material cybersecurity incidents. The audit committee provides updates regarding our cybersecurity program to the board of directors when material.

Item 2. Properties

Our headquarters is currently located in San Mateo, California and consists of approximately 3,000 square feet of office space under a lease that expires in June 2026. We believe that our facilities are adequate to meet our current needs. We plan to reassess our facilities needs on a quarterly basis.

Item 3. Legal Proceedings

From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. Our management believes that there are currently no claims or actions pending against us, the ultimate disposition of which would have a material adverse effect on our results of operations, financial condition or cash flows.

Item 4. Mine safety disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

On July 17, 2023, our Series A common stock began trading on the Nasdaq Global Market under the symbol "SGMT." Prior to that time, there was no public market for our common stock. There is no established public trading market for our Series B common stock.

Stockholders

As of March 5, 2026, there were 45 holders of record of our Series A common stock and 2 holders of record of our Series B common stock. The actual number of holders is greater than the number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and nominees.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We do not anticipate declaring or paying, in the foreseeable future, any cash dividends on our capital stock. We intend to retain all available funds and future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our board of directors, subject to applicable laws, and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

In addition, our ability to pay cash dividends on our capital stock in the future may be limited by the terms of any future debt or preferred securities we issue or any credit facilities we enter into.

Securities Authorized for Issuance under Equity Compensation Plans

Information about our equity compensation plans in Item 12 of Part III of this Annual Report on Form 10-K is incorporated herein by reference.

Recent Sales of Unregistered Equity Securities

There were no sales of unregistered securities during the year ended December 31, 2025.

Issuer Purchases of Equity Securities

None.

Item 6. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion and analysis of our financial condition and results of operations should be read together with the financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and analysis contains forward-looking statements that involve risks and uncertainties that could cause actual results or events to differ materially from those expressed or implied by such forward-looking statements as a result of many important factors, including those set forth in Part I of this Annual Report on Form 10-K under the caption "Risk Factors." Please also see the section titled "Forward-Looking Statements". We do not undertake any obligation to update forward-looking statements to reflect events or circumstances occurring after the date of this Annual Report.

Overview

We are a clinical-stage biopharmaceutical company developing novel therapeutics called fatty acid synthase (FASN) inhibitors that target dysfunctional metabolic and fibrotic pathways in diseases resulting from the overproduction of the fatty acid, palmitate. Our lead drug candidate, denifanstat, is an oral, once-daily pill and selective FASN inhibitor in development for the treatment of metabolic dysfunction-associated steatohepatitis (MASH), acne and select forms of cancer. Our second FASN inhibitor, TVB-3567, is a potent and selective small molecule FASN inhibitor in development for acne.

FASN inhibition for the treatment of MASH

The critical role of FASN overactivity in MASH makes it an attractive target for drug therapy. Our FASN inhibitor, denifanstat, targets multiple drivers of MASH by reducing steatosis, inflammation and fibrosis.

Phase 2b FASCINATE-2 clinical trial of denifanstat in MASH

Denifanstat met all primary and multiple secondary endpoints in the Phase 2b FASCINATE-2 clinical trial evaluating denifanstat in 168 biopsy-confirmed MASH patients with stage F2 or F3 fibrosis compared to placebo at week 52. We announced topline results in January 2024 and published the trial results in *The Lancet Gastroenterology & Hepatology* in October 2024. Denifanstat also demonstrated anti-fibrotic activity, including in patients with advanced fibrosis, as seen in the F3 modified intention to treat (mITT) population and qF4 patients (qF4 patients are AI-defined F4, based on the second harmonic generation (SGH) HistoIndex platform, which may encompass late stage F3 as well as F4 patients):

- Fibrosis improvement by ≥ 1 stage with no worsening of MASH (F3 mITT population: denifanstat 49% vs. placebo 13%, p=0.0032).
- Fibrosis improvement by ≥ 2 stages with no worsening of MASH (mITT population: denifanstat 20% vs. placebo 2%, p=0.0065; F3 mITT population: denifanstat 34% vs. placebo 4%, p=0.0065).
- A statistically significant difference in progression to cirrhosis (F4) (mITT population: denifanstat 5% vs. placebo 11%, p=0.0386).
- A statistically significant difference in fibrosis improvement by ≥ 1 stage with no worsening of MASH for patients on a stable background dose of a GLP-1 Receptor Agonist (mITT population: denifanstat 42% vs. placebo 0%, p=0.034).
- Decrease of 1 or 2 qFibrosis stages in 85% of qF4 patients as measured by AI-based pathology (SGH, HistoIndex).
- Statistically significant liver fibrosis regression in the portal and peri-portal regions (observed with AI-based digital pathology), which have been recently linked to major adverse liver outcomes (MALO) and mortality as measured by AI-based composite scores.

As in prior studies, denifanstat was generally well tolerated. No treatment-related serious adverse events (SAEs) were observed, and the majority of adverse events (AEs) were mild to moderate in nature (Grades 1 and 2). There were no Grade ≥3 treatment-related AEs and no drug-induced liver injury (DILI) signal in the study. The most common treatment-related AEs by system organ class (observed in ≥5% of patients in the study) were eye disorders, gastrointestinal disorders, and skin and subcutaneous tissue disorders. The incidence of treatment emergent adverse events (TEAEs) leading to treatment discontinuation was 19.6% in the denifanstat group compared to 5.4% in placebo.

Combination of denifanstat and resmetirom for the treatment of MASH

The Company is developing a combination of its oral once-daily FASN inhibitor, denifanstat, and the thyroid hormone receptor beta (THR-β) agonist, resmetirom (commercially available as Rezdiffra), for cirrhotic patients living with F4-stage MASH.

Phase 1 pharmacokinetic (PK) clinical trial of a combination of denifanstat and resmetirom

In December 2025, we announced completion of our Phase 1 PK trial of a combination of denifanstat and resmetirom. The Phase 1 PK was an open-label, 2-cohort study that enrolled 40 healthy adult participants. The trial objectives were to evaluate multiple-dose and

single-dose pharmacokinetics, identify any potential drug-drug interactions (DDI), and assess the safety and tolerability of the combination. The combination of denifanstat and resmetirom was generally well-tolerated over the duration of the study, with no safety signals. No SAEs occurred, and there were no clinically significant laboratory AEs, and no treatment-related discontinuations.

Our combination program builds upon preclinical data we presented at the European Association for the Study of the Liver (EASL) Congress in 2024 for two mouse models of MASH, showing that the combination of a FASN inhibitor (TVB-3664, a surrogate for denifanstat) and resmetirom, had a synergistic effect on important liver disease markers, including improvement of NAS by histologic analysis and more robust improvement in hepatic collagen content compared to the single agents. Synergistic activity of the combination was demonstrated in the rate of histological improvement (NAS ≥2 points), which was 33% for FASN inhibitor monotherapy, 25% for resmetirom monotherapy, and 80% for the combination of the two, a level of improvement that greatly exceeds a simple addition of the activity of the two drugs.

We plan to use these data to advance the development of the combination into a Phase 2 proof-of-concept efficacy trial for patients living with MASH with F4 fibrosis, expected to initiate in the second half of 2026, subject to consultation with regulatory authorities.

Acne

In addition to MASH, we are evaluating our FASN inhibitors in acne, a disorder in which dysregulation of fatty acid metabolism also plays a key role. Denifanstat is being developed for acne in China by our license partner for China, Ascletis BioScience Co. Ltd. (Ascletis), a subsidiary of Ascletis Pharma Inc. (Ascletis Pharma). Our potent and selective small molecule FASN inhibitor, TVB-3567, is currently in a first-in-human Phase 1 clinical trial for development of an acne indication. Acne is a promising therapeutic area for application of FASN inhibitors because FASN is required for sebum production, which is upregulated in acne and leads to exacerbation of acne lesions including development of nodules and cysts.

Phase 3 clinical trial of denifanstat in acne

In January 2026, Ascletis reported positive topline results in the open-label Phase 3 trial evaluating the long-term safety of ASC40 (denifanstat) tablets in patients with moderate to severe acne in China.

In December 2025, Ascletis announced that the China National Medical Products Administration (NMPA) accepted its New Drug Application (NDA) for denifanstat for the treatment of moderate to severe acne.

In June 2025, Ascletis announced that denifanstat met all primary and secondary endpoints in its Phase 3 trial in moderate to severe acne vulgaris in China. The Phase 3 clinical trial was a randomized, double-blind, placebo-controlled, multicenter clinical trial of 480 enrolled patients randomized 1:1 to receive denifanstat 50mg or placebo, once daily for 12 weeks.

Ascletis reported the following efficacy data from the Phase 3 trial:

- All primary endpoints were met, including:
    - the percentage of treatment success (defined as an Investigator's Global Assessment (IGA) score of 0 (clear) or 1 (almost clear) with at least a 2-point decrease from baseline) (denifanstat 33.2% vs. placebo 14.6%, $p<0.0001$).
    - the percentage change in total lesion count (denifanstat -57.4% vs. placebo -35.4%, $p<0.0001$).
    - the percentage change in inflammatory lesion count (denifanstat -63.5% vs. placebo -43.2%, $p<0.0001$).
- The secondary endpoint of change in non-inflammatory lesion count was also met (denifanstat -51.9% vs. placebo -28.9%, $p<0.0001$).

Ascletis reported that denifanstat was generally well-tolerated. Following 12 weeks of once-daily oral administration at 50 mg, the incidence rates of TEAEs were comparable between denifanstat and placebo.

Phase 1 clinical trial of TVB-3567

In June 2025, we initiated a first-in-human Phase 1 clinical trial of our potent and selective small molecule FASN inhibitor, TVB-3567, for development of an acne indication. The Phase 1 clinical trial is a randomized double-blind placebo-controlled trial designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of TVB-3567 in healthy participants with or without acne. The trial is comprised of several parts, including single ascending dose cohorts and multiple ascending dose cohorts in participants without acne, followed by testing in participants with acne including evaluation of pharmacodynamic biomarkers.

Subject to consultation with regulatory authorities, and contingent on the results of the Phase 1 trial, we anticipate initiating the Phase 2 trial of TVB-3567 in 2026.

Components of results of operations

Research and development expenses

Research and development expenses represent costs incurred in performing research, development and manufacturing activities in support of our own product development efforts and include internal personnel-related costs (such as salaries, employee benefits and stock-based compensation) for our personnel in research and development functions; as well as external costs, including costs related to acquiring, developing and manufacturing supplies for preclinical studies, clinical trials and other studies, including fees paid to contract manufacturing organizations (CMOs); costs and expenses related to agreements with contract research organizations (CROs), investigative sites and consultants to conduct non-clinical and preclinical studies and clinical trials; and professional and consulting services costs. Research and development expenses also include the costs of acquired product licenses and related technology rights where there is no alternative future use.

All research and development expenses are charged to operations as incurred in accordance with Accounting Standards Codification 730*, Research and Development*. We account for non-refundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received, rather than when the payment is made.

We expect our research and development expenses to increase substantially for the foreseeable future as we advance our drug candidates into and through preclinical studies and clinical trials, pursue regulatory approval and expand our pipeline.

