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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, 2024

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: 001-40384

Tourmaline Bio, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**83-2377352**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
27 West 24th Street, Suite 702 New York, NY	**10010**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (646) 481-9832

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	TRML	The Nasdaq Global Select 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, 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 ☒

As of June 28, 2024 (the last business day of the Registrant's second fiscal quarter), the Registrant's aggregate market value of its voting common equity held by non-affiliates was approximately $294.0 million based on the closing sale price of $12.86 per share as reported on The Nasdaq Global Market on that date. As of March 7, 2025, there were 25,685,429 shares of the Registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's definitive proxy statement (the "2025 Proxy Statement") for its 2025 Annual Meeting of Stockholders, which the Registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the Registrant's fiscal year ended December 31, 2024, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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EXPLANATORY NOTE

On October 19, 2023, the Delaware corporation formerly known as "Talaris Therapeutics, Inc." completed its previously announced merger transaction in accordance with the terms and conditions of the Agreement and Plan of Merger, dated as of June 22, 2023 (the "Merger Agreement"), by and among Talaris Therapeutics, Inc. ("Talaris"), Tourmaline Bio, Inc. ("Legacy Tourmaline") and Terrain Merger Sub, Inc., a direct wholly owned subsidiary of Talaris ("Merger Sub"), pursuant to which Merger Sub merged with and into Legacy Tourmaline, with Legacy Tourmaline surviving as a direct wholly owned subsidiary of Talaris and the surviving corporation of the merger (the "Reverse Merger"). Additionally, as a result of the Reverse Merger, (i) Legacy Tourmaline changed its name from "Tourmaline Bio, Inc." to "Tourmaline Sub, Inc.", and (ii) Talaris changed its name from "Talaris Therapeutics, Inc." to "Tourmaline Bio, Inc."

On October 19, 2023, in connection with the transactions contemplated by the Merger Agreement, Talaris filed a Certificate of Amendment to the Third Amended and Restated Certificate of Incorporation effecting a 1-for-10 reverse stock split of Talaris' common stock (the "Reverse Stock Split"). As a result of the Reverse Stock Split, the number of issued and outstanding shares of Talaris' common stock immediately prior to the Reverse Stock Split was reduced such that every 10 shares of Talaris' common stock held by a stockholder immediately prior to the Reverse Stock Split were combined and reclassified into one share of common stock after the Reverse Stock Split.

In this Report, unless the context indicates otherwise, the terms "Company," "we," "us," and "our" refer to Tourmaline Bio, Inc. (formerly known as Talaris Therapeutics, Inc.) and its consolidated subsidiaries. Unless otherwise noted, all references to shares of common stock and per share amounts prior to the Reverse Merger in this Annual Report on Form 10-K have been retroactively adjusted to reflect the conversion of shares in the Reverse Merger based on an exchange ratio of 0.07977 (after giving effect to the Reverse Stock Split).

Following the completion of the Reverse Merger, on June 30, 2024, Tourmaline Sub, Inc. merged with and into Tourmaline Bio, Inc., with Tourmaline Bio, Inc. as the surviving entity (the "Roll-Up Merger").

This Report contains references to trademarks belonging to other entities, which are the property of their respective holders. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

All statements other than statements of historical fact included in this Report, including, without limitation, statements under "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" regarding our financial position, business strategy and the plans and objectives of management for future operations, are forward-looking statements. When used in this Report, words and phrases such as "designed to," "intended to," "may," "might," "can," "will," "to be," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "project," "potential," "likely," "continue" and "ongoing," or the negative of such terms or other similar expressions, as they relate to us or our management, identify forward-looking statements.

Any statements in this Report, or incorporated herein, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are 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"), these forward-looking statements include statements regarding:

- the success, cost and timing of our development activities, non-clinical studies and clinical trials;
- the timing and outcome of our current and future clinical trials, and the reporting of data from those trials;
- the therapeutic potential of pacibekitug (also referred to as TOUR006) and future product candidates;
- the ability to obtain funding for our operations, including funding necessary to develop and commercialize our current and future product candidates, subject to regulatory approvals;
- our ability to extend our operating capital;
- the potential of our technologies and our ability to execute on our corporate strategy;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our reliance on third parties to manufacture and conduct preclinical studies and clinical trials of our current and future product candidates;
- the success of competing therapies that are or may become available;
- our ability to obtain regulatory approval for our product candidates and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- existing regulations and regulatory developments in the United States (the U.S.) and other jurisdictions;
- the strength and breadth of our patent portfolio;
- our ability to obtain and adequately protect intellectual property rights for our product candidates;
- potential claims relating to our intellectual property;
- our financial performance;
- our ability to develop and maintain our corporate infrastructure, including our ability to design and maintain an effective system of internal controls;
- our ability to remediate the existing material weaknesses in our internal control over financial reporting;
- our ability to attract and retain key scientific, medical, commercial and management personnel;
- our ability to continue to satisfy the listing requirements of The Nasdaq Stock Market and have our stock continue to trade thereon; and

- the effects of macroeconomic and geopolitical conditions and unforeseeable events, such as the war in Ukraine and hostilities in the Middle East, potential bank failures and global health crises.

These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to revise any forward-looking statements to reflect events or developments occurring after the date of this Report, even if new information becomes available in the future.

PART I

Item 1. Business.

Overview

We are a late-stage clinical biotechnology company focused on developing transformative medicines that dramatically improve the lives of patients with life-altering immune and inflammatory diseases. In doing so, we seek to identify and develop medicines that have the potential to establish new standards-of-care in areas of high unmet medical need.

Our initial product candidate is pacibekitug (also known as TOUR006), a fully human monoclonal antibody that selectively binds to interleukin-6 ("IL-6"), a key proinflammatory cytokine involved in the pathogenesis of many autoimmune and inflammatory disorders. The anti-IL-6 and anti-IL-6 receptor ("IL-6R") antibody class ("IL-6 class") has over two decades of clinical and commercial experience treating over a million patients with a variety of autoimmune and inflammatory diseases. To date, four anti-IL-6 or anti-IL-6R antibodies have been approved in the United States ("U.S."). These four anti-IL-6 or anti-IL-6R antibodies together generated more than $3.5 billion in global sales in 2024.

Pacibekitug is a long-acting anti-IL-6 antibody which we believe has best-in-class properties including a high binding affinity to IL-6, long half-life, and low observed immunogenicity. These characteristics may allow pacibekitug to achieve substantial IL-6 pathway suppression with relatively low amounts of drug exposure, potentially enabling delivery in a convenient, low volume, infrequently administered, subcutaneous injection.

We are pursuing two strategic paths for pacibekitug, the first of which is cardiovascular inflammation. We believe pacibekitug has the potential to transform the standard of care for patients living with high risk of cardiovascular disease by targeting key inflammatory pathways driving cardiovascular disease. Atherosclerotic cardiovascular disease ("ASCVD") is a leading cause of death globally. Preventing major adverse cardiovascular events ("MACE"), such as death, nonfatal myocardial infarction or nonfatal stroke, has the potential to significantly reduce global cardiovascular disease burden. IL-6 has been identified as a promising drug target for addressing the risk of MACE in ASCVD, and multiple external Phase 3 cardiovascular outcome trials investigating IL-6 blockade are ongoing. We believe that pacibekitug potentially offers a meaningfully enhanced product profile to these competitor programs with a potential for subcutaneous dosing once every three months.

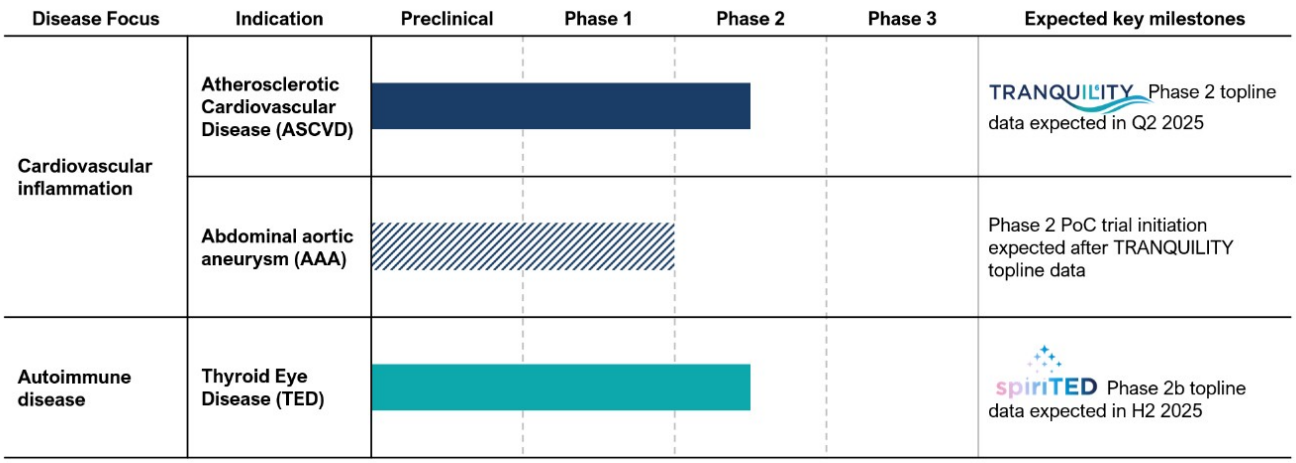
As previously announced in January 2024, we have reached alignment with the U.S. Food and Drug Administration ("FDA") on our ASCVD clinical development program, including our Phase 2 TRANQUILITY trial evaluating the reduction of high sensitivity C-reactive protein ("hs-CRP"), a validated biomarker for inflammation, with quarterly and monthly dosing of pacibekitug in patients with elevated hs-CRP and chronic kidney disease. In March 2024, the FDA cleared our Investigational New Drug application ("IND") related to our ASCVD clinical development program. The Phase 2 TRANQUILITY trial commenced in April 2024 and completed over-enrollment in December 2024. We expect to report topline data in the second quarter of 2025. Pending successful completion of the study, we expect that positive results from the Phase 2 TRANQUILITY trial will position pacibekitug to be Phase 3-ready for ASCVD.

Additionally we have nominated abdominal aortic aneurysm ("AAA") as an additional indication within our cardiovascular inflammation disease focus. We expect to provide additional details on a planned Phase 2 proof-of-concept trial in AAA after topline results from the Phase 2 TRANQUILITY trial are reported in the second quarter of 2025.

Our second strategic path is thyroid eye disease ("TED"). TED is an autoimmune disease characterized by autoantibody-mediated activation of the tissues surrounding the eye, causing inflammation and disfigurement which can be sight-threatening in severe cases. We have identified a substantial body of published clinical observations characterizing the beneficial off-label use of currently marketed IL-6 pathway inhibitors, namely Actemra® (tocilizumab), an anti-IL-6R monoclonal antibody, in reducing inflammation, eye-bulging, and levels of autoantibodies in patients with TED. However, no formal, industry-sponsored development effort studying the IL-6 class for the treatment of TED has been completed to date. We are currently evaluating pacibekitug in a pivotal Phase 2b trial in first-line TED, which we refer to as the spiriTED trial. We initiated the spiriTED trial in September 2023 and expect to report topline data in the second half of 2025.

Our Pipeline

The following figure summarizes our current development programs:



Note: The hatched bar represents a trial that has not yet commenced. The timing of clinical trial milestones is subject to change and additional discussion with the FDA

In addition, we continue to identify additional indication opportunities for pacibekitug and evaluate new in-licensing and acquisition opportunities for assets that we believe have standard-of-care changing potential for patients with immune, inflammatory and other diseases.

Our Strategy

We seek to identify and develop transformative medicines that have the potential to establish new standards-of-care in areas of high unmet medical need. We plan to apply a human data-focused approach to indication selection, identifying diseases where IL-6 pathway inhibitors have been used successfully in practice despite limited formal industry development and where we believe pacibekitug can potentially bring significant improvements over existing standards-of-care. We also plan to leverage insights from clinical trials as well as epidemiological and human genetic evidence with a goal of rapidly bringing pacibekitug into indications that have already been externally de-risked. We believe this focus on leveraging existing human data could allow us identify indications with high potential for clinical and commercial success and can maximize the value of pacibekitug.

The key elements of our strategy include:

- **In our cardiovascular inflammation strategy, advance pacibekitug through clinical development in patients with ASCVD and AAA**. We believe that pacibekitug has the potential to provide a differentiated product profile for the treatment of inflammatory risk in ASCVD with the potential for subcutaneous dosing once every three months. We initiated our Phase 2 TRANQUILITY clinical trial to assess the safety, pharmacokinetics ("PK"), and pharmacodynamics ("PD") of pacibekitug in patients with elevated hs-CRP and CKD in April 2024, completed over-enrollment in December 2024 and expect to report topline data in the second quarter of 2025. We expect to provide additional details on a planned Phase 2 proof-of-concept trial in AAA after reporting topline results from the Phase 2 TRANQUILITY trial.

- **Advance pacibekitug through clinical development in patients with TED**. Our initial product candidate, pacibekitug, has the potential for a differentiated product profile for the treatment of TED based on the literature supporting IL-6 pathway inhibition in active TED, a favorable long-term safety profile of the IL-6 class observed to date, and the potentially low administrative burden offered by infrequent, subcutaneous dosing. In September 2023, we initiated our pivotal Phase 2b spiriTED trial to assess the safety and efficacy of pacibekitug for the treatment of TED, and we expect to report topline results from this trial in the second half of 2025.

- **Maximize the potential of pacibekitug in additional indications where IL-6 inhibition has shown compelling evidence of clinical benefit**. We believe that pacibekitug has broad application beyond ASCVD, AAA and TED. We

aim to identify and develop in additional indications where IL-6 inhibition has shown evidence of clinical benefit, but has not entered industry-led clinical development, as well as indications where we could bring pacibekitug forward, capitalizing on external de-risking events.

- **Explore business development opportunities to selectively expand our product portfolio**. We continue to evaluate new in-licensing and acquisition opportunities for assets that we believe have standard-of-care changing potential for patients with immune, inflammatory and other diseases. We also plan to strategically evaluate potential collaborations with external parties to maximize the potential of pacibekitug.

Scientific Background

Overview of Autoimmune Disorders

The immune system plays a critical role in nearly every aspect of human health. In addition to providing protection against external pathogens such as viruses, bacteria, and fungi, the immune system is involved in the surveillance and elimination of internal threats such as pre-malignant and malignant lesions. Beyond providing protection, the immune system regulates key regenerative and homeostatic processes in healthy individuals on an ongoing basis.