General and administrative expenses

Our general and administrative expenses consist primarily of costs and expenses related to: personnel (including salaries, employee benefits and stock-based compensation) in our executive, finance and accounting and other administrative functions; legal services, including relating to intellectual property and corporate matters; accounting, auditing, consulting and tax services; insurance; information technology; and facility and other allocated costs not otherwise included in research and development expenses.

We expect our general and administrative expenses to increase for the foreseeable future as we increase our headcount and continue to grow our corporate infrastructure.

Other income

Other income consists primarily of interest income earned on our cash, cash equivalents and marketable securities offset by accretion of discounts to maturity on our marketable securities.

Results of operations

Comparison of the years ended December 31, 2025 and 2024

The following table summarizes our results of operations for the periods indicated (in thousands):

	Years Ended December 31,			
	2025	2024	$ Change	% Change
Operating expenses:				
Research and development	$ 39,054	$ 38,444	$ 610	2 %
General and administrative	17,835	16,010	1,825	11 %
Total operating expenses	56,889	54,454	2,435	4 %
Loss from operations	(56,889)	(54,454)	(2,435)	4 %
Total other income	5,851	8,887	(3,036)	(34)%
Net loss	$ (51,038)	$ (45,567)	$ (5,471)	12 %

Research and development – Research and development expenses for the years ended December 31, 2025 and 2024 were comprised of the following (in thousands):

	Years Ended December 31,			
	2025	2024	$ Change	% Change
External expenses				
Clinical development and research	$ 20,987	$ 23,912	$ (2,925)	(12)%
Manufacturing and non-clinical	11,405	8,488	2,917	34 %
External consulting and other	1,940	2,248	(308)	(14)%
Subtotal - external expenses	$ 34,332	$ 34,648	$ (316)	(1)%
Internal expenses				
Personnel costs	$ 3,591	$ 2,814	$ 777	28 %
Stock-based compensation	933	982	(49)	(5)%
Other internal operating expenses	198	—	198	100 %
Subtotal - internal expenses	$ 4,722	$ 3,796	$ 926	24 %
Total research and development expenses	$ 39,054	$ 38,444	$ 610	2 %

Research and development expenses increased by $0.6 million, or 2%, for the year ended December 31, 2025, compared to the year ended December 31, 2024. This increase was primarily due to (i) a $2.9 million increase in manufacturing and non-clinical expenses relating primarily to the $2.5 million up-front license fee recognized in connection with a license agreement with Assia Chemical Industries Ltd., and (ii) a $0.8 million increase in personnel costs due to an increase in headcount. These increases were partially offset by a net decrease in clinical development and research expenses of $2.9 million driven by lower clinical trial costs in connection with start-up activities for a Phase 3 trial of denifanstat in MASH, lower clinical trial expenses for the Phase 2b FASCINATE-2 trial as the trial was substantially complete in the first quarter of 2024 with topline results for the trial announced in January 2024, as well as lower costs for other denifanstat studies. The decrease in clinical development and research expenses were partially offset by an increase in clinical trial costs incurred for our Phase 1 clinical trial of TVB-3567, which was initiated in June 2025, and the Phase 1 PK clinical trial for the combination of denifanstat and resmetirom, which was initiated in September 2025.

External research and development expenses for the years ended December 31, 2025 and 2024 were comprised of the following (in thousands):

	Years Ended December 31,			
	2025	2024	$ Change	% Change
Denifanstat external research and development expenses	$ 28,248	$ 33,838	$ (5,590)	(17)%
TVB-3567 external research and development expenses	6,084	810	5,274	651 %
Total external research and development expenses	$ 34,332	$ 34,648	$ (316)	(1)%

General and administrative – General and administrative expenses increased by $1.8 million, or 11%, for the year ended December 31, 2025, compared to the year ended December 31, 2024 primarily due to (i) a $1.2 million increase in stock-based compensation expense driven by an increase in headcount and (ii) a $0.8 million increase in professional fees, driven by legal fees and the write-off of deferred financing costs related to the 2024 ATM Offering (defined below).

Other income – Other income decreased by $3.0 million, or 34%, for the year ended December 31, 2025, compared to the year ended December 31, 2024, primarily due to a decrease in interest income earned driven by a lower cash, cash equivalents and marketable securities balance as well as lower yields during the year ended December 31, 2025.

Liquidity and capital resources

Sources and uses of cash

Since our inception, we have devoted substantially all of our resources to researching, discovering and developing our pipeline of proprietary FASN inhibitors and other drug targets, organizing and staffing our company, performing business planning, establishing our intellectual property portfolio, raising capital and general and administration activities to support and expand such activities. We do not have any products approved for sale and have not generated any revenue from product sales. Our revenues to date have been generated solely from the license agreement with Ascletis.

To date, we have financed our operations primarily through public and private equity and debt financings, including our IPO of Series A common stock in July 2023 and our follow-on offering in January 2024, from which we received aggregate net proceeds of $190.9 million. Prior to becoming a public company, we raised $233.3 million in gross proceeds from the sale of our redeemable convertible preferred stock and convertible notes.

In August 2024, we entered into a Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co. to establish an at-the-market offering (2024 ATM Offering) through which we could offer and sell, from time to time at our sole discretion, up to $75.0 million of shares of our Series A common stock. In connection with the establishment of the 2025 ATM Offering (as defined below), we terminated the 2024 ATM Offering. No shares of Series A common stock were sold under the 2024 ATM Offering prior to such termination.

In August 2025, we entered into a Sales Agreement with Leerink Partners LLC to establish an at-the-market offering (2025 ATM Offering) through which we may sell, from time to time at our sole discretion, up to $75.0 million shares of our Series A common stock. There were no sales under the 2025 ATM Offering during the year ended December 31, 2025.

As of December 31, 2025, we had cash, cash equivalents and marketable securities of $113.1 million. We do not expect to generate any revenue from commercial product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our drug candidates, which we expect will take a number of years, if ever. We anticipate that we will continue to incur significant expenses for the foreseeable future as we continue to advance our drug candidates through preclinical and clinical trials; manufacture supplies for our preclinical studies and clinical trials; expand our corporate infrastructure, including the costs associated with being a public company; pursue regulatory approval of our drug candidates; hire additional personnel; acquire, discover, validate and develop additional drug candidates; and obtain maintain, expand and protect our intellectual property portfolio.

Until we can generate a sufficient amount of revenue from the commercialization of our drug candidates or additional revenue from collaboration agreements with third parties, if ever, we expect to finance our future cash needs through public or private equity or debt financings, third-party funding and marketing and distribution arrangements, as well as other collaborations, strategic alliances and licensing arrangements, or any combination of these approaches. The sale of equity or convertible debt securities may result in dilution to our stockholders and, in the case of preferred equity securities or convertible debt, those securities could provide for rights, preferences or privileges senior to those of our common stock. Debt financings may subject us to covenant limitations or restrictions on our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Our ability to raise additional funds may be adversely impacted by macroeconomic conditions, disruptions to and volatility in the credit and financial markets and geopolitical turmoil. There can be no assurance that we will be successful in acquiring additional funding at levels sufficient to fund our operations or on terms favorable or acceptable to us. If we are unable to obtain adequate financing when needed or on terms favorable or acceptable to us, we may be forced to delay, reduce the scope of or eliminate one or more of our research and development programs.

Our future capital requirements will depend on many factors, including:

- difficulties obtaining regulatory approval to commence a clinical trial or complying with conditions imposed by a regulatory authority regarding the scope or term of a clinical trial;
- conditions imposed on us by the FDA or other regulatory authorities regarding the scope or design of our clinical trials;
- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs, CMOs, and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly;
- insufficient supply of our drug candidates or other materials necessary to conduct and complete our clinical trials;
- difficulties obtaining institutional review board (IRB) or ethics committee approval to conduct a clinical trial at a prospective site;
- slow enrollment and retention rate of subjects in our clinical trials;
- the FDA or other regulatory authority requiring alterations to any of our study designs, our preclinical strategy or our manufacturing plans;
- governmental or regulatory delays and changes in regulatory requirements, policy and guidelines; serious and unexpected drug-related side effects related to the drug candidate being tested;
- lack of adequate funding to continue clinical trials;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of severe adverse effects in clinical trials of the same class of agents conducted by other companies;
- any changes to our manufacturing process, suppliers or formulation that may be necessary or desired;
- third-party vendors not performing manufacturing and distribution services in a timely manner or to sufficient quality standards;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, good clinical practice (GCP), or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; and
- failure of our third-party contractors, such as CROs and CMOs, or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner.

A change in the outcome of any of these or other variables could significantly change our costs and timing associated with the development of our drug candidates. Furthermore, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such change.

We rely and will continue to rely on third parties in the conduct of our preclinical studies and clinical trials and for manufacturing and supply of our drug candidates. We have no internal manufacturing capabilities, and we will continue to rely on third parties for our preclinical study and clinical trial materials. Given our stage of development, we do not yet have a marketing or sales organization or

commercial infrastructure. Accordingly, if we obtain regulatory approval for any of our drug candidates, we also expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution.

We enter into contracts in the normal course of business for products and services, including contract research and contract manufacturing services, which include provisions allowing for termination under certain conditions and timelines. These contracts generally do not include payments for early termination and are considered cancellable contracts.

Based on our current business plan, we believe that our existing cash, cash equivalents and marketable securities as of December 31, 2025, will be sufficient for us to fund our operating expenses for at least the next 12 months from the issuance of our audited financial statements.

Cash flows

The following table shows a summary of our cash flows for each of the periods presented below (in thousands):

	Years Ended December 31,	
	2025	2024
Net cash (used in) provided by:		
Operating activities	$ (45,650)	$ (42,435)
Investing activities	4,556	(61,683)
Financing activities	275	104,819
Net (decrease) increase in cash and cash equivalents	$ (40,819)	$ 701

Cash flows from operating activities - Net cash used in operating activities was $45.7 million for the year ended December 31, 2025, and primarily related to cash used to fund clinical development, manufacturing and other non-clinical activities for denifanstat, inclusive of start-up costs for a Phase 3 trial of denifanstat in MASH as well as the Phase 1 PK clinical trial for the combination of denifanstat and resmetirom, clinical development and manufacturing costs for TVB-3567, as well as costs associated with operating as a public company.

Net cash used in operating activities was $42.4 million for the year ended December 31, 2024, and primarily related to cash used to fund clinical development, manufacturing and other non-clinical activities for denifanstat, inclusive of clinical-batch manufacturing and other trial start-up costs for a Phase 3 trial of denifanstat in MASH, as well as costs to build out our corporate infrastructure and costs associated with being a public company.

Cash flows from investing activities - Net cash provided by investing activities was $4.6 million for the year ended December 31, 2025 and related to proceeds received from the sale and maturity of marketable securities of $111.4 million, partially offset by purchases of marketable securities of $106.8 million.

Net cash used in investing activities was $61.7 million for the year ended December 31, 2024 and related to purchases of marketable securities of $108.1 million, partially offset by proceeds received from the sale and maturity of marketable securities of $46.4 million.

Cash flows from financing activities - Net cash provided by financing activities was approximately $0.3 million for the year ended December 31, 2025, relating to proceeds from stock option exercises during the period.

Net cash provided by financing activities was $104.8 million for the year ended December 31, 2024, which primarily related to net cash proceeds of $105.7 million received from the sale of Series A common stock in our January 2024 follow-on offering and $0.1 million in proceeds from stock option exercises during the period, offset by the payment of financing costs related to the January 2024 follow-on offering of $1.0 million.

Critical accounting policies and estimates

We prepare our financial statements in accordance with accounting principles generally accepted in the United States of America. The preparation of financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, costs and expenses and related disclosures. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. Actual results could differ significantly from the estimates made and changes in estimates may occur.

While our significant accounting policies are described in more detail in Note 2 in our financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our financial statements.

Accrued research and development expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. The majority of our service providers require advance payments; however, some invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in the financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of the estimates with the service providers and make adjustments if necessary.

We base our expenses related to manufacturing, preclinical studies, clinical trials and other studies on our estimates of the services performed pursuant to contracts with research institutions, CROs and CMOs that conduct and manage such activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees when we have not yet been invoiced or otherwise notified of actual costs, we estimate the level of activity completed in each period. These estimates are based on the review of underlying contracts, discussions with key research and development personnel as to the progress of studies, and communications with the third-party service providers. We also monitor patient enrollment levels and related activities to the extent possible through discussions with CRO personnel to estimate clinical trial costs based on the best information available at each balance sheet date. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. There have been no material changes in estimates for the periods presented within this Annual Report on Form 10-K.

Stock-based compensation expense

We recognize stock-based compensation expense in an amount equal to the estimated grant date fair value of each option grant or stock award over the estimated period of service and vesting. This estimation of the fair value of each stock-based grant or issuance on the date of grant involves numerous assumptions by management. Although we calculate the fair value using the Black Scholes option pricing model, which is a standard option pricing model, this model still requires the use of numerous estimates, including, among others, the expected term of the award, the volatility of the underlying equity security, a risk-free interest rate, fair value of common stock, and expected dividends. The use of different values in connection with these estimates in the Black Scholes option pricing model could produce substantially different results.

For awards with service-based vesting conditions only, we recognize stock-based compensation expense on a straight-line basis over the requisite service or vesting period. For awards with service- and performance- based vesting conditions, we recognize stock-based compensation expense using the graded vesting method over the requisite service period beginning in the period in which the awards are deemed probable to vest, to the extent such awards are probable to vest. We recognize the cumulative effect of changes in the probability outcomes in the period in which the changes occur.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Due to the lack of trading history, our computation of expected stock volatility is based on the volatility rates of comparable publicly held companies over a period equal to the expected term of the option. We expect to continue to do so until such time we have adequate historical data regarding the volatility of our traded stock price. Our computation of expected term is determined using the simplified method, which represents the average of the contractual term of the options and the weighted-average expected vesting period. We believe that we do not have sufficient reliable exercise data in order to justify the use of a method other than the simplified method of estimating the expected exercise term of employee stock option grants. For non-employee stock option grants, we have the option to utilize either the expected term or the contractual term, determined on an award-by-award basis. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the

option. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends to stockholders and have no current intentions to pay cash dividends. The fair value of the common stock is determined based on the quoted market price of our Series A common stock.

Stock-based compensation expense is included in both research and development expenses and general and administrative expenses in the statements of operations and comprehensive loss. There have been no material changes in estimates, or our estimation methods, for the periods presented within this Annual Report on Form 10-K.

Emerging growth company and smaller reporting status

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act (the JOBS Act). Under the JOBS Act, emerging growth companies can delay the adoption of new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. Other exemptions and reduced reporting requirements under the JOBS Act for emerging growth companies include an exemption from the requirement to provide an auditor's report on internal controls over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, as amended, an exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation and less extensive disclosure about our executive compensation arrangements. We have elected to use the extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that (i) we are no longer an emerging growth company or (ii) we affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earliest of (i) the last day of our first fiscal year in which we have total annual gross revenues of $1.235 billion or more, (ii) December 31, 2028, (iii) the date on which we are deemed to be a large accelerated filer, under the rules of the SEC, which means the market value of equity securities that is held by non-affiliates exceeds $700.0 million as of the prior June 30th and (iv) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

We are also a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our stock held by non-affiliates is less than $250 million or (ii) our annual revenue is less than $100 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

Recently adopted accounting pronouncements

See "Notes to the Financial Statements—Note 2" included in our financial statements in Item 8 in this Annual Report for more information.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We are a smaller reporting company as defined by Rule 12b-2 of the Securities Exchange Act of 1934 and are not required to provide the information under this item.

Item 8. Financial Statements and Supplementary Data

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the stockholders and the Board of Directors of Sagimet Biosciences Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheet of Sagimet Biosciences Inc. (the Company) as of December 31, 2025, the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for the year then ended, and the related notes (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2025, and the results of its operations and its cash flows for the year then ended, in conformity with U.S. generally accepted accounting principles.

We also have audited the adjustments to the 2024 financial statements to retrospectively adopt ASU 2023-09 as described in Note 2. In our opinion, such adjustments are appropriate and have been properly applied. We are not engaged to audit, review, or apply any procedures to the 2024 financial statements of the Company other than with respect to the adjustments and, accordingly, we do not express an opinion or any other form of assurance on the 2024 financial statements taken as a whole.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audit. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audit, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audit included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audit also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2025.

Philadelphia, Pennsylvania
March 11, 2026

Report of Independent Registered Public Accounting Firm

To the stockholders and the Board of Directors of Sagimet Biosciences Inc.

Opinion on the Financial Statements

We have audited, before the effects of the adjustments to retrospectively apply the change in accounting discussed in Note 2 to the financial statements, the balance sheet of Sagimet Biosciences Inc. (the "Company") as of December 31, 2024, the related statement of operations and comprehensive loss, stockholders' equity, and cash flows, for the year ended December 31, 2024, and the related notes (collectively referred to as the "financial statements") (the 2024 financial statements before the effects of the retrospective adjustments discussed in Note 2 to the financial statements are not presented herein). In our opinion, the 2024 financial statements, before the effects of the adjustments to retrospectively apply the change in accounting discussed in Note 2 to the financial statements, present fairly, in all material respects, the financial position of the Company as of December 31, 2024, and the results of its operations and its cash flows for the year ended December 31, 2024, in conformity with accounting principles generally accepted in the United States of America.

We were not engaged to audit, review, or apply any procedures to the adjustments to retrospectively apply the change in accounting discussed in Note 2 to the financial statements, and accordingly, we do not express an opinion or any other form of assurance about whether such retrospective adjustments are appropriate and have been properly applied. Those retrospective adjustments were audited by the successor auditor.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

San Francisco, California
March 12, 2025

We began serving as the Company's auditor in 2015. In 2025 we became the predecessor auditor.

SAGIMET BIOSCIENCES INC.

BALANCE SHEETS

(in thousands, except for share and per share amounts)

	As of	
	December 31, 2025	December 31, 2024
Assets		
Current assets:		
Cash and cash equivalents	$ 35,021	$ 75,840
Short-term marketable securities	78,103	75,410
Prepaid expenses and other current assets	3,280	1,524
Total current assets	116,404	152,774
Long-term marketable securities	—	7,408
Operating lease right-of-use assets	78	77
Total assets	$ 116,482	$ 160,259
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,309	$ 1,425
Accrued expenses and other current liabilities	3,714	2,951
Operating lease liabilities	78	78
Total current liabilities	5,101	4,454
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Undesignated preferred stock, $0.0001 per share: 10,000,000 shares authorized; no shares issued and outstanding at December 31, 2025 and December 31, 2024	—	—
Series A common stock, $0.0001 per share: 500,000,000 shares authorized; 31,954,105 shares issued and outstanding at December 31, 2025; 30,674,855 shares issued and outstanding at December 31, 2024	3	3
Series B common stock, $0.0001 per share: 15,000,000 shares authorized; 567,494 shares issued and outstanding at December 31, 2025; 1,520,490 shares issued and outstanding at December 31, 2024	—	—
Additional paid-in capital	457,607	450,883
Accumulated deficit	(346,349)	(295,311)
Accumulated other comprehensive income	120	230
Total stockholders' equity	111,381	155,805
Total liabilities and stockholders' equity	$ 116,482	$ 160,259

The accompanying notes are an integral part of these financial statements.

SAGIMET BIOSCIENCES INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(in thousands, except for share and per share amounts)

	Years Ended December 31,	
	2025	**2024**
Operating expenses:		
Research and development	$ 39,054	$ 38,444
General and administrative	17,835	16,010
Total operating expenses	56,889	54,454
Loss from operations	(56,889)	(54,454)
Other income:		
Interest income and other, net	5,851	8,887
Total other income	5,851	8,887
Net loss	$ (51,038)	$ (45,567)
Net loss per share of Series A and Series B common stock outstanding, basic and diluted	$ (1.58)	$ (1.45)
Weighted-average shares of Series A and Series B common stock outstanding, basic and diluted	32,345,525	31,350,725
Net loss	$ (51,038)	$ (45,567)
Other comprehensive (loss) income:		
Net unrealized (loss) gain on marketable securities	(110)	200
Total comprehensive loss	$ (51,148)	$ (45,367)

The accompanying notes are an integral part of these financial statements.

SAGIMET BIOSCIENCES INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

(in thousands, except share amounts)

	Series A Common Stock		Series B Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance at January 1, 2024	21,375,402	$ 2	1,520,490	$ —	$ 340,777	$ (249,744)	$ 30	$ 91,065
Sale of Series A common stock, net of issuance costs of $7,796	9,000,000	1	—	—	104,704	—	—	104,705
Issuance of Series A common stock upon exercise of stock options	17,995	—	—	—	114	—	—	114
Issuance of Series A common stock for vesting of restricted stock units	281,458	—	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	5,288	—	—	5,288
Unrealized gain on marketable securities	—	—	—	—	—	—	200	200
Net loss	—	—	—	—	—	(45,567)	—	(45,567)
Balance at December 31, 2024	30,674,855	$ 3	1,520,490	$ —	$ 450,883	$ (295,311)	$ 230	$ 155,805
Issuance of Series A common stock for vesting of restricted stock units	281,462	—	—	—	—	—	—	—
Issuance of Series A common stock upon exercise of stock options	44,792	—	—	—	275	—	—	275
Conversion of Series B common stock to Series A common stock	952,996	—	(952,996)	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	6,449	—	—	6,449
Unrealized loss on marketable securities	—	—	—	—	—	—	(110)	(110)
Net loss	—	—	—	—	—	(51,038)	—	(51,038)
Balance at December 31, 2025	31,954,105	$ 3	567,494	$ —	$ 457,607	$ (346,349)	$ 120	$ 111,381

The accompanying notes are an integral part of these financial statements.

SAGIMET BIOSCIENCES INC.