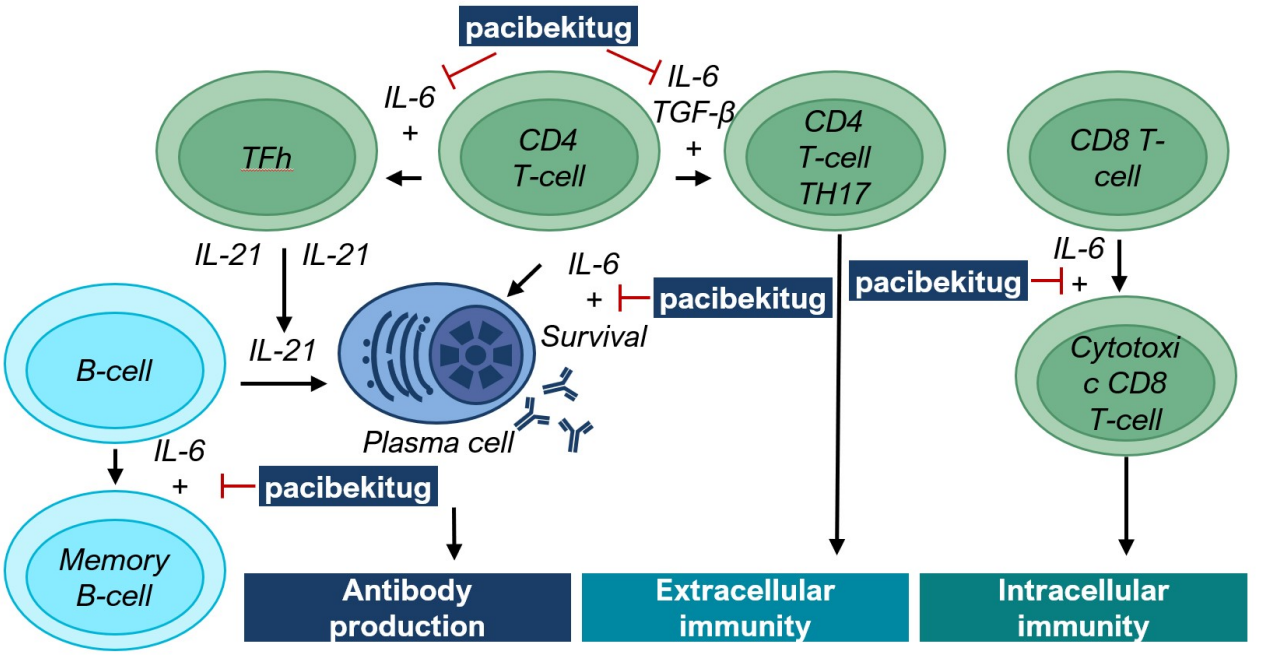
In patients with autoimmune diseases, the immune system inappropriately recognizes and attacks normal healthy tissues, resulting in inflammation, organ damage, debilitating symptoms and, in severe cases, death. To date over 80 autoimmune diseases have been documented, each with a wide range of clinical manifestations, pathophysiology, and severities. It is estimated that approximately 320 million people globally and approximately 24 million people in the U.S. are affected by an autoimmune disease.

The standard-of-care for immune-related disorders has been immunomodulatory and anti-inflammatory agents that are intended to prevent and control immune system overactivity. Recently, improved research and development efforts have resulted in targeted therapies that have shown greater efficacy while reducing treatment-limiting side effects, including those associated with broad immunosuppression. However, despite these advances, many patients with autoimmune diseases continue to be underserved. Existing targeted therapies may not fully address underlying disease biology or may have meaningful side effects.

IL-6: Mechanism of Action and Overview

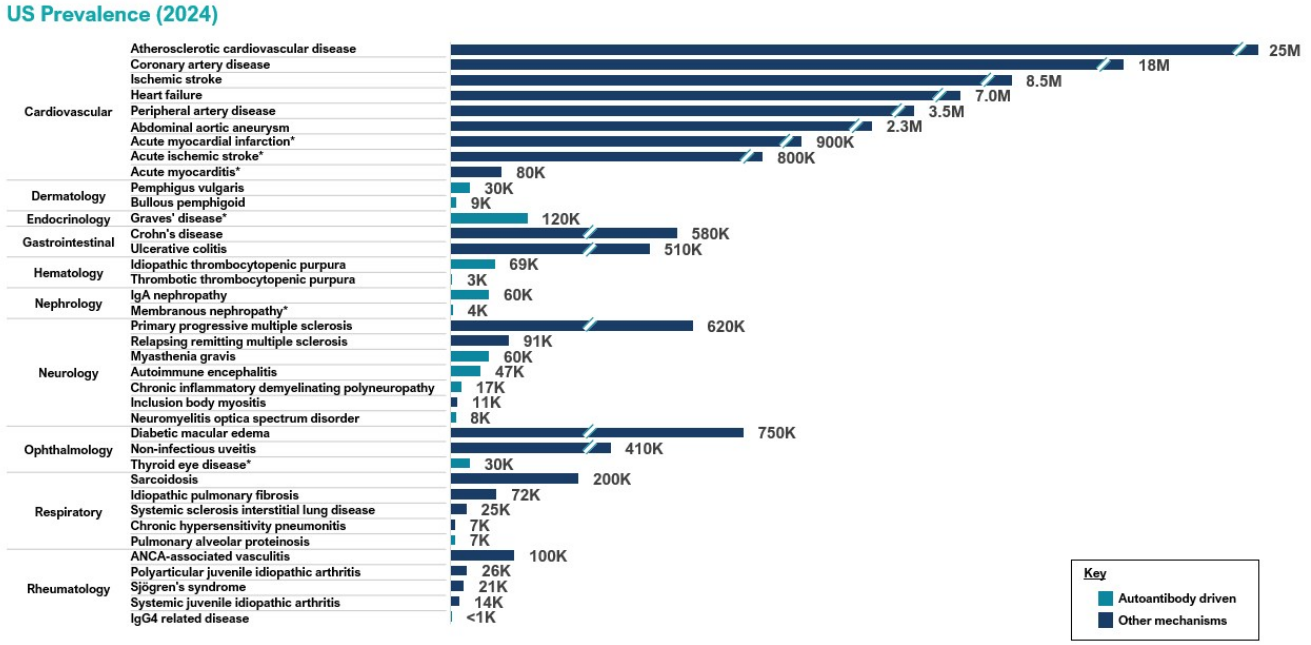
IL-6 is a pleiotropic cytokine which plays a key role in driving inflammation and cellular and humoral immune responses. In typical immunity, IL-6 is produced by various immune cells, including monocytes, macrophages, T cells, and B cells as well as fibroblasts and other non-immune cells, in response to cellular stresses and proinflammatory signals. Increased levels of IL-6 induce the acute phase inflammatory response, activating the innate immune system and providing a nonspecific response to infections and pathogens. IL-6 also plays a key role in activating the adaptive immune system by inducing proliferation and differentiation of B and T cells and release of additional inflammatory signals. IL-6 is a critical stimulation factor for B-cell and plasma cell survival, promoting antibody production. In addition, IL-6 serves as a key differentiating factor for T-cells, specifically promoting the development of Th17 cells and T follicular helper (“Tfh”) cells. Tfh cells also serve to promote B cell proliferation and antibody production.

Binding of IL-6 to IL-6R leads to recruitment of gp130, resulting in the downstream activation of a JAK/STAT-mediated signaling pathway which, depending on cell type, results in survival, proliferation, differentiation, and/or release of additional inflammatory signals. IL-6 is the exclusive binding partner of IL-6R and inhibition of either the ligand or the receptor blocks this signaling pathway. Clinical studies of IL-6 and IL-6R inhibitors have similarly produced observed reductions in C-reactive protein (“CRP”), an acute phase protein commonly used as a biomarker for IL-6 pathway activation and inflammation.



IL-6 mediates many autoimmune pathways including production of autoantibodies and proliferation of autoreactive T-cells; pacibekitug inhibits IL-6 from driving these pathways

Given the multiple roles of IL-6 in inflammation and immune cell activation, inhibiting IL-6 has emerged as an important therapeutic strategy for managing a wide range of immune disorders, including diseases caused by autoantibodies. Based on a review of the scientific literature and publicly reported clinical evidence, we believe that IL-6 may contribute to the disease pathobiology of over 30 diseases which may affect over 25 million patients in the U.S., including, but not limited to, those listed in the following figure:



*Incidence Number

Currently, there are four FDA approved therapies targeting the IL-6/IL-6R pathway: ACTEMRA® (tocilizumab), KEVZARA® (sarilumab), ENSPRYNG® (satralizumab-mwge), and SYLVANT® (siltuximab). Collectively, these therapies have been approved for nine indications: rheumatoid arthritis ("RA"), giant cell arteritis, juvenile idiopathic arthritis, polymyalgia rheumatica, cytokine release syndrome, multicentric Castleman's disease, neuromyelitis optica spectrum disorder ("NMOSD"), systemic sclerosis associated interstitial lung disease, and COVID-19. Collectively, these four anti-IL-6 or anti-IL-6R antibodies generated more than $3.5 billion in global sales in 2024.

Approved IL-6 pathway inhibitors:	Approved for the treatment of:
ACTEMRA® (tocilizumab)	RA, giant cell arteritis, systemic sclerosis-associated interstitial lung disease, polyarticular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, cytokine release syndrome, COVID-19
KEVZARA® (sarilumab)	RA, polymyalgia rheumatica
ENSPRYNG® (satralizumab)	NMOSD
SYLVANT® (siltuximab)	multicentric Castleman's disease

In addition, three biosimilars for tocilizumab have now been FDA approved, including TOFIDENCE® (Biogen), TYENNE® (Fresenius Kabi), and AVOTZMA® (Celltrion).

Our Product Candidate: Pacibekitug

We licensed pacibekitug, previously known as PF-04236921, from Pfizer Inc. ("Pfizer") in May 2022. Pacibekitug was originally developed from a hybridoma cell line using the Medarex UltiMAb transgenic mouse platform. The UltiMAb platform produces fully human monoclonal antibodies. The IgG1 isotype of the original clone was switched by Pfizer to IgG2 to reduce Fc receptor binding, thereby creating pacibekitug.

To date, pacibekitug has been tested by Pfizer in approximately 450 participants across six clinical trials, including over 400 autoimmune patients with RA, systemic lupus erythematosus ("SLE"), or Crohn's disease ("CD"). Across these studies, pacibekitug was generally well-tolerated, consistent with other therapies in the IL-6 class and had low rates of anti-drug antibodies ("ADAs") in the approximately 450 participants tested. We seek to leverage this large existing clinical dataset for pacibekitug, along with the extensive clinical experience with the IL-6 class, in our development programs. We believe this existing clinical dataset for pacibekitug serves as a basis for which the FDA will allow us to move directly into additional Phase 2 and/or pivotal trials in future selected development indications. To date, the FDA has cleared our INDs to support the initiation of the ongoing Phase 2 TRANQUILITY trial and ongoing pivotal Phase 2b spiriTED trial.

Potential Benefits of Pacibekitug

We believe pacibekitug presents a potentially best-in-class product profile for a wide range of indications where IL-6 biology is implicated. The potential benefits of pacibekitug may include:

- **Deep and sustained suppression of the IL-6 pathway**. In preclinical studies, pacibekitug has exhibited high affinity for IL-6 (kD in the picomolar range) and, in clinical studies, has exhibited a naturally occurring terminal half-life of 47 to 58 days. Pacibekitug has demonstrated meaningful suppression of IL-6 signaling at doses as low as 10mg as measured by hs-CRP. hs-CRP is an acute phase protein and a key downstream marker of IL-6 pathway signaling.

- **Low-volume, subcutaneous delivery**. Pacibekitug is expected to be subcutaneously administered with a 1mL or lower volume, making it a potentially more convenient therapy for patients and physicians compared to agents that require intravenous infusion or high-volume subcutaneous injection or infusion.

- **Infrequent dosing**. We expect pacibekitug will be dosed once every eight weeks or possibly every three months, depending on the indication, which is supported by prior studies conducted by Pfizer as well as our pharmacokinetic-pharmacodynamic modeling.

- **Low immunogenicity**. To date, low potential for immunogenicity has been observed for pacibekitug, with only two patients demonstrating evidence of treatment-emergent ADAs out of the approximately 450 participants dosed in completed Phase 1 and Phase 2 studies.

	Pacibekitug	Actemra (tocilizumab)		Kevzara (sarilumab)	Enspryng (satralizumab)	Sylvant (siltuximab)
Company	**Tourmaline**	Roche		Regeneron	Roche	EUSA
Antibody Type	**Human**	Humanized		Human	Humanized	Chimeric
Target	**IL-6**	IL-6 receptor		IL-6 receptor	IL-6 receptor	IL-6
Stage of development	**In Phase 2b**	Approved		Approved	Approved	Approved
Indications being pursued	**ASCVD, AAA, TED**	RA, GCA, PJIA, SJIA, CRS, SSc-ILD, COVID19		RA, PMR, PJIA, SJIA	NMOSD, AE, MOGAD, TED	MCD
Black box warning	**Drug not approved**	Yes		Yes	No	No
Terminal half-life	**47-58 days**	21.5 days[1]		Up to 10 days[1]	30 days[1]	20.6 days[1]
Anti-drug antibodies	**<1% of patients**	1-2% of patients[1]		14-19% of patients[1]	38-73% of patients (~20% increase in drug clearance) [1]	0-2% of patients[1]
Route of admin	**Subcutaneous (SC)**	IV	SC	SC	SC	IV
Standard dose	**≤50mg**	8-12mg/kg	162mg	200mg	120mg	11mg/kg
Dosing regimen	**Q8W / Q12W**	Q4W	QW / Q2W	Q2W	Q4W	Q3W

AAA: Abdominal Aortic Aneurysm; AE: Autoimmune Encephalitis; ASCVD: Atherosclerotic Cardiovascular Disease; COVID-19: Coronavirus Disease 2019; CRS: Cytokine Release Syndrome; GCA: Giant Cell Arteritis; MCD: Multicentric Castleman's Disease; MOGAD: Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease; NMOSD: Neuromyelitis Optica Spectrum Disorder; PJIA: Polyarticular Juvenile Idiopathic Arthritis; PMR: Polymyalgia Rheumatica; RA: Rheumatoid Arthritis; SJIA: Systemic Juvenile Idiopathic Arthritis; SSc-ILD: Systemic Sclerosis-Associated Interstitial Lung Disease; 1 As reported in the label or FDA review documents of the approved products; no head-to-head studies have been conducted against the approved products shown here, which have each been evaluated in indications other than those we are pursuing

Cardiovascular Inflammation

Cardiovascular disease ("CVD") is a group of disorders that affect the heart and blood vessels and includes coronary artery disease, heart failure, and stroke. CVD is a leading cause of morbidity and mortality, with an estimated 20 million cardiovascular-related deaths worldwide in 2021. CVD-related deaths continue to increase each year despite the wide availability of targeted treatment options, indicating that current therapies are not adequately addressing all risk factors as the global population continues to grow and age.

Cardiovascular Scientific Advisory Board

In October 2024 we announced the formation of our Cardiovascular Scientific Advisory Board ("CV SAB"). The CV SAB brings together academic and industry veterans with significant experience in cardiovascular medicine, clinical trial design and execution, and therapeutic innovation. This world-class group of experts is expected to provide strategic guidance and expertise as we advance our development efforts for pacibekitug within cardiovascular inflammation. Our CV SAB is currently comprised as follows:

- Deepak L. Bhatt, MD, MPH, MBA (CV SAB Chair) - Mount Sinai Fuster Heart Hospital
- Paul M. Ridker, MD, MPH - Harvard Medical School, Brigham and Women's Hospital
- Joshua A. Beckman, MD, MSc - University of Texas Southwestern
- Marc P. Bonaca, MD, MPH - University of Colorado, CPC Clinical Research
- Robin Choudhury, MA, DM - University of Oxford

- Dipender Gill, MD, PhD - Sequoia Genetics
- Douglas L. Mann, MD - Washington University School of Medicine
- James Min, MD - Cleerly, Inc.
- Pradeep Natarajan, MD, MMSC - Massachusetts General Hospital, Harvard Medical School
- Michael D. Shapiro, DO, MCR - Wake Forest University
- Michael Szarek, PhD - University of Colorado, CPC Clinical Research

ASCVD

Atherosclerosis, or the accumulation of fatty and fibrous material along the artery walls, is a significant contributing factor to approximately 80% of all cardiovascular deaths. Atherosclerotic plaques can acutely rupture, leading to blood clot formation in the artery and impairment of blood supply to vital organs, such as the heart or brain. Clinically, plaque ruptures manifest as fatal or nonfatal MACE such as myocardial infarction, or heart attack, and stroke.

A variety of risk factors are associated with the development of ASCVD including:

- Demographic factors such as family histories of ASCVD, race, and sex.
- Lifestyle factors including smoking, unhealthy diet, or lack of activity and exercise.
- Comorbidities including diabetes, obesity, chronic kidney disease, hypertension, and chronic inflammatory diseases.
- Biomarkers such as elevated cholesterol, hs-CRP, and triglyceride levels.

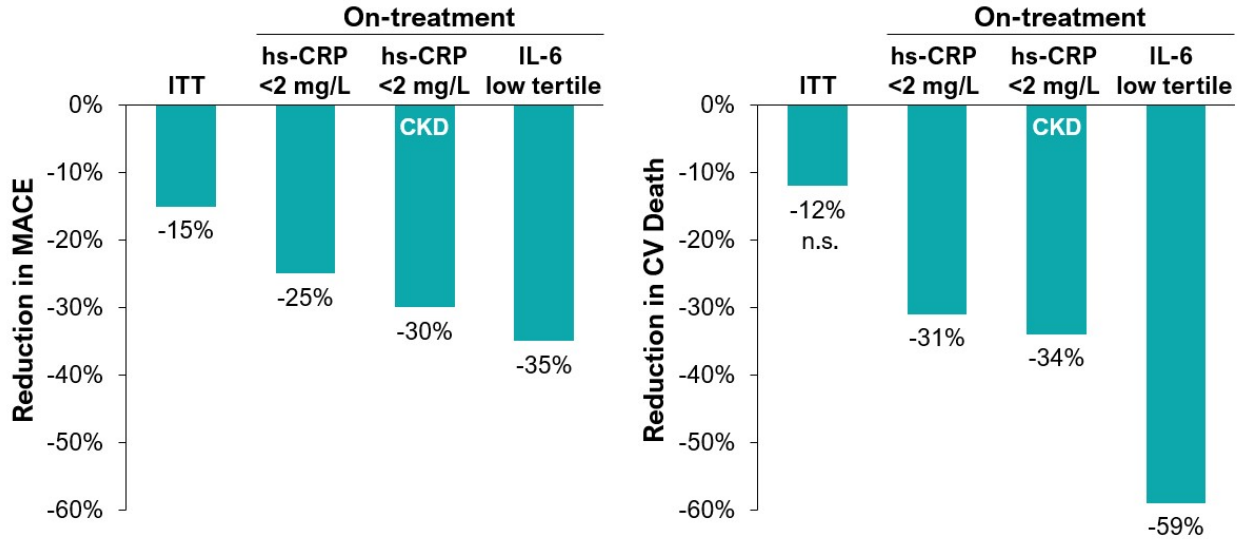
Current Treatment Paradigm for ASCVD

ASCVD treatment focuses on mitigating risk factors and includes lifestyle modifications, such as diet and exercise, and pharmacological interventions such as lipid lowering agents, antihypertensive agents, antiplatelet agents, and anticoagulants. In some cases, invasive procedures such as angioplasty or bypass surgery may be required for patients with more advanced disease. Most pharmacological interventions for ASCVD are once-daily, oral therapies, such as statins, a mainstay lipid-lowering therapy. Despite the wide availability of such agents, the overall disease burden remains high globally. Even in patients optimally managed with lifestyle modifications and pharmacologic therapies, a sizable subset of individuals with ASCVD continue to suffer from a high risk of MACE, indicating additional risk factors, such as inflammation, remain inadequately addressed. Additionally, adherence to these oral therapies is low as patients do not immediately experience the benefit of treatment. We believe a therapy with a longer dosing interval may be better suited for the treatment of ASCVD as it may better align with regular physician check-ins and improve patient adherence. Thus, we believe there is a significant unmet need for additional therapies with longer dosing intervals that target risk factors for ASCVD not currently addressed by current therapies, particularly inflammation.

Role of IL-6-driven Inflammation in ASCVD

The critical role of inflammation in ASCVD pathogenesis has been studied for over two decades. Pro-inflammatory monocytes home to atherosclerotic lesions and engulf lipoproteins and become foam cells that accumulate in plaques. Oxidized phospholipids and lipoproteins serve as inflammatory markers which can recruit and activate T-cell and humoral responses, further driving inflammation and atherosclerosis. Elevated hs-CRP is a known risk factor for ASCVD and is included in multiple guidelines for risk assessment for ASCVD. Chronic inflammatory conditions such as psoriasis, RA, and lupus are also risk factors. Across multiple cardiovascular outcomes studies, reduction of inflammation has been associated with improved outcomes and has been shown to be a more powerful predictor for therapeutic benefit than other biomarkers, such as cholesterol levels. Further, across a number of external cardiovascular outcomes trials, indirect inhibitors of IL-6-driven inflammation demonstrated statistically significant MACE reductions while outcomes trials of non-IL-6-related anti-inflammatory mechanisms did not produce statistically significant MACE reductions, highlighting the importance of IL-6 inhibition in targeting inflammation in CVD. These trials did not directly test an anti-IL-6 mechanism.

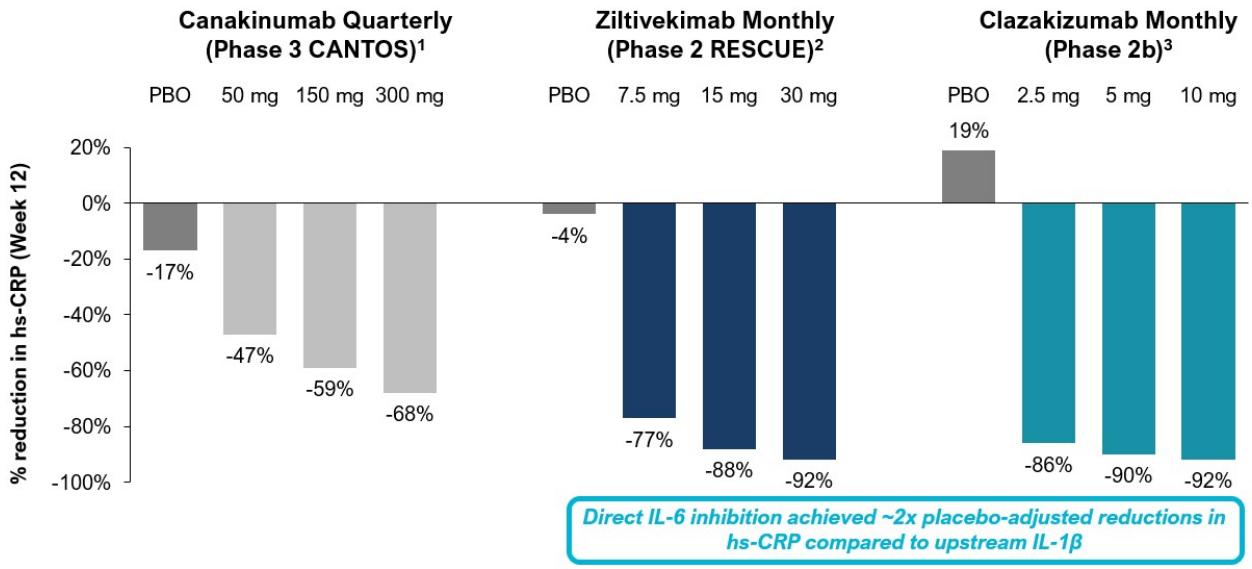
A targeted anti-inflammatory approach to treat CV disease was most recently supported by the third-party CANTOS study of canakinumab, a monoclonal antibody targeting IL-1ß, a key cytokine that can upregulate IL-6 levels. In three months, 150mg canakinumab achieved approximately 59% reduction in hs-CRP, without any discernable effect on other key risk factors such as low-density lipoprotein cholesterol; thus, the CANTOS study was the first significant investigation of a targeted anti-inflammatory approach for the treatment of ASCVD. In the large cardiovascular outcomes trial, 150mg canakinumab given once every three months provided a statistically significant 15% relative benefit compared to placebo in the secondary prevention of MACE in patients who had a previous myocardial infarction or stroke, confirming the therapeutic potential of a targeted, anti-inflammatory approach in CVD. Notably, the relative benefit versus placebo was 25% for the subgroup of patients who, following one treatment of canakinumab, had hs-CRP levels less than or equal to 2.0 mg/L, or within the normal range. This benefit was increased to 35% versus placebo for the subgroup of patients whose on-treatment IL-6 levels were in the lowest tertile following one dose of canakinumab. Notably, these trends in therapeutic benefit were also seen on reductions in cardiovascular death.



Results from CANTOS study of canakinumab in ASCVD. Reduction in MACE shown as 1-Hazard Ratio. MACE: major adverse cardiovascular events including CV death, myocardial infarction (MI), stroke. Overall CANTOS analysis presents data for 150mg dose group; values for CANTOS subanalyses combine all doses (50, 150, 300 mg). Ridker et al., NEJM (2017). Ridker et al., Lancet (2018). Adjusted for age, gender, smoking, hypertension, diabetes, BMI, baseline hs-CRP, baseline LDL-C. Ridker et al., Eur Heart J (2018). Adjusted for age, gender, smoking, hypertension, diabetes, BMI, baseline IL-6, baseline LDL-C. Ridker et al., JACC (2018).

As demonstrated in the CANTOS study, IL-6 is a key inflammatory cytokine in the pathology of ASCVD. Prior to CANTOS, the role of IL-6 in ASCVD had been characterized by over two decades of research. Patient IL-6 levels are a powerful predictor of future CV events, with one study showing that patients in the highest quartile of IL-6 levels were over twice as likely to have a CV event as patients in the lowest quartile. Additional genome and phenome-wide association studies have linked genes and phenotypes associated with higher IL-6 levels with greater cardiovascular risk. Nonclinical research has also implicated IL-6 in plaque erosion and rupture. CV system endothelial cells express IL-6 in response to inflammation, stress, and/or injury. Additionally, IL-6 has demonstrated the ability to upregulate cell adhesion molecules and plays a role in vascular permeability.

Following the results of the CANTOS study, the potential of an IL-6 targeted approach for ASCVD was further supported by the third-party Phase 2b RESCUE study of ziltivekimab, an anti-IL-6 monoclonal antibody, which showed up to 92% hs-CRP reductions for the 30 mg group at 12 weeks following monthly doses in an ASCVD patient cohort co-presenting with renal disease. By comparison, canakinumab only achieved as high as 68% reduction in hs-CRP.



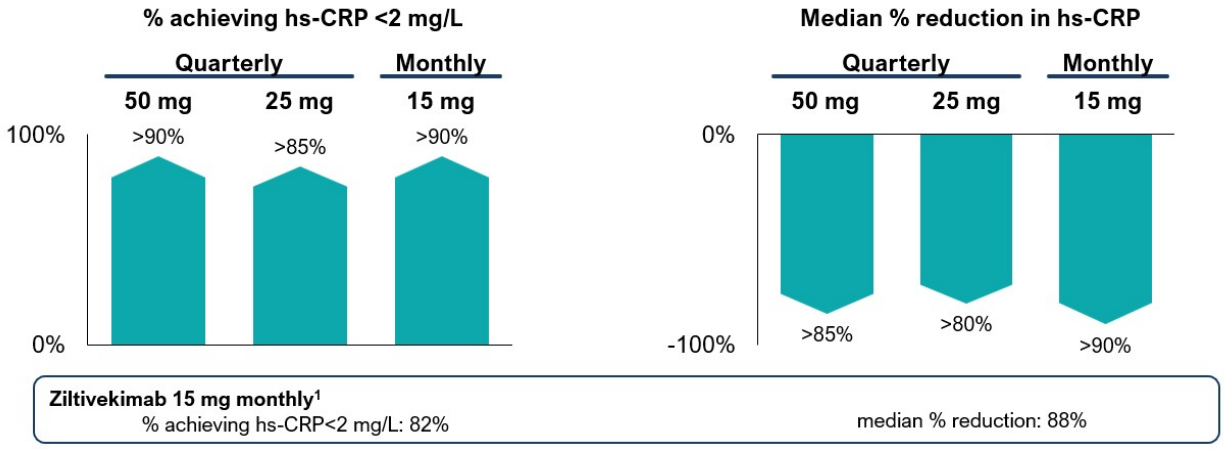
hs-CRP reductions after treatment with canakinumab, ziltivekimab and clazakizumab. 1. Ridker et al., NEJM (2017); median reductions reported . 2. Ridker et al., Lancet (2021); median reductions reported. 3. Chertow, Nature (2024):geometric mean ratios reported. Certain data in this slide are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross-trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein.

Multiple external Phase 3 cardiovascular outcome trials investigating IL-6 blockade are ongoing, and a positive readout from any of these trials could substantially validate the therapeutic hypothesis for IL-6 blockade in ASCVD. Novo Nordisk is currently testing ziltivekimab in four concurrent Phase 3 trials which we believe are de-risking opportunities for our own clinical development plan. For example, the ZEUS trial is testing ziltivekimab once every month in a 6,200 patient cardiovascular outcomes trial in ASCVD patients with chronic kidney disease.

Pacibekitug for the Treatment of ASCVD

We believe pacibekitug may offer a more convenient dosing profile for IL-6 inhibitors in the treatment of ASCVD. Competitor anti-IL-6 agents under development involve either intravenous administration or a subcutaneous administration once a month. In contrast, the targeted dosing regimen for pacibekitug is subcutaneous administration once every three months supported by its PK/PD modeling as shown in the figure below. Prior Phase 1 and Phase 2 trials of pacibekitug observed consistently lower levels of hs-CRP approximately three months following the last dose. A quarterly dosing regimen for pacibekitug would offer the potential to meaningfully improve patient convenience as well as optimize patient adherence to therapy due to the decreased drug administration burden.

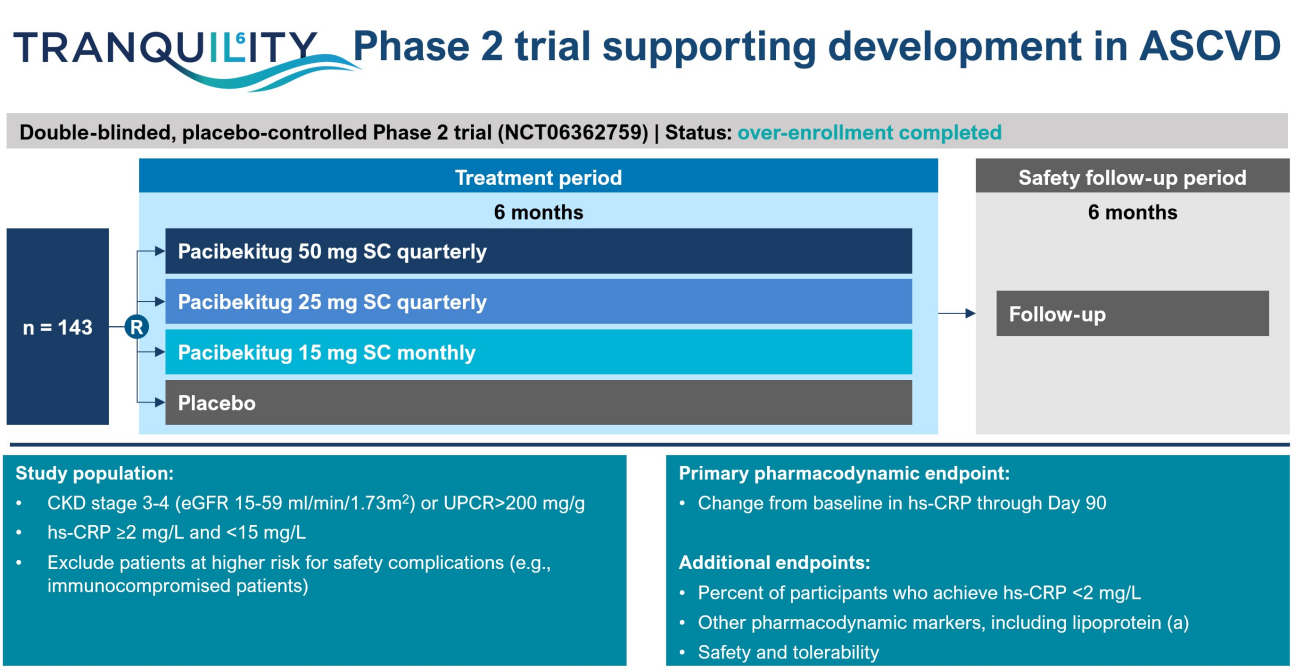
Results of pacibekitug PK/PD model developed from five studies in patients with RA, SLE, CD and healthy volunteers



ASCVD: atherosclerotic cardiovascular disease, RA: rheumatoid arthritis, SLE: systemic lupus erythematosus, CD: Crohn's disease. The PK and PK/PD models for pacibekitug were developed based on the data from 5 clinical trials (two phase 1 studies in healthy volunteers, one phase 1 trial in RA, one phase 2 trial in SLE, and one phase 2 trial in CD). A two-compartment model with first-order absorption and linear elimination and a mechanism-based indirect response model (in a relationship on hs-CRP) adequately described the PK and PK/PD relationships, respectively. Simulations were performed assuming an RA-like population with baseline hs-CRP >2 mg/L to 10 mg/L. Results at Day 90 are shown. 1. Ridker et al., Lancet (2021). Results after 12 weeks of treatment are shown. Certain data in this slide are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross-trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein.