STATEMENTS OF CASH FLOWS

(in thousands)

	Years Ended December 31,	
	2025	**2024**
Cash flows from operating activities		
Net loss	$ (51,038)	$ (45,567)
Adjustments to reconcile net loss to net cash used in operating activities:		
Accretion of discount on marketable securities, net	(389)	(1,253)
Non-cash operating lease expense	151	145
Stock-based compensation expense	6,449	5,288
Write-off of deferred financing costs	230	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(1,830)	(5)
Accounts payable, accrued expenses and other current liabilities	929	(907)
Operating lease liabilities	(152)	(136)
Net cash used in operating activities	(45,650)	(42,435)
Cash flows from investing activities		
Purchases of marketable securities	(106,864)	(108,087)
Sales and maturities of marketable securities	111,420	46,404
Net cash provided by (used in) investing activities	4,556	(61,683)
Cash flows from financing activities		
Proceeds from sale of Series A common stock, net of issuance costs	—	105,750
Payment of financing costs	—	(1,045)
Proceeds from exercise of stock options	275	114
Net cash provided by financing activities	275	104,819
Net (decrease) increase in cash and cash equivalents	(40,819)	701
Cash and cash equivalents at beginning of period	75,840	75,139
Cash and cash equivalents at end of period	$ 35,021	$ 75,840
Supplemental non-cash investing and financing activities:		
Deferred financing costs within accounts payable and accrued expenses	$ 9	$ —
Right-of-use assets obtained in exchange for operating lease obligations	$ 152	$ 149

The accompanying notes are an integral part of these financial statements.

1. Description of Business and Basis of Presentation

Sagimet Biosciences Inc. (the Company), a Delaware corporation headquartered in San Mateo, California, is a clinical-stage biopharmaceutical company developing novel therapeutics called fatty acid synthase (FASN) inhibitors that target dysfunctional metabolic and fibrotic pathways in diseases resulting from the overproduction of the fatty acid, palmitate. The Company's lead drug candidate, denifanstat, is an oral, once-daily pill and selective FASN inhibitor in development for metabolic dysfunction-associated steatohepatitis (MASH), acne and select forms of cancer. The Company's second FASN inhibitor, TVB-3567, is a potent and selective small molecule FASN inhibitor in development for acne.

In MASH, denifanstat met all primary and multiple secondary endpoints in FASCINATE-2, a Phase 2b clinical trial in F2/F3 MASH, was granted Breakthrough Therapy designation for the treatment of non-cirrhotic MASH with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) by the U.S. Food and Drug Administration (FDA) and has completed end-of-Phase 2 interactions with the FDA. In December 2025, the Company announced completion of its Phase 1 pharmacokinetic (PK) clinical trial of a combination of denifanstat and thyroid hormone receptor beta (THR-β) agonist, resmetirom, for development in MASH.

In acne, denifanstat met all primary and secondary endpoints in a Phase 3 trial in moderate to severe acne vulgaris conducted by the Company's license partner, Ascletis BioScience Co. Ltd. (Ascletis), in China. In December 2025, Ascletis announced that the China National Medical Products Administration (NMPA) accepted its New Drug Application (NDA) for denifanstat for the treatment of moderate to severe acne. In June 2025, the Company initiated a first-in-human Phase 1 clinical trial of Sagimet's second FASN inhibitor, TVB-3567, for development of an acne indication.

Basis of presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted (GAAP) in the United States. Any reference in these notes to applicable guidance is meant to refer to GAAP as found in the Accounting Standards Codification (ASC) and Accounting Standards Updates (ASU) promulgated by the Financial Accounting Standards Board (FASB).

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities as of the date of the financial statements and reported amounts of revenues and expenses during the reporting period. Such estimates include accruals of research and development expenses, accrued costs for services rendered under agreements with third-party contract research organizations (CROs) and stock option valuations and stock-based compensation. On an ongoing basis, the Company evaluates its estimates and judgments, which are based on historical and anticipated results and trends and on various other assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Emerging growth company status

The Company is an emerging growth company (EGC) as defined in the Jumpstart Our Business Startups Acts of 2012, as amended (the JOBS Act), and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not EGCs. The Company may take advantage of these exemptions until it is no longer an EGC under Section 107 of the JOBS Act and has elected to use the extended transition period for complying with new or revised accounting standards. As a result of this election, the Company's financial statements may not be comparable to those issued by companies that comply with the effective dates pursuant to public company FASB standards.

Liquidity

The accompanying financial statements have been prepared assuming the Company will continue as a going concern, which contemplates continuity of operations, realization of assets and the satisfaction of liabilities and commitments in the normal course of business. The Company will require substantial additional capital to fund its research and development and ongoing operating expenses. As of December 31, 2025, the Company has relied on public and private equity and debt financings and proceeds from licensing arrangements to fund its operations. The Company has incurred recurring losses and negative cash flows from operations since inception, and, as of December 31, 2025, had an accumulated deficit of $346.3 million and cash, cash equivalents and marketable securities of $113.1 million. The Company expects to incur additional losses and negative cash flows from operations for the foreseeable future.

In July and August 2023, the Company completed its initial public offering (IPO) and, inclusive of the partial exercise of the underwriters' overallotment option, the Company sold an aggregate of 6,026,772 shares of Series A common stock at a public offering price of $16.00 per share and received $86.2 million in net proceeds. In January 2024, the Company completed a follow-on offering whereby it sold 9,000,000 shares of its Series A common stock at a price of $12.50 per share and received $104.7 million in proceeds, net of issuance costs of $7.8 million.

In August 2024, the Company entered into a Controlled Equity Offering Sales Agreement with Cantor Fitzgerald & Co. to establish an at-the-market offering (2024 ATM Offering) through which the Company could sell, from time to time at its sole discretion, up to $75.0 million shares of its Series A common stock. In connection with the establishment of the 2025 ATM Offering (as defined below), the Company terminated the 2024 ATM Offering. No shares of Series A common stock were sold under the 2024 ATM Offering prior to such termination.

In August 2025, the Company entered into a Sales Agreement with Leerink Partners LLC to establish an at-the-market offering (2025 ATM Offering) through which the Company may sell, from time to time at its sole discretion, up to $75.0 million shares of its Series A common stock. There were no sales under the 2025 ATM Offering during the year ended December 31, 2025.

The Company expects that its cash, cash equivalents and marketable securities as of December 31, 2025 will be sufficient to fund the Company's operating expenses for at least the next 12 months from the issuance of these financial statements. In the future, the Company will need to raise additional funds until it is able to generate sufficient revenues to fund its development activities. The Company's future operating activities, coupled with its plans to raise capital or issue debt financing, may provide additional liquidity in the future, however these actions are not solely within the control of the Company, and the Company is unable to predict the outcome of these actions to generate the liquidity ultimately required.

2. Significant Accounting Policies

Segment information

The Company determines and presents operating segments based on the information that is regularly reviewed by the Chief Executive Officer, who is the Company's chief operating decision maker (CODM), in accordance with ASC 280, *Segment Reporting*. The Company has determined that it operates as a single business segment, developing and commercializing therapeutics for the treatment of MASH and other diseases where FASN plays a pathogenic role. Refer to Note 10, Segment Reporting for further information related to the Company's segment.

Concentration of credit risk

Financial instruments that potentially subject the Company to concentration of credit risk consist of cash, cash equivalents and marketable securities. The Company holds cash, cash equivalents and marketable securities at third-party financial institutions, that may from time to time, be in excess of Federal Deposit Insurance Corporation (FDIC) insurance limits. However, the Company believes its risk of loss is minimal as the majority of its cash, cash equivalents and marketable securities are held in custodial accounts at multiple large financial institutions which are well established and of high quality. The Company has not experienced any losses to date.

Cash and cash equivalents

The Company considers only those investments which are highly liquid, readily convertible to cash and purchased with an original maturity of three months or less to be cash equivalents. Marketable securities are those investments with original maturities in excess of three months. As of December 31, 2025 and 2024, cash and cash equivalents consisted of bank deposits, deposits in money market funds as well as investments in certain Agency securities.

Marketable securities

The Company classifies its marketable securities as available-for-sale and records such assets at estimated fair value in the balance sheets. The Company adopted ASU No. 2016-13, *Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses of Financial Instruments* on January 1, 2024. Marketable securities for which the estimated fair value is lower than amortized cost are evaluated for credit impairment. Credit impairment is recorded through the statements of operations and comprehensive loss via an allowance for credit losses account, and any remaining unrealized gains and losses are reported as a component of other comprehensive income (loss) within the statements of operations and comprehensive loss and as a separate component of stockholders' equity. The

Company classifies marketable securities with remaining maturities greater than three months but less than one year as current assets on the balance sheets, and those with remaining maturities greater than one year are classified as long-term marketable securities. For all marketable securities which the estimated fair value was lower than the amortized cost as of December 31, 2025 and 2024, the decline in fair value was determined to be primarily driven by a decline in market interest rates and not driven by credit impairment. As of December 31, 2025, the Company has not recognized any impairment or credit losses on its available for sale securities.

Leases

The Company determines if an arrangement is or contains a lease and the classification of that lease at contract inception. Specifically, the Company considers whether it controls the underlying asset and has the right to obtain substantially all the economic benefits or outputs from the asset. The Company enters into lease agreements for its office facility and accounts for its lease obligations under ASU No. 2016-02, *Leases* (Topic 842). The Company's operating lease asset is included in "operating lease right-of-use assets" (ROU assets) and the current portion of the operating lease liability is included in "operating lease liabilities" in the accompanying balance sheets. As of December 31, 2025 and 2024, the Company had no finance leases.

Operating lease ROU assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at the lease commencement date. Operating lease ROU assets are based on the corresponding lease liability adjusted for (i) payments made at or before the commencement date, (ii) initial direct costs incurred and (iii) tenant incentives under the lease. The Company does not account for renewals or early terminations unless it is reasonably certain to exercise these options at commencement. Operating lease expense is recognized on a straight-line basis over the lease term. The Company accounts for lease and non-lease components as a single lease component for operating leases. The Company does not record leases with terms of 12 months or less on the balance sheets.

As the implicit rate for the operating lease was not determinable, the Company used an incremental borrowing rate based on the information available at the lease commencement date in determining the present value of future payments. The Company's incremental borrowing rate was estimated to approximate the interest rate on a collateralized basis with similar terms and payments, in an economic environment where the leased asset is located. The Company determined the incremental borrowing rate by considering various factors, such as its credit rating, interest rates of similar debt instruments of entities with comparable credit rating, the lease term and the currency in which the lease was denominated.

Accrued research and development expense

Research and development expenses represent costs incurred in performing research, development and manufacturing activities in support of the Company's product development efforts and include personnel-related costs (such as salaries, employee benefits and stock-based compensation) for personnel in research and development functions; as well as external costs, including costs related to acquiring, developing and manufacturing supplies for preclinical studies, clinical trials and other studies, including fees paid to contract manufacturing organizations (CMOs); costs and expenses related to agreements with contract research organization (CROs), investigative sites and consultants to conduct non-clinical and preclinical studies and clinical trials; and professional and consulting services costs. Research and development expenses also include the costs of acquired product licenses and related technology rights where there is no alternative future use.

All research and development expenses are charged to operations as incurred in accordance with ASC 730, *Research and Development*. Non-refundable advance payments for goods or services that will be used in future research and development activities are deferred and expensed when the services have been performed or as the goods are delivered, rather than when the payment is made.