Pacibekitug Clinical Program in ASCVD

As previously announced in January 2024, we have reached alignment with the FDA on our ASCVD clinical development program for pacibekitug, including the Phase 2 TRANQUILITY trial evaluating hs-CRP reduction, a validated biomarker for inflammation, with quarterly and monthly dosing of pacibekitug in patients with elevated hs-CRP and CKD. In March 2024, the FDA cleared our IND related to our ASCVD clinical development program. The Phase 2 TRANQUILITY trial commenced in April 2024 and completed over-enrollment in December 2024. We expect to report topline data in the second quarter of 2025. Pending successful completion, we expect that positive results from the Phase 2 TRANQUILITY trial will position us to be ready Phase 3-ready for ASCVD.



Trial design for Phase 2 TRANQUILITY trial

Abdominal aortic aneurysm (AAA)

Affecting approximately 2 million patients in the United States, AAA is serious condition with high unmet need characterized by weakening and enlargement of the aorta, the largest blood vessel in the body. This expansion increases the risk of rupture which is a catastrophic and usually fatal event.

Current Treatment Paradigm for AAA

To prevent AAA rupture, surgery is recommended for large abdominal aortic aneurysms. The vast majority of patients with medium-sized AAA reach the recommended threshold for repair within three to five years. However, surgical repair, whether done via endovascular techniques or open surgery, is associated with near-term and long-term complications. There are no FDA-approved treatments to slow AAA growth. Addressing this treatment gap has been identified as a high priority among vascular specialists and researchers.

Role of IL-6-driven Inflammation in AAA

The totality of data provide compelling evidence to support the therapeutic potential of IL-6 inhibition to slow AAA growth. Naturally occurring human genetic variants that mimic low-dose IL-6 pathway inhibition have been associated with statistically significant reductions in the risk of developing abdominal aortic aneurysm. Epidemiological evidence is supportive as well. Higher circulating levels of IL-6 and higher aortic tissue levels of IL-6 have been associated with the presence of abdominal aortic aneurysm. In addition, higher levels of hs-CRP have been associated with a higher risk of AAA and increased AAA size. Finally, experimental evidence has been supportive of the potential therapeutic impact of IL-6 inhibition on AAA. In mouse models of AAA, genetic and pharmacological inhibition of IL-6 pathway signaling have been associated with decreased aneurysm expansion.

Pacibekitug for the Treatment of AAA

We believe pacibekitug has the potential be a first-in-disease treatment to slow the growth of AAA with a convenient infrequent, low volume, subcutaneous dosing regimen.

Pacibekitug Clinical Program in AAA

We are planning to initiate a Phase 2 proof of concept trial to evaluate the ability of pacibekitug to inhibit AAA growth. Serial imaging lies at the foundation of clinical care for patients with AAA, embedded firmly with clinical guidelines, and for our Phase 2 trial, we expect to leverage multimodality imaging to efficiently characterize pacibekitug. Dosing will be

informed by topline results from our Phase 2 TRANQUILITY trial, which we expect to report in the second quarter of 2025. We plan to discuss with the FDA the Phase 2 proof-of-concept design and share details of the forthcoming trial prior to trial initiation.

TED Overview

TED, also known as Graves' ophthalmopathy or thyroid-associated orbitopathy, is a debilitating autoimmune disorder that affects the eyes and surrounding tissues of patients. In the U.S., the annual incidence of TED is estimated to be approximately 16 per 100,000 females and 3 per 100,000 males, or approximately 30,000 new cases a year. TED occurs in two phases – the initial active phase, characterized by high inflammation which lasts between 6-36 months, and the subsequent inactive phase that is characterized by lower inflammation. TED can cause significant discomfort and can be sight-threatening if left untreated. Initial symptoms of TED may include dryness and irritation of the eyes, sensitivity to light, excessive tearing, diplopia and pain. As TED progresses, patients may develop retraction of their upper eyelids, swelling and redness around the eyes, and bulging of the eyes, also called proptosis. In severe cases, TED can be sight-threatening as a result of swelling and inflammation that can lead to compression of the optic nerve.

The underlying cause of TED is the production of stimulatory autoantibodies against thyroid-stimulating hormone receptor ("TSHR"), which activate TSHR-expressing fibroblasts and adipocytes around the eye, leading to aberrant cellular proliferation and production of cytokines that promote inflammation and tissue remodeling.

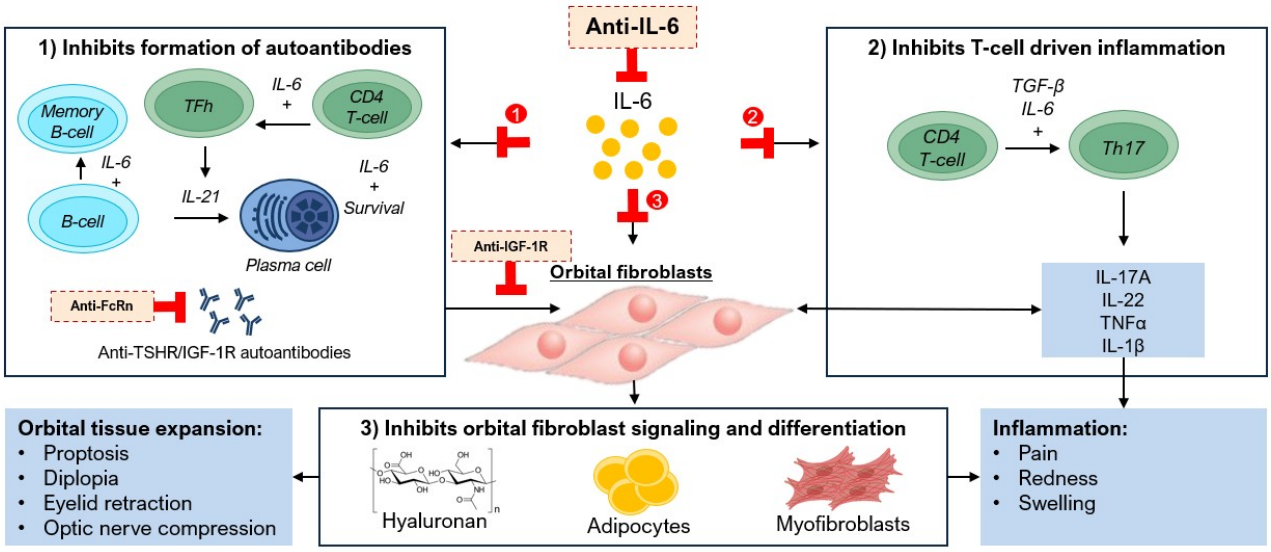
Levels of anti-TSHR antibody, specifically thyroid stimulating immunoglobulin ("TSI"), have been shown to be associated with the clinical features of TED and can influence its prognosis.

Recent studies have shown that the insulin-like growth factor 1 receptor ("IGF-1R") and TSHR form a receptor complex, with IGF-1R augmenting the signaling of TSHR. While the exact nature of the interaction between IGF-1R and TSHR is still being investigated, experimental evidence suggests that the effects of TSHR stimulating antibodies might only be partially blocked by an IGF-1R antagonist.

Autoantibodies that stimulate the TSHR have also been implicated in the disease pathology of Graves' disease, an autoimmune disorder that affects the thyroid gland. Graves' disease and TED are closely linked, and up to 95% of TED patients may have a history of Graves' hyperthyroidism at TED diagnosis. Some patients may also develop hyperthyroidism following presentation of TED symptoms.

Role of IL-6 in TED

IL-6 is believed to play a critical role in TED, including in autoantibody production, T cell-mediated inflammation, and orbital fibroblast activity. IL-6 and soluble IL-6R levels are elevated in patients with TED and correlate with disease activity. In a study of patients with Graves' disease, those who developed TED had significantly higher IL-6 levels than those who did not. In addition, elevated levels of biomarkers of IL-6 mediated signaling, such as hs-CRP, red blood cell distribution width, and neutrophil-to-lymphocyte ratio have been observed in patients with TED. Each of these markers represents distinct, downstream biological pathways modulated by IL-6, such as acute phase inflammation, iron metabolism, and immune cell regulation.



Current Treatment Paradigm for TED

Steroids, either oral or intravenous, are routinely used for the treatment of TED. While steroids may be an effective first-line treatment for some TED patients, as many as 50% of patients may not receive an adequate response and long-term use of steroids is associated with significant safety risks including weight gain, bone thinning, neuropsychiatric effects, hyperglycemia, and hypertension. For patients with moderate-to-severe TED that are unresponsive to steroids, orbital radiation and, in severe cases, surgical interventions such as decompression surgery or strabismus surgery may be required.

In 2020, the FDA approved the first targeted therapy for the treatment of TED: TEPEZZA® (teprotumumab), a monoclonal antibody that targets IGF-1R. In two randomized, double-masked, placebo-controlled trials, eight intravenous infusions of teprotumumab infused every three weeks led to proptosis response rates, defined as a ≥2 mm decrease in proptosis from baseline, in 71% and 83% of patients respectively, compared to 20% and 10% with placebo, respectively, at week 24. Based on our third-party and internal market research, the majority of TEPEZZA use appears to be reserved to later lines of treatment, primarily by oculoplastic surgeons, while front-line treatment providers, namely general ophthalmologists, have had limited uptake of TEPEZZA to date.

Limitations of Current IGF-1R Treatment

While IGF-1R treatments for TED may be promising and have demonstrated meaningful proptosis response rates for patients, we believe there remains a significant unmet need in light of the limitations of IGF-1R related treatments, including:

- **High patient and physician burden**. Teprotumumab's dosing regimen requires visits to an IV infusion center once every three weeks for a total of eight visits. Generalist ophthalmologists, who typically are the front-line treatment providers of TED, do not usually have direct access to an IV infusion center, and patients with significant diplopia or visual impairment may have difficulty traveling to centers.

- **Significant side effects**. Teprotumumab is associated with significant, debilitating side effects including nausea, muscle spasms, hyperglycemia, and hearing impairment, the latter of which has at times been reported as possibly permanent.

- **Incomplete durability of proptosis benefit**. Long-term follow-up of patients studied in teprotumumab's Phase 3 clinical trial showed that approximately 40% of patients did not sustain their proptosis response 48 weeks after their last infusion.

- **Incomplete treatment response rates**. Clinical trials of teprotumumab observed lower response rates on other clinically important aspects of TED besides proptosis, such as improvements in diplopia or inflammatory disease activity as measured by Clinical Activity Score ("CAS").

Hearing Disturbances Associated with IGF-1R Inhibition

IGF-1 pathway signaling is required for development and function of cell types in the inner ear, and thus is critical for the ability to hear. Loss-of-function genetic mutations in the IGF-1 pathway have been associated with sensorineural hearing loss and deafness.

Evidence of hearing impairment has been observed in clinical trials with IGF-1R inhibitors. Across the Phase 2 and Phase 3 clinical trials of teprotumumab (TEPEZZA), 10% of TEPEZZA-treated patients reported hearing-related adverse events. Other IGF-1R inhibitors have also reported hearing-related adverse events.

A meta-analysis published in April 2022 reported that hearing-related disturbances occurred in 15% of patients treated with TEPEZZA, of which 45% were reported as persistent. Another publication reports that hearing disturbances began to emerge after a mean of 3.6 infusions of TEPEZZA (out of the standard eight infusions per treatment course). Furthermore, as of December 2024, 1,121 cases of hearing and ear-related adverse events related to TEPEZZA treatment have been captured in the FDA's Adverse Event Reporting System (FAERS) database. These events have included reports of permanent deafness.

As of February 2025, over 220 lawsuits have been filed by patients who allege they suffered hearing loss due to treatment with TEPEZZA related to a failure by Horizon Therapeutics plc, which was acquired by Amgen, and which manufactured, promoted, and sold TEPEZZA prior to the acquisition, to adequately inform patients of the risk of hearing loss associated with TEPEZZA. In July 2023, the FDA required Horizon Therapeutics plc to update TEPEZZA's label to include a warning that states, "TEPEZZA may cause severe hearing impairment including hearing loss, which in some cases may be permanent. Assess patients' hearing before, during, and after treatment with TEPEZZA and consider the benefit-risk of treatment with patients."

Clinical Experience in TED with IL-6 Inhibition

There is a large and growing body of literature documenting successful clinical experiences with IL-6 pathway inhibition, namely the use of tocilizumab, an anti-IL-6R antibody, as an off-label treatment for TED. In over 50 investigator-led studies and retrospective analyses, spanning a total of over 400 patients with TED, IL-6 pathway inhibition was reported to offer meaningful improvement in proptosis, CAS, and/or diplopia. Substantial reductions in TSI levels have also been noted. Treatment was observed to be generally well-tolerated, with no major safety signals reported. In addition to this host of published literature, the European Group on Graves' orbitopathy ("EUGOGO") recommends tocilizumab for treatment of moderate-to-severe, steroid-resistant TED.

Together, this evidence highlights the consistent and beneficial use of IL-6 pathway blockade in the treatment of TED by leading physicians. Notably, many of the published treatment experiences were in patients with glucocorticoid-resistant TED, who were treated later in their disease course after a prolonged period of inflammation. We believe that first-line intervention earlier in the inflammatory phase may be an optimal approach to maximize the potential treatment benefit of blocking the IL-6 pathway.

A summary of published literature reporting on the off-label use of IL-6 pathway inhibition in TED is provided in the table below. This published literature listed below may not be indicative of future clinical results for pacibekitug.