The Company estimates its manufacturing, preclinical study, clinical trial and other study expenses based on the services performed pursuant to contracts with research institutions, CROs and CMOs that conduct and manage such activities on the Company's behalf. In accruing service fees when the Company has not yet been invoiced or otherwise notified of actual costs, the Company estimates the level of activity completed in each period. These estimates are based on the review of underlying contracts, discussions with key research and development personnel as to the progress of studies and communications with the third-party service providers. The Company also monitors patient enrollment levels and related activities to the extent possible through discussions with CRO personnel to estimate clinical trial costs based on the best information available at each balance sheet date. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. There have been no material changes in estimates for the periods presented.

Common stock warrants

From time to time, the Company has issued warrants to investors and creditors together with the Company's debt and equity financings. The Company accounts for warrants in accordance with the guidance contained in ASC 815, *Derivatives and Hedging*. Under ASC 815-40, warrants that meet the criteria for equity treatment are recorded in stockholders' equity. The warrants are subject to re-evaluation of the proper classification and accounting treatment at each reporting period. If the warrants no longer meet the criteria for equity treatment, they will be recorded as a liability and remeasured each period with changes recorded in the statement of operations and comprehensive loss. The Company values warrants using an option pricing model.

Stock-based compensation expense

The Company provides share-based payments in the form of stock options and restricted stock awards. For awards only subject to service conditions, the Company uses the straight-line attribution method for recognizing compensation expense over the requisite service period, which is generally the vesting period of the award. Compensation expense is recognized on awards ultimately expected to vest. Forfeitures are recorded when they occur.

For awards with performance vesting conditions, the Company evaluates the probability of achieving the performance condition at each reporting date. No compensation expense is recognized for awards subject to performance conditions until it is probable that the performance condition will be met. If the performance condition is probable of being achieved, the Company recognizes expense for such performance awards over the requisite service period using the accelerated attribution method.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Due to the lack of trading history, the Company's computation of expected stock volatility is based on the volatility rates of comparable publicly held companies over a period equal to the expected term of the option. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The Company's computation of expected term is determined using the simplified method, which represents the average of the contractual term of the options and the weighted-average expected vesting period. The Company believes that it does not have sufficient reliable exercise data in order to justify the use of a method other than the simplified method of estimating the expected exercise term of employee stock option grants. For non-employee stock option grants, the Company has the option to utilize either the expected term or the contractual term, determined on an award-by-award basis. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the option. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends to stockholders and has no current intentions to pay cash dividends.

The fair value of the common stock is determined based on the quoted market price of the Company's Series A common stock.

Income taxes

The Company accounts for income taxes using the asset and liability method. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates. In evaluating the ability to recover its deferred income tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. In the event the Company determines that it would be able to realize its deferred income tax assets in the future in excess of their net recorded amount, it would make an adjustment to the valuation allowance that would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period when such determination is made. As of December 31, 2025 and 2024, the Company has recorded a full valuation allowance on its deferred tax assets.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Net loss per share attributable to common stockholders

Basic and diluted net loss per share is computed using the two-class method required for multiple classes of common stock and participating securities. The Company's participating securities do not have a contractual obligation to share in the Company's losses. As such, the net loss was attributed entirely to common stockholders for all periods presented. Basic net loss per common share

attributable to common stockholders is calculated by dividing the net loss by the weighted-average number of common shares outstanding during the period, without consideration of potentially dilutive securities. Diluted net loss per share attributable to common stockholders is computed by dividing the net loss by the weighted-average number of common shares and potentially dilutive securities outstanding for the period. For purposes of the diluted net loss per share attributable to common stockholders' calculation, common stock options, restricted stock units and common stock warrants are considered to be potentially dilutive securities. As the Company has reported a net loss for the periods presented, basic and diluted net loss per share attributable to common stockholders is the same as all potentially dilutive securities would have an anti-dilutive impact.

The following table presents the calculation of basic and diluted net loss per share for the years ended December 31, 2025 and 2024 (in thousands, except share and per share data):

	Years Ended December 31,	
	2025	2024
Numerator:		
Net loss	$ (51,038)	$ (45,567)
Denominator:		
Weighted-average shares of Series A and Series B common stock outstanding, basic and diluted	32,345,525	31,350,725
Net loss per share of Series A and Series B common stock outstanding, basic and diluted	$ (1.58)	$ (1.45)

The following potentially dilutive securities have been excluded from the computation of diluted weighted-average shares of Series A and Series B common stock outstanding, as their effect would have been anti-dilutive:

	Years Ended December 31,	
	2025	2024
Options to purchase Series A common stock	5,722,326	4,462,517
Warrants to purchase Series A common stock	1,000	1,000
Restricted stock units	830,077	844,382
Total	6,553,403	5,307,899

Foreign currency translation

The Company considers the U.S. dollar to be its functional currency. Expenses denominated in foreign currencies are translated at the exchange rate on the date the expense is incurred. The effect of exchange rate fluctuations on translating foreign currency assets and liabilities into U.S. dollars is included in the statements of operations and comprehensive loss. Foreign exchange transaction gains and losses are included in the results of operations and are not material in the Company's financial statements.

Recently adopted accounting pronouncements

The Company considers the applicability and impact of all ASUs. ASUs not discussed below were assessed and either determined to be not applicable or expected to have a minimal impact on the Company's financial statements.

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740)—Improvements to Income Tax Disclosures*, a final standard on improvements to income tax disclosures. The standard requires disaggregated information about a reporting entity's effective tax rate reconciliation as well as information on income taxes paid. The standard is intended to benefit investors by providing more detailed income tax disclosures that would be useful in making capital allocation decisions and applies to all entities subject to income taxes. The new standard is effective for annual periods beginning after December 15, 2025 for EGCs under the JOBS Act. Early adoption is permitted for annual financial statements that have not yet been issued or made available for issuance. The Company elected to early adopt ASU 2023-09 on a retrospective basis beginning with this Annual Report. See Note 9, Income Taxes, for the updated disclosures as a result of adopting this ASU.

New accounting pronouncements not yet adopted

In November 2024, the FASB issued ASU 2024-03, *Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses*, which requires public business entities

to disclose, for interim and annual reporting periods, additional information about certain income statement expense categories. ASU 2024-03 is effective for annual periods beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. Early adoption is permitted and is effective on either a prospective basis or retrospective basis. The Company is currently evaluating the impact of the adoption of this standard on its financial statements and related disclosures.

One Big Beautiful Bill Act

On July 4, 2025, the One Big Beautiful Bill Act (OBBBA) was enacted in the United States. The OBBBA includes significant provisions, such as the permanent extension of certain expiring provisions of the Tax Cuts and Jobs Act and modifications to capitalization of research and development expenses, among others. The legislation has multiple effective dates, with certain provisions effective in 2025 and others implemented through 2027. The Company assessed the provisions of the OBBBA and included any changes that impacted the Company in its provision for income taxes for the year ended December 31, 2025. The OBBBA had no impact on the Company's financial statements and results of operations due to its cumulative tax loss and tax effect of a full valuation allowance against those balances. The Company will continue to assess the future potential impacts of this legislation on its deferred tax assets, financial statements and related disclosures.

3. Fair Value Measurements and Fair Value of Financial Instruments

The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1 - Quoted prices in active markets for identical assets or liabilities.

Level 2 - Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3 - Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

As of December 31, 2025 and 2024, financial assets measured at fair value on a recurring basis consisted of cash equivalents and marketable securities. Cash equivalents consist primarily of money market funds and other investments that are readily convertible into cash and have maturities of three months or less at the time of acquisition. The fair value of cash equivalents was $34.7 million and $75.3 million as of December 31, 2025 and, 2024, respectively. The Company considers marketable securities with maturities greater than three months at the time of acquisition to be available for sale securities. The fair value of available for sale securities was $78.1 million and $82.8 million as of December 31, 2025, and 2024, respectively. These available-for-sale securities have expected maturities ranging from 0.5 to 12.0 months, and securities with an expected maturity greater than 12 months as of the balance sheet date, are classified in long-term. There were no available-for-sale securities with expected maturities greater than 12 months as of December 31, 2025. The fair value of marketable securities, which are Level 2 financial instruments, is based upon market prices quoted on the last day of the fiscal period or other observable market inputs. The Company obtains pricing information from its investment manager and generally determines the fair value of investment securities using standard observable inputs, including reported trades, broker-dealer quotes, bids and/or offers.

The Company evaluates securities with unrealized losses, if any, to determine whether the decline in fair value has resulted from credit loss or other factors, including various qualitative factors. As of December 31, 2025, the Company has not recognized any impairment or credit losses on the Company's available for sale securities. While the Company classifies these securities as available for sale, the Company does not intend to sell its investments and based on its current plans, the Company currently believes it has the ability to hold these investments until maturity.

The carrying values of the Company's accounts payable and accrued expenses and other current liabilities approximate their fair values due to the short-term nature of these liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

The Company's Level 3 liabilities that are measured at fair value on a recurring basis consist of the Series A common stock warrant liability related to the warrant to purchase 1,000 shares of Series A common stock with an exercise price of $69.94 per share and an expiration date of July 18, 2026, the third anniversary date of the closing of the Company's IPO. The fair value of the Series A common stock warrant liability was immaterial as of December 31, 2025 and 2024, as well as the change in fair value during the years ended December 31, 2025 and 2024. There were no transfers within the hierarchy during the periods presented.

The following tables set forth the Company's financial assets that were measured at fair value on a recurring basis by level within the fair value hierarchy (in thousands):

		December 31, 2025			
	Valuation Hierarchy	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Assets					
Cash equivalents:					
Money market funds	Level 1	$ 33,219	$ —	$ —	$ 33,219
Corporate debt securities	Level 2	1,499	—	—	1,499
Total cash equivalents		34,718	—	—	34,718
Short-term marketable securities:					
Commercial paper	Level 2	18,061	14	(4)	18,071
Corporate debt securities	Level 2	1,500	3	—	1,503
U.S. Treasury securities	Level 2	50,340	92	—	50,432
Agency securities	Level 2	2,033	1	—	2,034
Asset-backed securities	Level 2	6,049	16	(2)	6,063
Total short-term marketable securities		77,983	126	(6)	78,103
Total cash equivalents and marketable securities		$ 112,701	$ 126	$ (6)	$ 112,821

		December 31, 2024			
	Valuation Hierarchy	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Assets					
Cash equivalents:					
Money market funds	Level 1	$ 72,800	$ —	$ —	$ 72,800
U.S. Treasury securities	Level 2	2,477	—	—	2,477
Total cash equivalents		75,277	—	—	75,277
Short-term marketable securities:					
Commercial paper	Level 2	14,447	25	(1)	14,471
Corporate debt securities	Level 2	6,909	7	—	6,916
U.S. Treasury securities	Level 2	27,493	123	—	27,616
Agency securities	Level 2	21,345	12	(2)	21,355
Asset-backed securities	Level 2	5,030	22	—	5,052
Total short-term marketable securities		75,224	189	(3)	75,410
Long-term marketable securities:					
U.S. Treasury securities	Level 2	4,884	36	—	4,920
Asset-backed securities	Level 2	2,480	8	—	2,488
Total long-term marketable securities		7,364	44	—	7,408
Total cash equivalents and marketable securities		$ 157,865	$ 233	$ (3)	$ 158,095

4. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	As of	
	December 31, 2025	December 31, 2024
Prepaid clinical costs	$ 973	$ 436
Prepaid research and development costs	1,395	48
Prepaid insurance	431	577
Deferred financing costs	282	306
Other	199	157
Total prepaid expenses and other current assets	$ 3,280	$ 1,524

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	As of	
	December 31, 2025	December 31, 2024
Accrued payroll-related costs	$ 1,617	$ 1,358
Accrued clinical costs	561	528
Accrued research and development costs	1,242	516
Accrued general and administrative costs	267	544
Other	27	5
Total accrued expenses and other current liabilities	$ 3,714	$ 2,951

6. Commitments and Contingencies

License and other agreements

Ascletis BioScience Co. Ltd

In January 2019, the Company entered into a license agreement that became effective in February 2019 with Ascletis BioScience Co. Ltd. (Ascletis), a subsidiary of Ascletis Pharma Inc. (Ascletis Pharma), a biotechnology company incorporated in the Cayman Islands and headquartered in Hangzhou, China. Ascletis Pharma, through a subsidiary, was the lead investor in the Company's Series E redeemable convertible preferred stock financing in February 2019. The parties entered into this agreement with the intention to develop, manufacture, and commercialize the Company's proprietary FASN inhibitor, denifanstat, which Ascletis refers to as ASC40. Under the terms of the license agreement, the Company granted Ascletis and its affiliates an exclusive, royalty-bearing sublicensable right and license under the Company's intellectual property to develop, manufacture, commercialize and otherwise exploit denifanstat and other products containing denifanstat-related compounds in Greater China, consisting of the People's Republic of China, Hong Kong, Macau and Taiwan.

The Company is eligible to receive development and commercial milestone payments from Ascletis in aggregate of up to $122.0 million as well as tiered royalties ranging from percentages in the high single digits to mid-teens on future net sales of denifanstat in Greater China. The license and the research and development services components of this license agreement are representative of a relationship with a customer, and therefore, the Company evaluated the license agreement under the provisions of ASC 606, *Revenue from Contracts with Customers*. The developmental and commercial event-based milestone payments represent variable consideration, and the Company used the most likely amount method to estimate this variable consideration because the potential milestone payment is a binary event, as the Company will either receive the milestone payment or it will not. Given the high degree of uncertainty around achievement of these milestones, the Company determined the milestone amounts to be fully constrained and will not recognize revenue until the uncertainty associated with these payments is resolved. Any consideration related to royalties will be recognized if and when the related sales occur. The Company re-assesses the transaction price in each reporting period and when events whose outcomes are resolved or other changes in circumstances occur.

In July 2023, the Company entered into an Assignment and Assumption Agreement with Ascletis and Ascletis' affiliate Gannex Pharma Co., Ltd. (Gannex) under which Ascletis, while remaining responsible for performance under the license agreement, assigned

all of its rights and obligations under the license agreement to Gannex and Gannex assumed such rights and obligations, effective as of October 2019.

Assia Chemical Industries Ltd.

In September 2025, the Company entered into a term sheet with Assia Chemical Industries Ltd. (Assia), doing business as TAPI Technology & API Series (TAPI), a subsidiary of Teva Pharmaceutical Industries Ltd. and in December 2025, the Company entered into a license agreement with TAPI replacing the term sheet (License Agreement). Under the agreement, TAPI granted the Company a global, exclusive license to certain intellectual property rights covering innovative forms of TAPI's resmetirom active pharmaceutical ingredient (API) for Sagimet's technical evaluation and manufacture, and, if elected by the Company, further development of a fixed-dose combination (FDC) product containing denifanstat and resmetirom.

Upon execution of the term sheet in September 2025, a non-refundable up-front payment of $2.5 million was due, which was paid and recognized in research and development expense during the year ended December 31, 2025. Pursuant to the License Agreement, the Company is obligated to pay TAPI potential additional manufacturing-related milestones of up to $5.5 million as well as a low single-digit royalty on net sales of the FDC product. The License Agreement terminates upon the date certain TAPI know-how ceases to be confidential information or the last of the TAPI patents expires, whichever is later, unless earlier terminated by either party in accordance with the terms of the License Agreement.

Facility Lease Agreement

In March 2019, the Company executed a 38-month non-cancelable operating lease agreement for 3,030 square feet of office space for its headquarters facility in San Mateo, California, which commenced April 1, 2019. In December 2021, the lease agreement was amended to extend the term of the lease through June 2024; in April 2024, the Company amended the lease agreement to (i) extend the lease through June 30, 2025 and (ii) increase the monthly lease payment to approximately $13,000 beginning on July 1, 2024, which resulted in an increase in the Company's operating lease right-of-use asset and corresponding operating lease liability of $0.1 million on the amendment date. In May 2025, the Company amended the lease agreement to extend the term of the lease through June 2026, which resulted in an increase in the Company's operating lease right-of-use asset and corresponding operating lease liability of $0.2 million on the amendment date.

Operating lease costs were $0.2 million and $0.2 million for the years ended December 31, 2025, and 2024, respectively.

The following is a schedule by year of future maturities of the Company's operating lease liabilities (in thousands):

	December 31, 2025
2026	$ 80
Total lease payments	80
Less: interest	(2)
Total	$ 78

Supplemental cash flow information related to leases was as follows (in thousands):

	Year Ended December 31,	
	2025	2024
Cash paid for amounts included in the measurement of lease liabilities:		
Operating cash flows from operating leases	$ 159	$ 159

Weighted-average remaining lease term and discount rate were as follows as of December 31, 2025:

Weighted-average remaining lease term	0.5 years
Weighted-average discount rate	9 %

Guarantees and indemnifications

In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. In addition, the Company has entered into indemnification agreements with members of its board of directors and its executive officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2025, the Company does not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded related liabilities.

Legal Proceedings

From time to time, the Company may become involved in various legal proceedings that arise in the ordinary course of its business. The Company records a liability for such matters when it is probable that future losses will be incurred and that such losses can be reasonably estimated. Significant judgment by the Company is required to determine both probability and the estimated amount. The Company is not party to any material legal proceedings as of December 31, 2025.

7. Stockholders' Equity

Common stock

As of December 31, 2025 and 2024, the Company had authorized 500,000,000 shares of Series A common stock, $0.0001 par value per share, and 15,000,000 shares of Series B common stock, $0.0001 par value per share. Holders of Series A common stock are entitled to one vote and Series B common stock are not entitled to vote. Upon the voluntary or involuntary liquidation, dissolution or winding up of the Company, the net assets of the Company will be distributed pro rata to the holders of Series A common stock and Series B common stock. Each share of Series B common stock is convertible, at any time at the option of the holder, into one share of Series A common stock, unless that holder would beneficially own a number of Series A common stock in excess of 4.99% of the total number of shares of Series A common stock then issued and outstanding.

In December 2025, certain holders of the Company's Series B common stock elected to convert 952,996 shares of the Company's Series B common stock into Series A common stock.

Undesignated preferred stock

As of December 31, 2025 and 2024, the Company had authorized 10,000,000 shares of undesignated preferred stock, $0.0001 par value per share, of which none were issued and outstanding.

8. Stock-Based Compensation

The 2023 Stock Option and Incentive Plan (2023 Plan) was adopted by the board of directors, approved by the Company's stockholders on July 4, 2023, and became effective on July 13, 2023, replacing the 2017 Equity Incentive Plan. The number of shares initially reserved for issuance under the 2023 Plan was 2,585,968. The number of shares will automatically increase each January 1, by (i) 4% of the outstanding number of shares of the Company's Series A common stock on the immediately preceding December 31 or (ii) a lesser number of shares as determined by the compensation committee of the board of directors. In accordance with the 2023 Plan, the shares reserved for issuance automatically increased by 855,016 shares on January 1, 2024, and by 1,226,994 shares on January 1, 2025. As of December 31, 2025, the aggregate maximum number of shares reserved for issuance under the 2023 Plan was 4,667,978, of which 1,395,328 shares were available for future grants. Option grants issued under the 2023 Plan are exercisable for up to 10 years from the date of issuance.

In connection with the 2023 Plan, the number of shares reserved for issuance under the 2023 Plan was automatically increased by 1,278,164 shares, effective January 1, 2026.

In March 2024, the Company established a pool of 1,000,000 shares of Series A common stock (Inducement Pool) from which equity grants in the form of options and restricted stock units may be issued as inducement for new employees to accept employment offers from the Company or for individuals returning to employment after a bona fide period of non-employment with the Company. Inducement Pool grants are granted outside of the 2023 Plan and do not require approval from the Company's stockholders pursuant to

the Nasdaq inducement grant exception in accordance with Nasdaq Listing Rule 5635(c)(4). In February 2025, the Company increased the number of shares available for issuance by 300,000 shares, increasing the total number of shares available for issuance under the Inducement Pool to 1,300,000 shares. As of December 31, 2025, 361,217 shares were available for future grants from the Inducement Pool.

Total stock-based compensation recorded in the statements of operations and comprehensive loss related to stock options, restricted stock units and the ESPP (defined below) for employees and non-employees was as follows (in thousands):

	Years Ended December 31,	
	2025	2024
Stock options	$ 5,334	$ 4,227
Restricted stock units	1,106	1,061
Employee stock purchase plan	9	—
Total stock-based compensation expense	$ 6,449	$ 5,288
Included in:		
General and administrative expense	$ 5,516	$ 4,306
Research and development expense	933	982
Total stock-based compensation expense	$ 6,449	$ 5,288

Stock options

The Company grants stock options which consist of (i) time-based options, which vest and become exercisable, subject to the participant's continued employment or service through the applicable vesting date and (ii) performance-based options, which vest based on performance measures against predetermined objectives that include successful completion of qualified equity offerings or announced topline results for clinical trials and positive clinical results over a specified performance period. The Company's time-based options have various vesting schedules that range from vesting immediately to vesting over a four-year period.

The following table summarizes stock option activity (in thousands, except share and per share data):

	Number of Shares Underlying Outstanding Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in Years)	Aggregate Intrinsic Value [1]
Outstanding, January 1, 2025	4,462,517	$ 6.58	7.4	$ 619
Granted	1,337,219	4.92		
Exercised	(44,792)	6.14		
Forfeited/expired	(32,618)	19.88		
Outstanding, December 31, 2025[2]	5,722,326	$ 6.12	7.1	$ 3,799
Vested and expected to vest, December 31, 2025	5,722,326	$ 6.12	7.1	$ 3,799
Exercisable at December 31, 2025	3,685,879	$ 6.55	6.3	$ 1,424

(1) Aggregate intrinsic value represents the difference between the fair value of the Company's Series A common stock on the last day of the fiscal period and the exercise price, multiplied by the number of options outstanding.

(2) Includes 477,467 performance-based options with a weighted-average exercise price of $6.44, all of which were fully vested and exercisable.

During the years ended December 31, 2025 and 2024, the weighted average grant-date fair value per share of stock options granted was $3.84 and $3.26, respectively. The total intrinsic value of stock options exercised during the years ended December 31, 2025 and 2024 was $0.2 million and $0.1 million, respectively. Additionally, during the years ended December 31, 2025 and 2024, cash received from the exercise of stock options was $0.3 million and $0.1 million, respectively.