Study Details					Key Endpoints		
First author	Study Drug	Year	Study type	Number treated	Proptosis response rate	CAS response rate	% reduction in autoantibodies
Perez-Moreiras	TCZ	2021	Retrospective	54	78	89	75
Sánchez-Bilbao	TCZ	2020	Observational	48	NR	NR	NR
Atienza-Mateo	TCZ	2018	Multicenter	29	NR	NR	NR
Farde	TCZ	2024	Retrospective	23	64	NR	75
Lee	TCZ	2024	Prospective	19	11	47	56
Pérez-Moreiras	TCZ	2014	Prospective	18	72	100	76
Pérez-Moreiras	TCZ	2018	Randomized Controlled	15	93	60	NS
de la Fuente Bursón	TCZ	2020	Retrospective	15	NR	NR	NR
Pereira	TCZ	2023	Retrospective	14	NR	NR	NR
Habroosh	TCZ	2024	Prospective	13	100	31	68
Boutzios	TCZ	2023	Observational	12	NR	NR	84
Pampin-Sánchez	TCZ	2022	Retrospective	11	75	73	NR
Moi	TCZ	2022	Retrospective	10	Clear improvement	80	75
Cortez	TCZ	2022	Prospective	10	10	100	81
Guo	TCZ	2024	Retrospective	10	NR	NR	NR
Silkiss	TCZ	2020	Case Series	9	Clear improvement	56	74
Smith	TCZ	2021	Retrospective	9	78	100	54
Bielefeld	TCZ	2019	Observational	8	NR	NR	NR
Ceballos-Marcias Jose	TCZ	2020	Case Series	8	NR	75	41
Bennedjai	TCZ	2020	Retrospective	7	NR	NR	73
Moás	TCZ	2022	Observational	7	NR	NR	92
Toro-Tobon	TCZ	2023	Retrospective	6	50	NR	NR
de Pablo Gomez	TCZ	2018	Case Series	5	NR	60	NR
Navarrete	SAR	2022	Retrospective	5	NR	NR	NR
Ribi	TCZ	2017	Case Series	3	33	67	NR
Maldiney	TCZ	2020	Case Series	3	67	NR	NR
Stevens	TCZ	2022	Retrospective	3	100	67	NR
Russell	TCZ	2017	Case Series	2	NR	0	NR
Sy	TCZ	2017	Case Series	2	Clear improvement	50	69
Copperman	TCZ	2019	Case Series	2	100	0	NR
Coy	TCZ	2019	Case Series	2	NR	50	NR
Sierra Osorio	TCZ	2020	Case Series	2	100	100	NR
Park	TCZ	2021	Case Series	2	100	100	NR
Abeillon-du Payrat	TCZ	2022	Case Series	2	100	50	NR
Butnaru	TCZ	2013	Case Report	1	NR	100	NR
Gómez Rodríguez	TCZ	2014	Case Report	1	NR	100	NR
Bielefeld	TCZ	2017	Case Report	1	Clear improvement	NR	NR
Canas	TCZ	2018	Case Report	1	100	NR	NR
Pascual-Campa	TCZ	2018	Case Report	1	NR	NR	NR
Garreta Fontelles	TCZ	2019	Case Report	1	NR	NR	93
Mehmet	TCZ	2020	Case Report	1	0	NR	NR
Kaplan	TCZ	2020	Case Report	1	NR	0	85
Cayon-Blanco	TCZ	2020	Case Report	1	NR	100	NR
Tran	TCZ	2020	Case Series	1	NR	NR	NR
Ruiz	TCZ	2021	Case Report	1	NR	NR	NR
Albrashdi	TCZ	2022	Case Report	1	100	NR	NR
Cezara	TCZ	2022	Case Report	1	NR	0	NR
Mohamed	TCZ	2022	Case Series	1	0	0	NR
Moleiro	TCZ	2022	Case Report	1	100	NR	86
Almazrouei	TCZ	2023	Case Report	1	NR	NR	NR
Cuculescu	TCZ	2023	Case Report	1	Clear improvement	0	NR
Nirmalan	TCZ	2023	Case Series	1	NR	NR	NR
Pramono	TCZ	2023	Case Report	1	NR	NR	NR
Rymuza	TCZ	2024	Case Report	1	100	0	8
				Weighted mean	**68%**	**72%**	**72%**
				Smith 2017 (Tepro Phase 2)	**71%**	**69%**	**N/A**
				Douglas 2020 (Tepro Phase 3)	**83%**	**59%**	**N/A**

Published literature reporting on the off-label use of IL-6 pathway inhibitors supports the potential of IL-6 blockade to offer meaningful effects upon proptosis and CAS. Proptosis response rate is generally defined in the data outlined here as a ≥2 mm proptosis improvement in the worse eye at baseline without any worsening in the other eye. CAS response rate is generally defined in the data outlined here as a CAS of 0 or 1. Studies referenced in this table represent investigator-led studies and were not designed with the intent of generating evidence for an approval of tocilizumab or sarilumab in TED. The majority of these studies were not designed with power to detect statistical significance. NR: not reported. TCZ: tocilizumab. SAR: sarilumab

Pacibekitug for the Treatment of TED

We seek to establish pacibekitug as a new standard-of-care for the first-line treatment of TED. We believe pacibekitug has the potential to offer attributes of an ideal first-line therapy for TED, including:

- **Broad, deep, and durable effects**. Based on the strong evidence implicating IL-6's central role in TED, we believe pacibekitug offers the potential for meaningful and durable benefit across multiple efficacy outcome measures relevant to TED, such as proptosis, CAS, and diplopia.

- **A generally well-tolerated product without a risk of hearing loss**. Based on the extensive safety experience with IL-6 pathway inhibitors as a class and the available safety data to date for pacibekitug, we believe that pacibekitug, at

the dosing regimens being evaluated, has the potential to be generally well-tolerated in TED without a risk of hearing loss.

- **An anti-inflammatory mechanism, well-suited for use early in disease**. Given the natural pathology of TED, pacibekitug's anti-inflammatory mechanism may be best suited for early use in the active inflammatory phase of disease, which has a time-limited window before tissue injury and fibrosis occur.

- **A patient-centric experience**. We plan to dose pacibekitug as a subcutaneous, low-volume (≤1 mL) injection once every eight weeks, which we believe will provide substantial improvements to ease of access and ease of use over the current standard of care.

We estimate that 15,000 to 20,000 patients out of the incident population in the U.S. have moderate to severe, active, inflammatory TED that may be appropriate candidates for treatment with an advanced therapy such as pacibekitug.

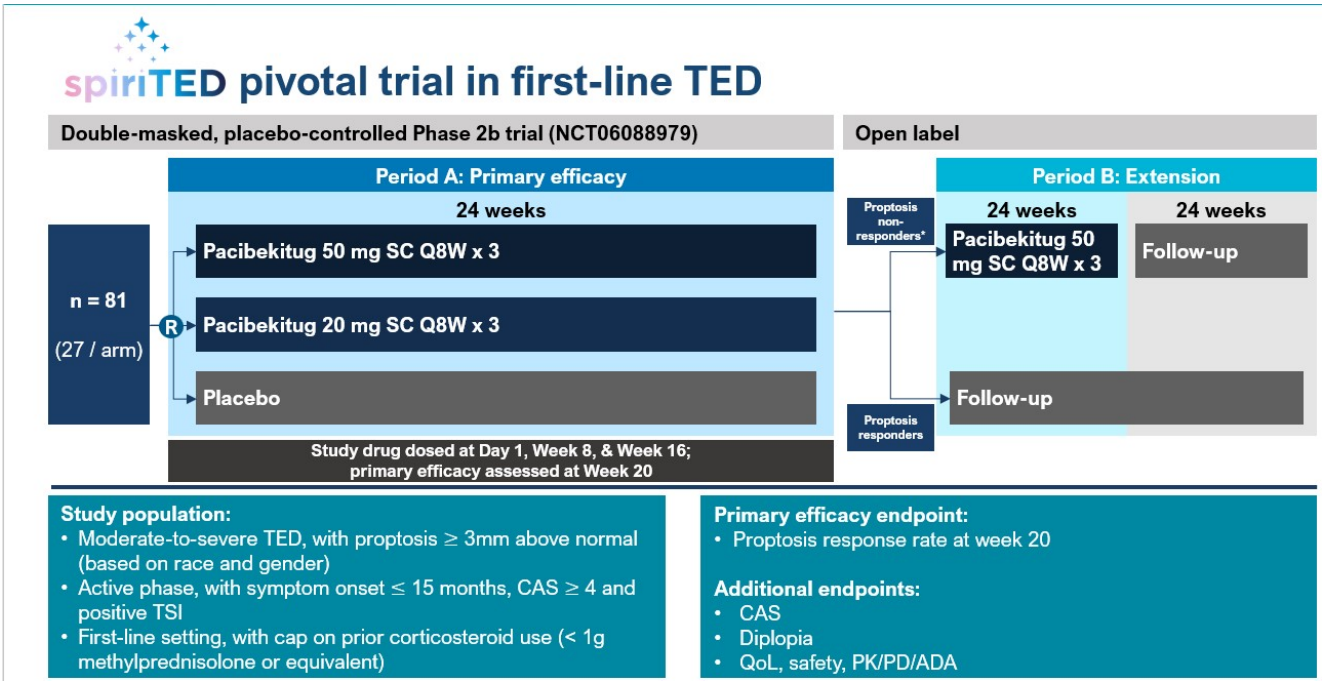
Pacibekitug Clinical Program in TED

We have initiated our first pivotal trial in TED, which we refer to as the spiriTED trial. This trial is a randomized, double-masked, placebo-controlled, dose-ranging Phase 2b study in adult patients with active, moderate-to-severe TED. We are enrolling approximately 81 participants with baseline proptosis at least 3 mm greater than the normal range for race and sex, baseline CAS score of 4 or greater on the 7-point scale, and TED symptom onset of approximately one year or less prior to entering the study. Participants must also have TSI positivity. The study protocol specifies additional inclusion and exclusion criteria.

In the Primary Efficacy Period (24-week duration), participants receive pacibekitug (20mg or 50mg) or placebo, administered subcutaneously every eight weeks at Day 1, Week 8, and Week 16. The primary endpoint of the study is the proptosis response rate at Week 20, defined as the percentage of participants who achieve at least a 2 mm reduction in proptosis from baseline in the study eye without worsening in the fellow eye and without need for rescue therapy or intervention. Additional endpoints include other efficacy outcomes (such as CAS and diplopia), safety, PK, PD, and ADA testing.

In the Extension Period, participants not experiencing a proptosis response (and not having received any rescue therapy or intervention) after completing the 24-week Primary Efficacy Period will receive 50mg of pacibekitug in an open-label fashion every eight weeks for three administrations. All participants (regardless of whether they receive pacibekitug) will be followed through week 72.

We expect to report topline results for the spiriTED's Primary Efficacy Period in the second half of 2025. Initiation of a Phase 3 trial in TED will be dependent upon results from the Phase 2b spiriTED trial.



Trial design for Phase 2b spiriTED trial *Any participant who receives rescue therapy/intervention in Period A will not receive pacibekitug in Period B and will instead undergo follow-up only.

Previous Clinical Experience with Pacibekitug

Prior to our in-licensing of pacibekitug in May 2022, Pfizer had treated approximately 450 study participants with pacibekitug across six clinical trials including Phase 2 studies in SLE and CD.

The following table summarizes the previous studies conducted by Pfizer:

Study Description	Subjects Who Received Pacibekitug	Doses Tested
Single Ascending Dose PK Study in Healthy Participants	36	7, 22, 44, 112, 284, 500, 700 mg IV, single dose
Multiple Ascending Dose PK Study in Participants with Rheumatoid Arthritis Receiving Methotrexate	31	1, 10, 30, 100, 250 mg IV Q4W
Single Dose PK Study of Pacibekitug Administered Subcutaneously to Healthy Participants	10	200mg SC, single dose
Phase 2 Dose-ranging Study in Participants with Moderate to Severe CD who are Anti-TNF Inadequate Responders	178	10, 50, 200 mg SC Q4W
Phase 2 Open-label Extension Study in Participants with Moderate to Severe CD	191	50, 100 mg SC Q8W
Phase 2 Dose-ranging Study in Participants with Active Generalized Systemic Lupus Erythematosus	138	10, 50, 200 mg SC Q8W

Phase 1 trial in healthy volunteers

Study design:

Pacibekitug was studied by Pfizer in a first-in-human Phase 1, randomized, placebo-controlled, double-masked, single ascending dose study in healthy volunteers. A total of 48 participants were enrolled; 12 received placebo and 36 received seven different fixed intravenous doses of pacibekitug: 7, 22, 44, 112, 284, 500, and 700mg. Participants were followed until their serum levels of pacibekitug were below the lower limit of quantitation ("LLOQ") and all treatment-related adverse events had resolved. The study was not powered for statistical significance.

PK/PD:

Pacibekitug's exposure PK increased in a dose-proportional manner across the dose range tested. Mean terminal elimination half-life was similar across dose groups, ranging from 47-58 days. A dose-dependent reduction in high-sensitivity CRP ("hs-CRP") was observed. hs-CRP is an indicator of inflammation and a downstream signal of IL-6 pathway activation. Maximal hs-CRP reductions relative to baseline were observed on Day 7 or Day 14 post dose across the various dose groups. Given the low baseline levels of Free IL-6 hs-CRP in this healthy population, the full PD effect of pacibekitug was not able to be observed compared to later studies in patients with inflammatory diseases.

Safety Data:

Pacibekitug in doses up to 500 mg appeared to be generally well-tolerated in this study with no dose limiting adverse effects, clinically significant laboratory abnormalities, or clinically relevant vital sign or ECG changes. During the study, three serious adverse events ("SAEs") were reported by two participants. An SAE of spontaneous abortion that was considered potentially treatment-related by the sponsor was reported in the sexual partner of a participant in the 284 mg pacibekitug arm. One participant in the 700 mg pacibekitug arm reported 2 SAEs (tonsillitis and acute pancreatitis), both of which were considered treatment-related. At least 67% of subjects in each pacibekitug group experienced at least one AE compared to 58% in the placebo group. Headache and fatigue were the most frequently reported AEs (all causalities and treatment-related). The most frequently reported treatment-related AEs by Medical Dictionary for Regulatory Activities (MedDRA) version 13.1 system organ class were infections and infestations and gastrointestinal disorders, reported by 8 and 11 subjects in the pacibekitug groups and 1 and 0 subjects in the placebo group, respectively.

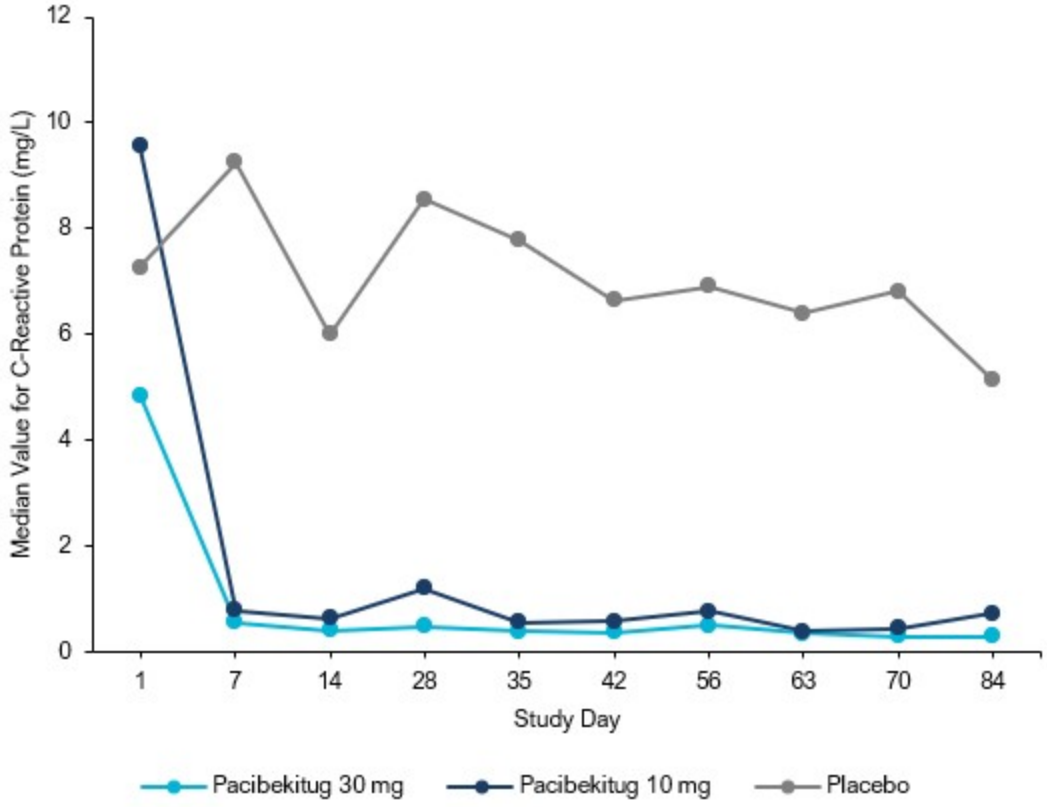
Phase 1 trial in RA patients

Trial design:

Pacibekitug was studied by Pfizer in a Phase 1 randomized, placebo-controlled, double-masked, escalating dose study investigating multiple ascending doses of intravenous pacibekitug in RA patients receiving methotrexate. A total of 40 participants were treated 9 received placebo and 31 received 3 monthly IV doses of pacibekitug at a set dosing level: 1, 10, 30, 100, or 250 mg. Participants were followed until their serum levels of pacibekitug were below the LLOQ and all treatment-related AEs had resolved. The study was not powered for statistical significance.