As of December 31, 2025, there was $8.3 million of unrecognized compensation expense, which is expected to be recognized over a remaining weighted-average period of 2.1 years.

Restricted stock units

The Company's restricted stock units generally vest over a four-year period in equal amounts on an annual basis, provided the employee remains continuously employed with the Company. The fair value of the restricted stock units is equal to the closing price of the Company's Series A common stock on the grant date.

The following table summarizes restricted stock unit activity:

	Restricted Stock Units	Weighted-Average Grant Date Fair Value
Outstanding, January 1, 2025	844,382	$ 2.96
Granted	267,157	4.85
Vested/released	(281,462)	2.96
Outstanding, December 31, 2025	830,077	$ 3.57

As of December 31, 2025, the total unrecognized compensation expense related to unvested restricted stock units was $2.3 million, which is expected to be recognized over a remaining weighted-average period of 2.3 years.

Valuation assumptions

The fair value of each stock option granted was estimated on the date of grant using the Black-Scholes option pricing model using the following assumptions:

	Years Ended December 31,	
	2025	2024
Expected volatility	95 - 96 %	91 - 96 %
Risk-free interest rate	3.8 - 4.3 %	3.6 - 4.5 %
Dividend yield	—	—
Expected term (in years)	5.3 - 6.0	5.3 - 6.1

The expected term is determined using the simplified method, which represents the average of the contractual term of the options and the weighted-average expected vesting period. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the option. The expected stock volatility rate is based on the volatility rates of comparable publicly held companies over a period equal to the expected term of the option. The Company utilizes a dividend yield of zero based on the fact that the Company has never paid cash dividends to stockholders and has no current intentions to pay cash dividends.

Employee stock purchase plan

The 2023 Employee Stock Purchase Plan (the ESPP) was adopted by the board of directors in July 2023 with an initial total of 215,497 shares of Series A common stock reserved for issuance. Under the ESPP plan, the amount of shares reserved automatically increases each January 1 through January 1, 2033, by the least of (i) 215,497 shares of Series A common stock, (ii) 1% of the outstanding number of shares of the Company's Series A common stock on the immediately preceding December 31 or (iii) such lesser number of shares of Series A common stock as determined by the administrator of the ESPP. In accordance with the ESPP, the shares reserved for issuance automatically increased by 213,754 shares on January 1, 2024, and by 215,497 shares on January 1, 2025. As of December 31, 2025, the aggregate maximum number of shares reserved for issuance under the ESPP was 644,748. No shares of Series A common stock have been issued under the ESPP to date.

In connection with the ESPP, the number of shares reserved for issuance under the ESPP was automatically increased by 215,497 shares effective January 1, 2026.

9. Income Taxes

For the years ended December 31, 2025, and 2024, the Company did not record a provision or benefit for federal or state income taxes, as the Company has incurred a net loss for all periods presented and the Company has provided a full valuation allowance against

its net deferred tax assets. The Company did not pay any income taxes in any jurisdiction for the years ended December 31, 2025 and 2024.

A reconciliation between the federal statutory tax rates and the Company's effective tax rate for the years ended December 31, 2025, and 2024, is as follows:

	Years Ended December 31,			
	2025		2024	
Federal income taxes at statutory rates	$ 10,718	21.00 %	$ 9,569	21.00 %
Research and development credits	156	0.30	1,976	4.34
Stock-based compensation	216	0.42	(593)	(1.30)
Changes in unrecognized tax benefits	164	0.32	89	0.20
Section 162(m) limitations	(522)	(1.02)	(108)	(0.24)
Other	(3)	(0.01)	(5)	(0.01)
Change in valuation allowance	(10,729)	(21.01)	(10,928)	(23.99)
Effective income tax rate	$ —	— %	$ —	— %

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The following table presents significant components of the Company's net deferred tax assets as of December 31, 2025 and 2024 (in thousands):

	As of December 31,	
	2025	2024
Deferred tax assets:		
Net operating loss carryforwards	$ 46,665	$ 35,045
Capitalized start-up costs and research expenses	18,169	20,137
Research and development credits	8,824	8,265
Accruals, reserves and other	313	270
Stock compensation	3,439	2,674
Lease liabilities	16	16
Total gross deferred assets	77,426	66,407
Valuation allowance	(77,410)	(66,391)
Total deferred tax assets	16	16
Deferred tax liabilities:		
Right-of-use assets	(16)	(16)
Total deferred liabilities	(16)	(16)
Net deferred tax assets	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2025, and 2024. The valuation allowance increased $11.0 million and $11.3 million during the years ended December 31, 2025 and 2024, respectively.

As of December 31, 2025, the Company had U.S. federal net operating loss carryforwards (NOLs) of approximately $213.6 million which may be available to offset future U.S. federal income. U.S. Federal NOLs incurred in taxable years beginning prior to January 1, 2018 of approximately $91.0 million expire beginning in 2029 while U.S. federal NOLs incurred in taxable years beginning after December 31, 2017 of approximately $122.6 million will have an indefinite carryforward period, subject to annual limitations. As of December 31, 2025, the Company also had state NOL carryforwards of approximately $26.3 million which may be available to offset future state income and expire at various years beginning in 2028.

As of December 31, 2025, the Company had U.S. federal research and development tax credit (R&D credit) carryforwards of approximately $8.5 million available to reduce future tax liabilities which expire at various years beginning with 2028. As of December 31, 2025, the Company had state credit carryforwards of approximately $3.2 million available to reduce future tax liabilities which do not expire.

Under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage point change (by value) in its equity ownership by "5% shareholders" over a rolling three-year period, the corporation's ability to use its pre-change NOLs, R&D credits and certain other tax attributes to offset its post-change income or taxes may be limited. This could limit the amount of NOLs, R&D credit carryforwards or other applicable tax attributes that the Company can utilize annually to offset future taxable income or tax liabilities. The Company has not performed a Section 382 analysis through December 31, 2025, and as such, the Company is not able to determine the impact of any potential limitations on the usage of the Company's NOLs and tax credit carryforwards. To the extent that an assessment is completed in the future, the Company's ability to utilize tax attributes could be restricted on a year-by-year basis and certain attributes could expire before they are utilized.

The Company applies the two-step approach to recognizing and measuring uncertain tax positions. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates it is more likely than not that the position will be substantiated on audit, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount, which is more than 50% likely of being realized upon ultimate settlement. Income tax positions must meet a more likely than not recognition threshold at the effective date to be recognized upon the adoption of ASC 740 and in subsequent periods. This interpretation also provides guidance on measurement, de-recognition, classification, interest and penalties, accounting in interim periods and transition.

A reconciliation of the unrecognized tax benefits for the years ended December 31, 2025 and 2024, is as follows (in thousands):

	Years Ended December 31,	
	2025	2024
Unrecognized tax benefits as of the beginning of the year	$ 2,186	$ 1,784
Decrease related to prior year tax positions	(151)	(251)
Increase related to current year tax positions	306	653
Unrecognized tax benefits as of the end of the year	$ 2,341	$ 2,186

No amount of the unrecognized tax benefits, if recognized, would reduce the Company's annual effective tax rate because the benefits are in the form of deferred tax assets for which a full valuation allowance has been recorded. The Company does not anticipate a significant change to its unrecognized tax benefits over the next 12 months.

The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2025, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations and comprehensive loss. There are no ongoing examinations by taxing authorities at this time.

The Company files U.S. and state income tax returns with varying statutes of limitations. The Company's tax years from inception in 2006 will remain open to examination due to the carryover of the unused NOLs and tax credits. The Company does not have any tax audits or other proceedings pending.

10. Segment Reporting

Operating segments are defined as components of an entity about which discrete financial information is evaluated regularly by the CODM in deciding how to allocate resources and assess performance. The Company operates and manages its business as one business segment, which is development and commercialization of therapeutics for the treatment of MASH, acne and other diseases where FASN plays a pathogenic role. Accordingly, the Company has one reportable segment. The Company has a single management team that reports to the Chief Executive Officer, the Company's CODM, who comprehensively manages the entire Company. The accounting policies of the segment are the same as those described in the summary of significant accounting policies.

When evaluating the Company's financial performance, the CODM is regularly provided with more detailed expense information than what is included in the Company's statements of operations and comprehensive loss. The CODM uses net loss, as reported in the

statements of operations and comprehensive loss, in evaluating the performance of the segment. Decisions regarding resource allocation are made primarily during the annual budget planning process and reallocated as needed throughout the year. The measure of segment assets is reported on the balance sheets as total assets.

The following table shows the Company's segment net loss, including the significant expense categories regularly provided to and reviewed by the CODM, as computed under U.S. GAAP, for the years ended December 31, 2025, and 2024 (in thousands):

	Years Ended December 31,	
	2025	2024
Denifanstat external research and development expenses	$ 28,248	$ 33,838
TVB-3567 external research and development expenses	6,084	810
External general and administrative expenses	8,760	8,001
Personnel costs	7,150	6,517
Stock-based compensation	6,449	5,288
Other segment items [(1)]	(5,653)	(8,887)
Segment net loss	$ 51,038	$ 45,567

(1) Other segment items consist of (i) interest and other income, net and (ii) other internal operating research and development expenses.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

(a) Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, (Exchange Act), that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive officer and principal financial officer, to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Our management, with the participation of our Chief Executive Officer and our Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), as of the end of the period covered by this Annual Report. Based on such evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that as of December 31, 2025 our disclosure controls and procedures were effective to provide reasonable assurance that the information to be disclosed by us in this Annual Report was (a) reported within the time periods specified by the SEC rules and regulations, and (b) communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding any required disclosure.

(b) Management's Report on Internal Control over Financial Reporting

Management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rule 13a-15(f) under the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. Because of its inherent limitations, our internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with applicable policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2025. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in the original Internal Control—Integrated Framework updated in 2013. Based on that assessment, our management concluded that, as of December 31, 2025, our internal control over financial reporting was effective.

(c) Attestation Report on Internal Control over Financial Reporting

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm because we are an "emerging growth company," and may take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not "emerging growth companies" including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act.

(d) Changes in Internal Control over Financial Reporting

During the quarter ended December 31, 2025, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15(d)-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

(e) Inherent Limitations on Effectiveness of Controls

Our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving the desired control objectives. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in

evaluating the cost-benefit relationship of possible controls and procedures. Similarly, an evaluation of controls cannot provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud, if any, have been detected.

Item 9B. Other information

(a) None.

(b) During the fourth quarter of the fiscal year ended December 31, 2025, no director or "officer" as defined in Rule 16a-1(f) under the Exchange Act adopted or terminated any Rule 10b5-1 trading plan or arrangements or any non-Rule 10b5-1 trading plan or arrangements, in both cases as defined in Item 408(a) of Regulation S-K.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2026 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2025.

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. A current copy of the code is posted on the Investors and Media, Corporate Governance section of our website, which is located at www.sagimet.com. We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Business Conduct and Ethics by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of The Nasdaq Global Market, by filing a Current Report on Form 8-K with the SEC, disclosing such information.