PK/PD:

Pacibekitug exposure increased approximately in proportion with dose. Accumulation of pacibekitug exposure, in terms of increases in Cmax after each 4-week dosing interval, was nearly constant from dose to dose and consistent with time-linear PK. Mean terminal elimination half-lives were 36-49 days across pacibekitug treatment groups. Greater serum CRP concentration reductions from baseline were observed in pacibekitug treatment groups compared with placebo from Day 7 to Day 84 and reductions appeared to be dose-related. Mean percent reductions from baseline were >80% (and up to 96%) in the higher pacibekitug dose groups. A single 10 mg intravenous dose of pacibekitug led to rapid and substantial decrease in CRP as shown in the figure below. Maximal reductions in CRP concentrations relative to baseline were generally observed by day 7 or day 14 across the various treatment groups. The time required for CRP levels to return to baseline appeared to increase as dose increased.



Median serum concentration of hs-CRP over time, with intravenous doses of study drug administered on day 1, 28, and 56 to RA subjects

Safety Data:

All doses of pacibekitug tested in the study appeared to be generally well-tolerated. During the study, three participants reported five treatment-emergent SAEs: two participants in the 30 mg pacibekitug arm and one in the 100 mg pacibekitug arm. The observed SAEs were plantar fasciitis, plantar abscess, pneumonia, chest pain (all in the 30 mg arm) and road traffic accident (100 mg arm). Proportions of subjects with treatment-emergent and treatment-related AEs were similar between placebo and pacibekitug treatment groups (100.0% vs 80.6%, and 44.4% vs 51.6%, respectively). A slightly greater proportion of pacibekitug-treated subjects experienced upper respiratory tract infection, increases in alanine transaminase ("ALT") and aspartate transaminase ("AST"), and leukopenia treatment-emergent adverse effects ("TEAEs"), compared with placebo-treated subjects (25.8% vs 11.1%, 12.9% vs 0%, 12.9% vs 0%, and 9.7% vs 0%, respectively). No subjects with increased ALT or AST TEAEs met study criteria for abnormal laboratory values (i.e., >3 × upper limit of normal). Of the 4 subjects with TEAEs related to either hypercholesterolemia or dyslipidemia during the study, all responded well to the addition of lipid-lowering treatment with a reduction in serum lipid levels.

Phase 1 trial in healthy volunteers for single subcutaneous dose

Trial design:

Pfizer investigated pacibekitug in a Phase 1, single center, open-label study to investigate the safety, tolerability, and PK of a single dose level of subcutaneously administered pacibekitug in 10 healthy adult participants (all male). A dose of 200 mg SC was chosen for this study (2 concurrent 100 mg doses). The study was not powered for statistical significance.

Safety Data:

There were no SAEs, deaths, dose reductions, or discontinuations due to AEs during the study. A single 200 mg total dose of pacibekitug administered SC appeared to be well-tolerated in this study.

PK:

The PK profile of pacibekitug was characterized by a prolonged absorption rate followed by a mono-exponential decline in plasma concentrations. Comparison of exposure at similar doses following IV and SC administrations indicates that SC bioavailability is relatively high. The estimated dose-normalized AUCinf following the SC dose of 262 mg.h/mL/mg was similar to the average AUCinf of 249 mg.h/mL/mg following IV administration in healthy participants across a range of doses from 7 to 700 mg in the phase 1 single ascending dose trial of IV pacibekitug. The mean terminal elimination half-life was approximately 52 days.

Phase 2 trial in SLE patients

Trial design:

Pacibekitug was investigated by Pfizer in SLE through a Phase 2 randomized controlled trial, and results from this study have been published in a peer-reviewed medical journal. This Phase 2 trial was a multicenter, randomized, placebo-controlled, dose-ranging, double-masked, clinical study evaluating patients with active, generalized SLE. Participants were randomized to subcutaneous doses of pacibekitug: 10, 50, and 200 mg or placebo in a 1:1:1:1 ratio. The study included a 24-week treatment period and a 28-week follow-up period. Participants received study treatment on Day 1, Week 8, and Week 16. A total of 183 participants received at least 1 dose of study treatment (45 participants in the 10 mg pacibekitug group, 47 participants in the 50 mg pacibekitug group, 46 participants in the 200 mg pacibekitug group, and 45 participants in the placebo group). The primary endpoint of the study was the proportion of patients achieving a response on the SLE Responder Index (SRI-4) criteria at Week 24. The study was designed with 80% power to detect a 25% difference in the SRI-4 response rate between pacibekitug and placebo using a one-sided alpha of 0.05.

Safety:

Safety data results from this study supported the use of 10 and 50mg doses of pacibekitug. During the double-masked treatment period, the most commonly reported TEAEs (excluding infections or injection site reactions ("ISRs")) across all treatment groups were headache (8.7%), nausea (8.2%), and diarrhea (6.6%), and the most frequently reported infectious TEAEs were upper respiratory tract infection (13.7%), cystitis (5.5%), and pharyngitis/laryngitis (5.5%). A total of 15 participants across the study experienced at least 1 ISR: 8 participants in the 50 mg pacibekitug arm, 3 participants in the placebo arm and 2 participants each in the 10 mg and 200 mg pacibekitug arms. More subjects experienced SAEs in the placebo (5 subjects, 11.1%) and 200 mg (5 subjects, 10.9%) groups compared to the 10 mg (2 subjects, 4.4%) and 50 mg groups (1 subject, 2.1%). There were 4 deaths in the study (1 in the 10 mg arm and 3 in the 200 mg arm). Causes of death were suspected pulmonary embolism in the 10 mg arm, and cardio-respiratory arrest, sepsis with pulmonary embolism, and disseminated tuberculosis in the 200 mg arm. In the interest of the safety of participants in the study, dosing in the 200 mg arm was prematurely terminated, based on an unblinded recommendation from the internal review committee for this study.

SLE has an elevated risk of serious complications, such as infection and thromboembolism. This risk is further amplified in patients who have higher severity of inflammation and/or are in the midst of an active disease flare, as the patients in this study were. Additional confounding data was introduced from a high rate of concomitant medication use, such as systemic corticosteroids which may increase the risk for complications including infection and thromboembolism. Additionally, the 200 mg pacibekitug arm had a disproportionately higher rate of comorbidities at baseline, such as SLE-associated cardiorespiratory involvement and neuropsychiatric involvement. Despite these confounding factors, we do not intend to pursue treatment with a 200 mg dose of pacibekitug.

Efficacy Data:

The study did not meet the primary endpoint for efficacy on SRI-4, though the 10 mg pacibekitug treatment arm did see a numerical trend with a 60% response rate compared to 40% in the placebo arm (p=0.076, which is not statistically significant).

PK/PD:

Pacibekitug exposure increased dose-proportionally and mean terminal half-life ranged between 40-44 days. Dose proportional hs-CRP reductions were observed and serum hs-CRP levels were continuously suppressed from week 2

through week 24 in the treatment period. Median percentages of change of hs-CRP were 2.5%, -56.0%, -80.0%, and -93.0% at Week 24 in the placebo, 10, 50, and 200 mg pacibekitug treatment groups, respectively.

Phase 2 trials in Crohn's Disease patients

Trial design:

Pacibekitug was investigated by Pfizer in CD through a Phase 2 randomized controlled trial and a companion open-label extension ("OLE") trial. Results from these studies have been published in a peer-reviewed medical journal. The Phase 2 trial was a multi-center, parallel, dose-ranging, randomized, double-masked, placebo-controlled study evaluating patients with moderate to severe CD who were inadequate responders to anti-tumor necrosis factor ("TNF") therapy. Participants were randomized to subcutaneous doses of pacibekitug: 10, 50, 200 mg or placebo in a 1:1:1:1 ratio. Participants received study treatment on Day 1 and Day 28 of the 12-week induction period. The primary endpoint of induction study was the proportion of patients achieving a ≥70-point reduction in CD Activity Index ("CDAI") score ("CDAI-70"). After completing the induction period, participants could either enter the 28-week follow-up period or enter the OLE study. 247 participants received at least 1 dose of study treatment (67 participants in the 10 mg pacibekitug group, 71 participants in the 50 mg pacibekitug group, 40 participants in the 200 mg pacibekitug group, and 69 participants in the placebo group). Due to safety concerns from results of the SLE study, dosing of the 200 mg arm was prematurely terminated. The OLE study included a 48-week treatment period and a 28-week follow-up period. In the OLE, 191 participants received pacibekitug on Day 1 and every 8 weeks through Week 40. All participants received subcutaneous 50 mg pacibekitug on Day 1. Dose escalation to 100 mg was allowed for non-responders starting at 8 weeks; if such an individual did not experience a response within 8 weeks after this dose escalation, they were discontinued from the active treatment period. Responders who subsequently relapsed were also eligible for dose escalation to 100 mg. The OLE study was not powered for statistical significance.

Safety:

Safety results from this study supported the use of 10 mg, 50 mg, and 100 mg pacibekitug. At least 1 TEAE and at least 1 SAE were reported by 86.6% and 14.6%, respectively, of all participants during the first 12 weeks of the study. The most common TEAEs across all participants during this treatment period were CD (11.7%), abdominal pain (11.3%), nasopharyngitis (9.3%), and headache (8.5%). ISRs were infrequent, and there was no apparent imbalance in rates across treatment arms. There was 1 death in the 50 mg pacibekitug arm due to respiratory failure secondary to pneumonia following post-operative complications of colectomy in a participant with chronic obstructive pulmonary disease, which was assessed as unrelated to study treatment by the investigator. The most common SAEs across treatment arms were CD (15 participants), condition aggravated (6 participants), anal fistula and anal abscess (3 participants each), and abdominal pain (2 participants), and all other SAEs were experienced by only 1 participant across treatment arms; there were no apparent imbalances in the incidences of SAEs across treatment arms.

Across the 191 participants in the OLE, the median drug exposure was 378 days. At least 1 TEAE was reported by 89.5% of participants during the treatment period and 74.2% of participants during the follow-up period. At least 1 SAE was reported by 30.4% of participants during the treatment period and 20.6% of participants during the follow-up period. The most frequently reported TEAEs during the treatment period were CD (27.7%), abdominal pain (16.2%), and nasopharyngitis (12.0%). The incidence of ISRs during the treatment period was 4.7% and 11.0% of 50 mg pacibekitug-treated participants and 100 mg pacibekitug-treated participants respectively. The most common SAEs were worsening of CD (26 participants), followed by condition aggravated (13 participants). During the follow-up period, the most common TEAEs were worsening of CD (19.4%) and abdominal pain (7.7%). The most common SAEs were worsening of CD (17 participants) and condition aggravated (5 participants). No participants died during the OLE study in either the treatment period or follow-up period.

PD and Efficacy Data:

Serum hs-CRP levels were continuously suppressed from week 2 through week 12 in the induction period. Median percent change from baseline in serum hs-CRP were -12.3%, -66.4%, -86.3%, and -95.5% at Week 12 in the placebo, 10, 50, and 200 mg treatment groups, respectively.

The CDAI-70 response rates for the 50 mg pacibekitug arm were significantly greater than placebo at Week 8 (49.3% vs 30.6%, one-sided $p < 0.05$) and Week 12 (47.4% vs 28.6%, one-sided $p < 0.05$) and met the primary endpoint. The primary

endpoint was not met for the 10 mg dose of pacibekitug. Due to halting of dosing in the 200mg pacibekitug arm, efficacy analysis was not conducted for this treatment group.

Immunogenicity:

Across the six studies described above, limited immunogenicity has been observed to date. Across the approximately 450 healthy volunteers and patients treated with pacibekitug, two study participants had samples that were confirmed ADA positive following pacibekitug treatment. Both participants' ADAs were confirmed positive for neutralizing antibodies. Neither of the two participants experienced any AE or SAE that could be related to ADAs, and no discernible impact on PK was observed. Two additional participants had samples at baseline that were confirmed ADA positive but without any increase in ADA titer following pacibekitug treatment.

License Agreement with Pfizer

In May 2022, we entered into a license agreement (the "Pfizer License Agreement") with Pfizer, pursuant to which we obtained an exclusive, sublicensable, royalty-bearing, worldwide right to use and license under certain know-how for the development, commercialization and manufacture of PF-04236921 (the "Compound", now known as pacibekitug), and any pharmaceutical or biopharmaceutical product incorporating the Compound (the "Product"), for the treatment, diagnosis, or prevention of any and all diseases, disorders, illnesses and conditions in humans and animals. Pfizer is free to use the licensed know-how for any purpose other than those exclusively licensed to us.

We are responsible for the development, manufacture, regulatory strategy and commercialization of the Product worldwide. We are obligated to use commercially reasonably efforts to develop and seek regulatory approval for at least one Product in certain specified major markets. We are also obligated to use commercially reasonable efforts to commercialize a Product in each major market where it has received regulatory approval.

In consideration for the license and other rights we received under the Pfizer License Agreement, we paid Pfizer an upfront payment of $5.0 million and granted Pfizer 7,125,000 Series A preferred units of Tourmaline Bio, LLC, which subsequently converted to 7,125,000 shares of our Series A convertible preferred stock, which was the equivalent to 15% of all of our capital stock on a fully-diluted basis at the time of issuance. In addition, in May 2023, we issued 8,823,529 additional shares of our Series A convertible preferred stock to Pfizer pursuant to an anti-dilution provision within the Pfizer License Agreement. Subsequent to the issuance of these additional shares of Series A convertible preferred stock, the anti-dilution provision is no longer in force and effect. These shares of Series A convertible preferred stock were converted into 1,272,214 aggregate shares of our common stock upon consummation of the Reverse Merger.

As additional consideration for the license, we are obligated to pay Pfizer up to $128.0 million upon the achievement of specific development and regulatory milestones. We are also obligated to pay Pfizer up to $525.0 million upon the first achievement of specific sales milestones. We are also obligated to pay Pfizer a marginal royalty rate in the low-double digits (less than 15%), subject to specified royalty reductions. The royalty term, on a Product-by-Product and country-by-country basis, begins on the first commercial sale of such Product and expires upon the later of twelve years following the date of the first commercial sale or the expiration of regulatory exclusivity protecting such Product. In the event we complete a Significant Transaction (as defined in the Pfizer License Agreement), we will be obligated to pay Pfizer a one-time payment in the low-eight digits (up to $20.0 million); the amount of such payment is based on the timing of the transaction. As of December 31, 2024, we do not owe any milestones or royalties under the Pfizer License Agreement, and no such milestone or royalties have been paid to date.

The Pfizer License Agreement shall expire, unless earlier terminated, upon the last to expire royalty term, and at such time our license will become fully paid-up, irrevocable and perpetual. Each party shall have the right to terminate the Pfizer License Agreement in its entirety in the event of a material breach by the other party if the breaching party fails to cure such breach within a specified cure period after written notice. Pfizer may terminate the Pfizer License Agreement on a Product-by-Product and country-by-country basis if we have materially breached our diligence obligations. Each party shall have the right to terminate the Pfizer License Agreement in the event of a bankruptcy event. We have the right to terminate the Pfizer License Agreement at our convenience in its entirety or on a country-by-country basis (except with respect to the major market countries) upon a specified notice period based on the time of the termination.

License Agreement with Lonza

In May 2022, we entered into a license agreement (the "Lonza License Agreement") with Lonza Sales AG ("Lonza"), pursuant to which we obtained a worldwide, non-exclusive, sublicensable (subject to certain conditions) license under certain know-how to market, sell, offer for sale, distribute, import and export products containing pacibekitug ("Product"). We also obtained a non-exclusive, sublicensable (subject to certain conditions) license under certain licensed know-how to use, develop, and manufacture (including have manufactured in accordance with the terms of the Lonza License Agreement) Product at premises approved by Lonza.

In consideration for the licenses and other rights we received under the Lonza License Agreement, we are obligated to pay Lonza a royalty in the low-single digits on the Net Sales (as defined in the Lonza License Agreement) of Product, and the royalty rate shall be based on the entity manufacturing the drug substance contained in the Product. Royalties are payable on a Product-by-Product basis and a country-by-country basis for ten years following the first commercial sale of a Product in a certain country. In addition, we may owe Lonza a low six figure annual fee following the occurrence of a specified event depending on which entity manufactures the drug substance, all as specified in the Lonza License Agreement.

The Lonza License Agreement shall continue in full force and effect unless terminated in accordance with the terms of the Lonza License Agreement. Each party shall have the right to terminate the Lonza License Agreement in its entirety in the event of a breach by the other party if the breach is irremediable or the breaching party fails to cure such breach within a specified cure period after written notice. Each party shall have the right to terminate the Lonza License Agreement in the event of a bankruptcy event of the other party. We shall have the right to terminate the Lonza License Agreement at our convenience upon a specified notice period. Lonza shall have the right to terminate the Lonza License Agreement in the event of a change of control of us or we contest the secret or substantial nature of the licensed know-how.

Reverse Merger with Talaris

On June 22, 2023, privately-held Tourmaline Sub, Inc. (formerly Tourmaline Bio, Inc., "Legacy Tourmaline") entered into an Agreement and Plan of Merger (the "Merger Agreement") with Talaris Therapeutics, Inc. ("Talaris"), a publicly traded company, and Terrain Merger Sub, Inc., a direct, wholly owned subsidiary of Talaris ("Merger Sub"). On October 19, 2023, Legacy Tourmaline completed the merger with Talaris in accordance with the terms of the Merger Agreement, pursuant to which, among other matters, Merger Sub merged with and into Legacy Tourmaline, with Legacy Tourmaline surviving as a wholly owned subsidiary of Talaris (such transaction, the "Reverse Merger"). The Reverse Merger was intended to qualify for federal income tax purposes as a tax-free reorganization under the provisions of Section 368(a) of the Internal Revenue Code of 1986, as amended.

Immediately prior to the effective time of the Reverse Merger, Talaris effected a 1-for-10 reverse stock split of its common stock.

Pursuant to the terms of the Merger Agreement, immediately prior to the effective time of the Reverse Merger, each share of Legacy Tourmaline's Series A convertible preferred stock was converted into a share of Legacy Tourmaline common stock. At the effective time of the Reverse Merger, Talaris issued an aggregate of approximately 15,877,090 shares of common stock to Legacy Tourmaline's stockholders, based on an exchange ratio of 0.07977 shares of common stock for each share of Legacy Tourmaline's capital stock, including those shares of Legacy Tourmaline's common stock issued upon the conversion of the Series A convertible preferred stock and those shares of Legacy Tourmaline's common stock issued in the Pre-Merger Financing Transaction (as described below), resulting in approximately 20,336,741 shares of common stock of the combined company being issued and outstanding immediately following the effective time of the Reverse Merger. In connection with the Reverse Merger, the Amended and Restated Investor Rights Agreement, dated May 2, 2023, between Tourmaline and certain of its stockholders and the Amended and Restated Investors' Rights Agreement, dated September 22, 2020, between Talaris and certain of its stockholders, were terminated.

Immediately prior to the completion of the Reverse Merger, pursuant to a securities purchase agreement, Legacy Tourmaline issued 4,092,035 shares (as effected by the exchange ratio described above) of Legacy Tourmaline's common stock in a private placement for gross proceeds of $75.0 million (the "Pre-Merger Financing Transaction").

The issuance of the shares of our common stock issued to the former stockholders of Legacy Tourmaline was registered with the Securities and Exchange Commission ("SEC") on our Registration Statement on Form S-4 (File No. 333-273335), as amended.

In connection with the completion of the Reverse Merger, Talaris changed its name from "Talaris Therapeutics, Inc." to "Tourmaline Bio, Inc.," Legacy Tourmaline changed its name to "Tourmaline Sub, Inc.," and we began conducting the business conducted by Legacy Tourmaline.

The shares of our common stock listed on The Nasdaq Global Market, previously trading through the close of business on Thursday, October 19, 2023 under the ticker symbol "TALS," commenced trading on The Nasdaq Global Select Market on a post-Reverse Stock Split adjusted basis under the ticker symbol "TRML" on October 20, 2023.

On June 30, 2024, Tourmaline Sub, Inc. was merged with and into Tourmaline Bio, Inc., with Tourmaline Bio, Inc. as the surviving entity.

Sales and Marketing

We do not currently have our own marketing, sales or distribution capabilities. In order to commercialize pacibekitug or any future product candidate, if approved for commercial sale, we would have to develop a sales and marketing infrastructure or make arrangements with third parties to perform these services for it. We may opportunistically seek strategic collaborations to maximize the commercial opportunities for pacibekitug or any future product candidates inside and outside the U.S.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of pacibekitug. Furthermore, there is limited capacity at contract manufacturers that operate under the current good manufacturing practice ("cGMP") requirements of the FDA to meet our timelines and production needs. We currently rely and intend to continue to rely on contract development and manufacturing organizations ("CDMOs"), for drug substance, drug product, and labeling/packaging. Currently, we contract with three well-established third-party manufacturers, one for the manufacture of our drug substance, another for the manufacture of our drug product, and a third for labeling and packaging. We may engage additional third-party manufacturers to support any clinical trials for pacibekitug as well as commercialization of pacibekitug, if approved, in the U.S. or other jurisdictions. In addition, as our production needs increase, we may recruit additional experienced personnel to manage the CDMOs producing our product candidate and other product candidates or products that we may develop in the future.

We rely on CDMOs to perform all chemistry, manufacturing, and controls ("CMC") activities. Our agreements with CDMOs may obligate them to develop or transfer upstream and downstream processes, develop or transfer drug product manufacturing processes, develop or transfer suitable analytical methods for release and stability testing and qualify these methods for use with our products, produce drug substance for preclinical testing, and produce drug substance or drug product under cGMP for use in clinical studies among other activities. In addition, we rely on CDMOs to operate facilities that meet regulatory requirements for production and testing of clinical and commercial products and to work closely with us to validate manufacturing processes prior to commercial launch. We qualify CDMOs prior to initiation of cGMP regulated activities and periodically thereafter as part of the supplier qualification program. We oversee CDMOs by performing technical and quality assurance review and/or approval of cGMP documentation, establishing quality agreements to define responsibilities and expectations for goods and services, and observing production and testing activities as a person-in-plant, among other activities.

Competition

We seek to develop our product candidates in a highly competitive and ever-changing environment for biopharmaceuticals. We face and will continue to face competition from products with similar mechanisms of action, as well as products that work differently from ours but are being developed for the treatment of the same indications that we are pursuing. These competitors may impact our ability to recruit patients into our clinical trials on schedule or limit the uptake of our products, if successfully approved. Furthermore, many of these competitors may have access to greater financial, human and other resources than we do, as well as more regulatory and operational experience than we currently possess. New drug candidates continue to be developed and discovered, which could render our programs obsolete or non-competitive in the future.

Competition in IL-6

There are four FDA-approved products that block IL-6 or IL-6R, including tocilizumab (ACTEMRA®), siltuximab (SYLVANT®), sarilumab (KEVZARA®), and satralizumab-mwge (ENSPRYNG®). In addition, three biosimilars for tocilizumab have now been FDA approved, including TOFIDENCE® (Biogen), TYENNE® (Fresenius Kabi), and AVOTZMA® (Celltrion).

There are multiple IL-6 inhibitors in active clinical development (but not yet approved in the U.S.) including: ARGX-109 (argenx), clazakizumab (CSL Behring), levilimab (Biocad), olokizumab (R-Pharm), ziltivekimab (Novo Nordisk), and FB704A (Oneness Biotech Co).

Competition in ASCVD

Several classes of therapies are routinely used for the treatment of ASCVD. Examples of such therapy classes include (but are not limited to) statins and other therapies for dyslipidemia, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, other antihypertensive agents, aspirin, and anti-platelet agents. These therapies are largely once-daily, oral therapies. Recently, low-dose colchicine (LoDoCo®), a broad anti-inflammatory medicine, and bempedoic acid (Nexletol®), another lipid lowering agent, were approved for the treatment of ASCVD. Both are once-daily, oral medicines. Additionally, subcutaneously administered agents with longer dosing intervals inhibiting proprotein convertase subtilisin/kexin type 9 ("PCSK9") have been approved in the last decade. These agents include alirocumab (Praluent®), evolocumab (Repatha®), and inclisiran (Leqvio®). Glucagon-like peptide 1 ("GLP-1") receptor agonists and GLP-1/ glucose-dependent insulinotropic polypeptide ("GIP") co-agonists are also approved to reduce the risk of cardiovascular events in patients with type 2 diabetes and/or obesity. These therapies are typically subcutaneously administered once weekly with oral formulations also available. We are not aware of any targeted, anti-inflammatory therapies approved for ASCVD.

We are aware of two IL-6 antibodies currently being developed for the treatment of ASCVD. Novo Nordisk is developing ziltivekimab, a monthly, subcutaneously administered monoclonal antibody targeting IL-6, in two Phase 3 ASCVD cardiovascular outcomes trials. The ZEUS trial is testing ziltivekimab in patients with ASCVD, chronic kidney disease, and residual inflammatory risk. The ARTEMIS trial is testing ziltivekimab in patients with a recent myocardial infarction. Novo Nordisk also has two additional, ongoing Phase 3 trials testing ziltivekimab in heart failure. CSL Behring is developing clazakizumab, a monthly, subcutaneously administered monoclonal antibody targeting IL-6, in a Phase 3 cardiovascular outcomes trial in end-stage kidney disease patients with diabetes or ASCVD. In addition, we are aware of companies developing nucleotide binding oligomerization domain-like receptor family pyric domain-containing 3 ("NLRP3") inhibitors for the treatment of ASCVD. NLRP3 inhibitors are expected to lower hs-CRP levels and are also proposed to have other cardiometabolic effects. Companies we are aware of with ongoing CV-related trials of NLRP3 inhibitors include Novartis, Roche, Ventyx Therapeutics, Nodthera and Novo Nordisk (in partnership with Ventus Therapeutics). Other therapies being developed to reduce other risk factors (outside of IL-6-drive inflammation) for ASCVD include (but are not limited to) incretin-targeted agents, lipoprotein(a)-targeted agents, and angiopoietin-like protein 3-targeted agents.

Competition in AAA

Treatment for AAA is limited to surgical options. We are not aware of any pharmacological therapies approved for AAA or any ongoing, industry-sponsored studies evaluating a systemic therapy in AAA.

Competition in TED

To date, teprotumumab is the only FDA-approved agent for the treatment of TED. There are multiple other agents in various stages of development for the treatment of TED. These include, but are not limited to:

- Roche is developing satralizumab, currently being evaluated in ongoing Phase 3 studies.

- Viridian Therapeutics, Inc. ("Viridian") is developing veligrotug (also known as VRDN-001), a monoclonal antibody targeting IGF-1R and delivered by intravenous infusion, has reported results for two Phase 3 trials and plans to file for FDA approval. Viridian is also developing VRDN-003, an anti-IGF-1R antibody delivered by subcutaneous administration, currently in Phase 3 studies.

- Acelyrin, Inc. ("Acelyrin") is developing lonigutamab (VB-421), a monoclonal antibody targeting IGF-1R, delivered by subcutaneous administration, and previously announced plans to initiate two Phase 3 trials. In February 2025, Alumis Inc. announced a merger with Acelyrin and updated development plans for lonigutamab. As disclosed, Acelyrin plans to re-evaluate the development program for lonigutamab to confirm its differentiation in a capital efficient manner.

- Amgen is developing a subcutaneous form of teprotumumab, currently in a Phase 3 study. Amgen is also developing AMG732, a subcutaneous therapy with undisclosed mechanism of action, currently in a Phase 1 study.

- Sling Therapeutics, Inc. is developing linsitinib, a small molecule IGF-1R inhibitor, and has reported results from its Phase 2b study.

- Innovent Biologics, Inc. is developing IBI311, a monoclonal antibody targeting IGF-1R, delivered by intravenous infusion, currently under review by the China National Drug Administration.

- Minghui Pharmaceutical, Inc. is developing MHB018A, a monoclonal antibody targeting IGF-1R, delivered by subcutaneous administration. Phase 1b/2 data have been released along with plans to initiate Phase 3 trials in 2025.

- Lirum Therapeutics, Inc. is developing LX-101, an IGF-1 bound to methotrexate, currently in Phase 1 oncology studies, but with plans to develop in TED.

- argenx is developing efgartigimod, an antibody fragment targeting FcRn, currently being evaluated in ongoing Phase 3 studies.

- Immunovant, Inc. and Harbour BioMed are developing batoclimab (IMVT-1401/HBM9161), a monoclonal antibody targeting FcRn, currently being evaluated in ongoing Phase 3 studies.

- Lassen Therapeutics is developing LASN01, a monoclonal antibody targeting IL-11R, currently being evaluated in a Phase 2 study.

- Lundbeck is developing Lu AG22515, a recombinant fusion antibody targeting CD40L, currently being evaluated in a Phase 1b study.

- GenSci is developing GenSci098, a monoclonal antibody targeting TSHR, currently in a Phase 1 study.

- Regeneron is collaborating with the Massachusetts Eye and Ear Infirmary to study aflibercept, a soluble decoy receptor that binds vascular endothelial growth factor-A ("VEGF"-A), VEGF-B and placental growth factor, in a Phase 2 study.

- Kriya Therapeutics, Inc. is developing a gene therapy program, currently in preclinical studies.

- Crinetics Pharmaceuticals, Inc. is developing a TSHR antagonist, currently in preclinical studies.

- Septerna, Inc. is developing a TSHR negative allosteric modulator, currently in preclinical studies.

Intellectual Property

We pursue a layered intellectual property strategy, including patents, trademarks, and trade secret rights, to protect our company name and our pacibekitug platform, including its use in treating various indications of interest to us.

Our future commercial success depends, in part, on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; to defend and enforce our patents and other intellectual property; to preserve the confidentiality of our trade secrets; and to operate without infringing, misappropriating or violating the valid and enforceable patents and other intellectual property rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products, or from developing competing diagnostic technologies, may depend on the extent to which we have rights under valid and enforceable patents, trade secrets or other intellectual property rights that cover these activities. We cannot be sure that patents will issue with respect to any of the pending patent applications or, with respect to any patent applications that we may file or license in the future, nor can we be sure that any of the patents we do obtain will be commercially useful in

protecting any products that we ultimately attempt to commercialize, or any method of making or using such products. Moreover, we may be unable to obtain patent protection for certain of our indications. See the section titled "Risk Factors —Risks Related to Our Intellectual Property" in this Report for a more comprehensive description of risks related to our intellectual property.

Patents

An issued patent provides its owner (or its licensee) with a right to exclude others from making, using or selling that which is claimed in the patent, for a specified period of time (the "term" of the patent), in the jurisdiction in which the patent is issued. In the U.S., and in many other countries, patents have a presumptive term of 20 years from their effective filing date (which is the earliest non-provisional filing date to which the patent claims priority). However, many jurisdictions, including the U.S., require the payment of periodic maintenance fees in order for patents to remain in force for the full 20-year term; some jurisdictions require periodic annuities to be paid even to maintain pendency of an application. The U.S. also has provisions that require a patent term to be shortened if its claims are too similar to another patent owned by the same party that has a shorter term. The U.S. and certain other jurisdictions also have provisions that permit extension of patent terms for patents that claim a drug or drug product, or its approved use, if the patent was issued before clinical trials were completed and certain other requirements were satisfied. In the U.S., such extension is called a Patent Term Extension, or PTE, and it is limited to a period of not more than five years, or a period that would extend the patent so that the total patent term including the PTE does not exceed 14 years after the date of regulatory approval; only one patent can be extended per product approval. The U.S. also offers a different form of patent term extension, known as Patent Term Adjustment, or PTA, whereby a particular patent's term is automatically extended beyond the 20-year date if the U.S. Patent and Trademark Office caused delay during its examination; however, potentially available PTA is reduced by any amount of any delay caused by the patent applicant.