Insider Trading Arrangements and Policies

We have adopted insider trading policies and procedures governing the purchase, sale, and other dispositions of securities of Sagimet by directors, officers, and employees that we believe are reasonably designed to promote compliance with insider trading laws, rules and regulations, and applicable Nasdaq listing standards. Our insider trading policy states, among other things, that our directors, officers, and employees are prohibited from trading in such securities while in possession of material, nonpublic information. In addition, with regard to trading in our own securities, it is our policy to comply with the federal securities laws and the applicable exchange listing requirements. The foregoing summary of our insider trading policies and procedures does not purport to be complete and is qualified by reference to our insider trading policy attached hereto as Exhibit 19.1 and incorporated herein.

Item 11. Executive Compensation

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2026 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2025.

Item 12. Security Ownership of Certain Beneficial Owners and Management Related Stockholder Matters

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2026 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2025.

Item 13. Certain Relationships and Related Party Transactions, and Director Independence

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2026 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2025.

Item 14. Principal Accountant Fees and Services

Our independent public accounting firm is KPMG LLP, Philadelphia, Pennsylvania (PCAOB Auditor ID: 185). The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2026 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2025.

PART IV

Item 15. Exhibits

The following documents are filed as part of this Annual Report on Form 10-K:

(1) Financial Statements

For a list of the financial statements included in this Annual Report on Form 10-K, see the Index to Financial Statements, which is incorporated by reference herein.

(2) Financial Statement Schedules

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits

The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the signature page. The exhibits listed in the Exhibit Index are incorporated by reference herein.

Item 16. Form 10-K Summary

We have elected not to include summary information.

Exhibit Number	Description	Method of Filing
3.1	Eleventh Amended and Restated Certificate of Incorporation of Sagimet Biosciences Inc.	Incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-41742) filed on July 18, 2023
3.2	Second Amended and Restated Bylaws of Sagimet Biosciences Inc.	Incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-41742) filed on July 18, 2023
4.1	Form of Series A Common Stock Certificate of Sagimet Biosciences Inc.	Incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
4.2	Form of Series B Common Stock Certificate of Sagimet Biosciences Inc.	Incorporated by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
4.3	Description of Capital Stock	Incorporated by reference to Exhibit 4.3 to the Company's Form 10-K (File No. 001-41742) filed on March 25, 2024
10.1•	Sagimet Biosciences Inc. 2007 Equity Incentive Plan	Incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.2•	Forms of Grant Notice, Stock Option Agreement and Notice of Exercise under the 2007 Equity Incentive Plan	Incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.3•	Sagimet Biosciences Inc. 2017 Equity Incentive Plan	Incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.4•	Forms of Grant Notice, Stock Option Agreement and Notice of Exercise under the 2017 Equity Incentive Plan	Incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.5•	Sagimet Biosciences Inc. 2023 Stock Option and Incentive Plan	Incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.6•	Forms of Incentive Stock Option Agreement, Non-Qualified Stock Option Agreement for Non-Employee Directors and Non-Qualified Stock Option Agreement for Company Employees under the Sagimet Biosciences Inc. 2023 Stock Option and Incentive Plan	Incorporated by reference to Exhibit 10.6 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.7•	Forms of Restricted Stock Unit Award Agreement for Non-Employee Directors and Restricted Stock Unit Award Agreement for Company Employees under the Sagimet Biosciences Inc. 2023 Stock Option and Incentive Plan	Incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.8•	Form of Restricted Stock Award Agreement under the Sagimet Biosciences Inc. 2023 Stock Option and Incentive Plan	Incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023

10.9•	Amended and Restated Sagimet Biosciences Inc. 2023 Employee Stock Purchase Plan	Filed herewithin.
10.10•	Sagimet Biosciences Inc. 2023 Non-Employee Director Compensation Policy	Incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.11•	Form of Indemnification Agreement by and between Sagimet Biosciences Inc. and its directors	Incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.12•	Form of Indemnification Agreement by and between Sagimet Biosciences Inc. and its executive officers	Incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.13•	Sagimet Biosciences Inc. Senior Executive Cash Incentive Bonus Plan	Incorporated by reference to Exhibit 10.21 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.14•	Exclusive License and Development Agreement by and between Sagimet Biosciences Inc. and Ascletis BioScience Co. Ltd., dated as of January 18, 2019	Incorporated by reference to Exhibit 10.22 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.15*	Assignment and Assumption Agreement, by and among Sagimet Biosciences Inc., Ascletis BioScience Co., Ltd. and Gannex Pharma Co., Ltd., effective October 25, 2019	Incorporated by reference to Exhibit 10.29 to the Company's Registration Statement on Form S-1/A (File No. 333-272901) filed on July 10, 2023
10.16*	Patent Assignment Agreement by and between Sagimet Biosciences Inc. and Gannex Pharma Co., Ltd., effective October 25, 2019	Incorporated by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.17*	Amended and Restated Patent Assignment Agreement by and between Sagimet Biosciences Inc. and Gannex Pharma Co., Ltd., dated July 2, 2023	Incorporated by reference to Exhibit 10.24 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on July 10, 2023
10.18	Lease Agreement by and between Sagimet Biosciences Inc. and Casiopea Bovet, LLC, dated as of March 1, 2019, as amended by the First Amendment to Lease Agreement, dated December 14, 2021	Incorporated by reference to Exhibit 10.23 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.19	Amended and Restated Nominating Agreement, dated as of April 15, 2021, by and among Sagimet Biosciences Inc., Baker Brothers Life Sciences, L.P. and 667, L.P. as amended by Amendment No. 1 to Amended and Restated Nominating Agreement, dated as of June 22, 2023, by and among Sagimet Biosciences Inc., Baker Brothers Life Sciences, L.P. and 667, L.P.	Incorporated by reference to Exhibit 10.25 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023
10.20	Amended and Restated Investors' Rights Agreement, by and among Sagimet Biosciences Inc. and certain of its stockholders, dated December 21, 2020	Incorporated by reference to Exhibit 10.26 to the Company's Registration Statement on Form S-1 (File No. 333-272901) filed on June 23, 2023

10.21	Amended and Restated Warrant to Purchase Stock, by and between Sagimet Biosciences Inc. and Banc of California, Inc., dated January 4, 2024	Incorporated by reference to Exhibit 10.28 to the Company's Registration Statement on Form S-1 (File No. 333-276664) filed on January 23, 2024
10.22•	Form of Inducement Option Award Agreement	Incorporated by reference to Exhibit 10.28 to the Company's Annual Report on Form 10-K (File No. 001-41742) filed on March 12, 2025
10.23	Second Amendment to Lease Agreement by and between Sagimet Biosciences Inc. and Casiopea Bovet, LLC, dated as of April 5, 2024	Incorporated by reference to Exhibit 10.29 to the Company's Annual Report on Form 10-K (File No. 001-41742) filed on March 12, 2025
10.24	Third Amendment to Lease Agreement by and between Sagimet Biosciences Inc. and Casiopea Bovet, LLC, dated as of May 5, 2025	Incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on File 10-Q (File No. 001-41742) filed on August 13, 2025
10.25•	Second Amended and Restated Executive Employment Agreement by and between Sagimet Biosciences Inc. and David Happel, dated June 6, 2025	Incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on File 10-Q (File No. 001-41742) filed on August 13, 2025
10.26•	Amended and Restated Executive Employment Agreement by and between Sagimet Biosciences Inc. and Thierry Chauche, dated June 6, 2025	Incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on File 10-Q (File No. 001-41742) filed on August 13, 2025
10.27•	Second Amended and Restated Executive Employment Agreement by and between Sagimet Biosciences Inc. and Eduardo Martins, dated June 6, 2025	Incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on File 10-Q (File No. 001-41742) filed on August 13, 2025
10.28•	Second Amended and Restated Executive Employment Agreement by and between Sagimet Biosciences Inc. and Elizabeth Rozek, dated June 6, 2025	Incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on File 10-Q (File No. 001-41742) filed on August 13, 2025
10.29	Sales Agreement Dated as of August 14, 2025 between Leerink Partners LLC and Sagimet Biosciences Inc.	Incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-41742) filed on August 14, 2025
19.1	Sagimet Biosciences Inc. Insider Trading Policy	Incorporated by reference to Exhibit 19.1 to the Company's Annual Report on Form 10-K (File No. 001-41742) filed on March 25, 2024
23.1	Consent of KPMG LLP	Filed herewith
23.2	Consent of Deloitte & Touche LLP	Filed herewith
24.1	Power of Attorney (included on signature page)	Filed herewith
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	Filed herewith

31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002	Filed herewith
32.1	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2022	Furnished herewith
97.1	Sagimet Biosciences Inc. Compensation Recovery Policy	Incorporated by reference to Exhibit 97.1 to the Company's Annual Report on Form 10-K (File No. 001-41742) filed on March 25, 2024
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document	Filed herewith
101.SCH	Inline XBRL Taxonomy Extension Schema Document	Filed herewith
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	Filed herewith
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	Filed herewith
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	Filed herewith
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	Filed herewith
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	Filed herewith

- Indicates management contract or compensatory plan.

* Portions of this exhibit (indicated by [***]) have been omitted because the registrant has determined that the information is both not material and is the type that the registrant treats as private and confidential.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this Annual Report to be signed on its behalf by the undersigned, thereunto duly authorized.

SAGIMET BIOSCIENCES, INC.

Date: March 11, 2026

By:/s/ David Happel
David Happel
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 11, 2026

By:/s/ Thierry Chauche
Thierry Chauche
Chief Financial Officer
(Principal Financial and Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of David Happel and Thierry Chauche his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ David Happel **David Happel**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 11, 2026
/s/ Thierry Chauche **Thierry Chauche**	Chief Financial Officer (Principal Financial and Accounting Officer)	March 11, 2026
/s/ George Kemble, PhD **George Kemble, PhD**	Chairman of the Board	March 11, 2026
/s/ Anne Phillips, MD **Anne Phillips, MD**	Director	March 11, 2026
/s/ Beth Seidenberg, MD **Beth Seidenberg, MD**	Director	March 11, 2026
/s/ Elizabeth Grammer, Esq. **Elizabeth Grammer, Esq.**	Director	March 11, 2026
/s/ Jennifer Jarrett **Jennifer Jarrett**	Director	March 11, 2026
/s/ Paul Hoelscher **Paul Hoelscher**	Director	March 11, 2026
/s/ Tim Walbert **Tim Walbert**	Director	March 11, 2026

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David Happel, certify that:

1. I have reviewed this Form 10-K of Sagimet Biosciences Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d). Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2026

By: /s/ David Happel
David Happel
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) OR 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Thierry Chauche, certify that:

1. I have reviewed this Form 10-K of Sagimet Biosciences Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: March 11, 2026

By: /s/ Thierry Chauche
Thierry Chauche
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Sagimet Biosciences Inc. (the "Company") for the year ended December 31, 2025 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, to the best of his knowledge, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 11, 2026

By: /s/ David Happel

David Happel
President and Chief Executive Officer
(Principal Executive Officer)

Date: March 11, 2026

By: /s/ Thierry Chauche

Thierry Chauche
Chief Financial Officer
(Principal Financial and Accounting Officer)

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