Our patent portfolio currently includes solely owned provisional patent application filings in the U.S., international patent applications and non-provisional patent applications in Taiwan covering the use of pacibekitug for treating specified ocular and inflammatory indications. Given our pre-commercial state of development, we cannot be certain that any of the patent application filings in our portfolio will provide meaningful protection for any drug or indication we ultimately attempt to commercialize. Non-provisional filings in the U.S. and other jurisdictions that claim the benefit of the provisional filings would have a presumptive twenty-year term extending into 2043 or 2044.

We intend to pursue patent protection, whether through in-licensing or our own development, for future drug candidates and specific aspects of our treatment methods. We may also pursue additional patent protection for features of our pacibekitug platform, though we will rely on confidentiality and trade secret protections for certain aspects of that platform.

We have sought patent protection in the U.S., Taiwan, and internationally through Patent Cooperation Treaty ("PCT") related to the use of pacibekitug in targeting specific diseases. As of the date of this prospectus, our patent portfolio consists of eight U.S. provisional applications, four pending PCT applications, and four pending Taiwan non-provisional applications. Two of the provisional applications were filed less than one year ago, and the PCT and Taiwan applications claim benefit of priority to the other provisional applications. The non-provisional applications are projected to expire in 2043 or 2044, prior to consideration of any additional patent term. We intend to pursue, when possible, further composition, method of use, dosing, formulation, and other patent protection directed to pacibekitug and any new products developed. We may also pursue patent protection with respect to manufacturing and drug development processes and technology.

Trademarks

We plan to register our rights in the Tourmaline mark in the U.S. and various other jurisdictions. We expect to pursue trademark protection for additional marks in the future for products that we commercialize.

Trade Secrets and Confidential Information

For certain of our technologies, we rely on unpatented trade secrets and confidential know-how to develop and maintain our competitive position. However, trade secrets are notoriously difficult to protect. Breaches of trade secret or confidentiality provisions can be challenging to detect, and even more challenging to prove. We seek to protect our proprietary information, in part, through confidentiality and non-competition agreements with employees, consultants, partners, and other advisors. These agreements may be breached and we may not be able to successfully defend our rights. Moreover, we may not be able to secure adequate remedies for harm caused by such breach. Furthermore, our trade secrets

or confidential information may be independently developed by a third party, and it may not have any ability to restrain or secure any remedy from them. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. See the section titled "Risk Factors—Risks Related to Intellectual Property" for a more comprehensive description of risks related to our trade secrets and confidential information.

Government Regulation

The FDA and other regulatory authorities at federal, state, and local levels, as well as in foreign jurisdictions, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring, and post-approval reporting of all pharmaceutical products. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of any product candidate.

FDA Drug Approval Process

In the U.S., the FDA regulates biologics under both the Federal Food, Drug and Cosmetic Act and the Public Health Services Act and their implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve a pending Biologics License Application ("BLA"), withdrawal of an approval, imposition of a clinical hold, issuance of untitled or warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, injunctions, debarment, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before biologic product candidates may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current good laboratory practices regulations ("GLPs");
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an institutional review board ("IRB") or ethics committee for each clinical site before the trial may commence at that particular site;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices ("GCP") to establish the safety and efficacy of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials that includes substantial evidence of safety and efficacy in the target patient population, and identity, strength, quality, purity and potency of the proposed biologic product candidate for its intended purpose from results of nonclinical testing and clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCPs; and
- FDA review and approval, or licensure, of the BLA to permit commercial marketing of the product for particular indications for use in the U.S.

Preclinical and Clinical Development

Prior to beginning a clinical trial in the U.S., we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans within a specific defined clinical study or studies. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, PK, pharmacology, and PD characteristics of the product candidate; CMC information; and any available human data or literature to support the use of the investigational product. An IND must be cleared before human clinical trials may begin in the US. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. In such a case, the IND may be placed on clinical hold until the IND sponsor and the FDA resolve the outstanding concerns or questions. The FDA also may impose a partial clinical hold that would limit a trial, for example, to certain doses or for a certain length of time or to a certain number of subjects. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. For new indications, a separate new IND may be required. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial, its informed consent form and other communications to study subjects before the clinical trial begins at that site. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB must monitor the study until completed, including any changes to the study plans while it is being conducted.

Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, the clinical trial is not being conducted in accordance with the FDA's or IRB's requirements, if the drug has been associated with unexpected serious harm to subjects or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides advice to the sponsor on whether or not a study should move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. Information about some clinical trials, including a description of the trial and trial results, must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if SAEs occur.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism, distribution and elimination of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.

- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and labeling.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval

of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate and must 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 product candidate. In addition, the sponsor must develop and validate analytical methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

In addition, under the Pediatric Research Equity Act ("PREA"), a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

BLA Submission, Review and Approval

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's CMC and proposed labeling, among other things. The submission of a BLA requires payment of a substantial application user fee to FDA, unless a waiver or exemption applies.

Once the FDA receives an application, it has 60 days to review the BLA to determine if it is substantially complete to permit a substantive review, before it accepts the BLA for filing. If the FDA determines that a BLA is incomplete, the filing may be refused and must be re-submitted for consideration. Once the submission is accepted for filing, the FDA begins an in-depth review of the BLA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has 10 months from acceptance of filing in which to complete its initial review of a standard BLA and respond to the applicant, and six months from acceptance of filing for a priority BLA. The FDA does not always meet its PDUFA goal dates. The review process and the PDUFA goal date may be extended by three months or longer if the FDA requests that the BLA sponsor provides additional information or clarification regarding information already provided in the submission before the PDUFA goal date.

After the BLA is accepted for filing, the FDA reviews a BLA to determine, among other things, whether a product is safe and effective, and whether the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued quality, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions.

Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application 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 a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. 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 a BLA and conducts any necessary inspections, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter, which indicates that the review cycle is complete, will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a REMS, to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-market studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Expedited Development and Review Programs

Any marketing application for a biologic submitted to the FDA for approval may be eligible for FDA programs intended to expedite the FDA review and approval process, such as priority review, fast track designation, breakthrough therapy and accelerated approval.

A product is eligible for priority review if the FDA determines that it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For products containing new molecular entities, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for frequent interactions with the FDA review team to expedite development and review of the product. The FDA may also review sections of the BLA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor and FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the BLA. The review clock does not begin until the final section of the BLA is submitted. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

In addition, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug or biologic that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Products designated as breakthrough therapies are eligible for intensive guidance from the FDA on an efficient development program, organizational commitment to the development and review of the product including involvement of senior managers, and, like fast track products, are also eligible for rolling review of the BLA. Both fast track and breakthrough therapy products may also be eligible for accelerated approval and/or priority review if relevant criteria are met.

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product 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 clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. The FDA may require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period, which could adversely impact the timing of the commercial launch of the product.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review and approval will not be shortened. Furthermore, priority review, fast track designation, breakthrough therapy designation, and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Orphan Drug Designation

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

If a product that has orphan designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan exclusivity does not prevent FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application fee.

A designated orphan product may not receive orphan exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the U.S. may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer 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 products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, requirements relating to quality control and quality assurance, record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors 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, which impose certain procedural and documentation requirements upon us and our third-party manufacturers.

Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the U.S.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur 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; imposition of post-

market studies or clinical studies 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 a product, mandated modification of promotional materials or issuance of corrective information, issuance by FDA or other regulatory authorities of safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product, or complete withdrawal of the product from the market or product recalls;

- fines, warning or untitled letters or holds on post-approval clinical studies;

- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;

- product seizure or detention, or refusal of the FDA to permit the import or export of products; or

- injunctions, consent decrees or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively 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 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. Such off-label uses are common across medical specialties. 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. However, manufacturers and third parties acting on their behalf are prohibited from marketing or promoting drugs in a manner inconsistent with the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Biosimilars and Reference Product Exclusivity

The Biologics Price Competition and Innovation Act of 2009 ("BPCIA") created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of litigation.

Other U.S. Healthcare Laws and Compliance Requirements

In the U.S., our current and future operations are subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare and Medicaid Services ("CMS") other divisions of the U.S. Department of Health and Human Services ("HHS") (such as the Office of Inspector General, Office for Civil Rights and the Health Resources and Service Administration), the U.S. Department of Justice ("DOJ") and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, our clinical research, sales, marketing and scientific/educational grant programs may be subject to the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy and security provisions of the Health Insurance Portability and Accountability Act ("HIPAA") and similar state laws, each as amended, as applicable. our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors and customers may be subject to healthcare laws, regulations and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, price reporting, and physician sunshine laws. Some of our pre-commercial activities are subject to some of these laws.

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, in whole or in part, 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 therapeutic product manufacturers on 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, the intent standard under the Anti-Kickback Statute was amended by the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations of the Anti-Kickback Statute can result in significant civil and criminal fines and penalties, imprisonment, and exclusion from federal healthcare programs. In addition, the ACA codified case law that 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 ("FCA").

The federal false claims and civil monetary penalty laws, including the FCA, which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, including federal healthcare programs, such as Medicare and Medicaid, 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, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. For instance, historically, 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, off-label, and thus generally non-reimbursable, uses. Penalties for federal civil FCA violations may include up to three times the actual damages sustained by the government, plus significant mandatory civil penalties, and exclusion from participation in federal healthcare programs.

HIPAA created additional federal criminal statutes that prohibit, among other things, 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, willfully obstructing a criminal investigation of a healthcare offense, 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.

Like the Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and its implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates, which are independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity as well as their covered subcontractors. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways, are often not pre-empted by HIPAA, and may have a more prohibitive effect than HIPAA, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act (the "Sunshine Act") within the ACA, 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) report annually to CMS 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 health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties. In addition, many states also govern the reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

Many states have similar statutes or regulations to the above federal laws that may be broader in scope and may apply regardless of payor. We may also be subject to 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, and/or state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, drug pricing or marketing expenditures. These laws may differ from each other in significant ways and may not have the same effect, further complicating compliance efforts. Additionally, to the extent that we have business operations in foreign countries or sell any of our products in foreign countries and jurisdictions, including Canada or the E.U., we may be subject to additional regulation.

We may develop products that, once approved, may be administered by a physician. Under currently applicable U.S. law, certain products not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain biopharmaceutical products, that are medically necessary to treat a beneficiary's health condition. As a condition of receiving Medicare Part B reimbursement for a manufacturer's eligible drugs, the manufacturer is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program.

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private 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 U.S. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to our products in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological 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 and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, 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 and biotechnology 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.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future governmental regulations that apply to us, it may be subject to significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, 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, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and results of operations.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may obtain regulatory approval. In the U.S. and in foreign markets, sales of any products for which we 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 products. In the U.S., third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the U.S., and commercial payors are critical to new product acceptance.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors, which decide which therapeutics they will pay for and establish reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor's determination that use of a therapeutic is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

We cannot be sure that coverage or reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Reimbursement may impact the demand for, or the price of, any product for which we obtain regulatory approval.

Third-party payors are increasingly challenging the price, examining the medical necessity, and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. We may need to conduct expensive pharmacoeconomic

studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the 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 reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develops.

Different pricing and reimbursement schemes exist in other countries. In the E.U., governments influence the price of biopharmaceutical 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 product candidate to currently available therapies. Other member states allow companies to establish their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become 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 product candidates for which we 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, the increasing influence of health maintenance organizations, and additional legislative changes in the U.S. has increased, and we expect will continue to increase, the pressure on healthcare pricing. The downward pressure on the rise in healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. 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 receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the U.S. and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product candidates for which marketing approval is obtained. Among policy makers and payors in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, on August 16, 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law, which among other things, (1) directs HHS to negotiate the price of certain high-expenditure, single-source biologics that have been on the market for at least 11 years covered under Medicare (the "Medicare Drug Price Negotiation Program") and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA includes certain exemptions to the Medicare Drug Price Negotiation Program, including a limited exemption for products with orphan drug designation. This exemption applies only to products with one orphan drug designation that is (i) for a rare disease or condition and (ii) is approved for indication(s) for such rare disease or condition. By limiting price negotiation exemption to products with only one orphan drug designation, the IRA may decrease our interest in pursuing orphan drug designation for our product candidates in multiple indications. The IRA also, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025 and eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. These provisions began to take effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon prices of the first ten drugs that were subject to price negotiations, although the Medicare Drug Price Negotiation Program is currently subject to legal challenges. On January 17, 2025, HHS selected fifteen additional products covered under Part D for price negotiation in 2025. Each year thereafter, more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program.

The ACA has substantially changed healthcare financing and delivery by both governmental and private insurers. The ACA, among other things, increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs; required collection of rebates for drugs paid by Medicaid managed care organizations; required manufacturers to participate in a coverage gap discount program, under which they must agree to offer point-of-sale discounts (increased to 70 percent, effective as of January 1, 2019) off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; imposed a non-deductible annual fee on pharmaceutical manufacturers or importers who sell certain "branded prescription drugs" to specified federal government programs, implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected expanded the types of entities eligible for the 340B drug discount program; expanded eligibility criteria for Medicaid programs; created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There have been legal and political challenges to certain aspects of the ACA. It is possible that the ACA and IRA may be subject to judicial or Congressional challenges in the future.

We anticipate that the ACA, if substantially maintained in its current form, will continue to result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Further legislation or regulation could be passed that could harm our business, financial condition and results of operations. Other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect beginning on April 1, 2013 and, due to subsequent legislative amendments, will stay in effect through 2032 unless additional Congressional action is taken.

Additionally, there has been increasing legislative and enforcement interest in the U.S. with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, on December 7, 2023, an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act was announced. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. Individual states in the U.S. have also become increasingly active in passing legislation and implementing regulations designed to control biopharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

The current administration is pursuing policies to reduce regulations and expenditures across government including at HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. These actions may include directives to reduce agency workforce, rescinding a Biden administration executive order tasking the Center for Medicare and Medicaid Innovation ("CMMI") to consider new payment and healthcare models to limit drug spending and eliminating the Biden administration's executive order that directed HHS to establishing an AI task force and developing a strategic plan. Additionally, in its June 2024 decision in Loper Bright Enterprises v. Raimondo ("Loper Bright"), the U.S. Supreme Court overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper Bright decision could result in additional legal challenges to current regulations and guidance issued by federal agencies applicable to our operations, including those issued by the FDA. Finally, Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program created under the IRA.

The U.S. Foreign Corrupt Practices Act

The U.S. Foreign Corrupt Practices Act of 1977, as amended ("FCPA"), prohibits any individuals and entities from paying, providing, offering, or authorizing payment or provision of money or anything of value, directly or indirectly, to any officer, employee, agent, or representative of any non-US government or public international organization, or any political party or candidate for the purpose of influencing any act or decision of the foreign governmental entity in order to obtain or retain business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with accounting provisions requiring the maintenance of 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.

Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that it is in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Other Regulations

We are also subject to numerous federal, state and local laws relating to such matters as privacy, information security, safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees and Human Capital Resources

As of March 7, 2025, we had 74 full-time employees, including 11 who hold Ph.D. or M.D. degrees. Of these full-time employees, 54 employees are engaged in research and development and 20 employees are engaged in management or general and administrative activities. None of our employees are subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relationship with our employees to be good.

Core Values

We strive to live by our core values every day: (1) we have passion for our mission; (2) we believe respect and inclusion are core to the success of our team; (3) we overcome obstacles to deliver results for patients; and (4) we push the envelope.

Conduct and Ethics

At Tourmaline, we are committed to fostering a culture of integrity and ensuring each of our employees is equipped with resources to help them do the right thing. We believe it is imperative that the board of directors and senior management strongly support a no-tolerance stance for workplace harassment, biases and unethical behavior. All employees are required to review and agree to abide by our company's Code of Conduct, whistleblower policy, anti-corruption policy, insider trading policy, and other corporate policies upon hire and on an annual basis thereafter.

Retention, Training and Development

The development, attraction and retention of our employees is a critical success factor for Tourmaline. We cultivate a culture of learning and offer formal and informal training and development opportunities for employees at all levels. We actively promote from within and continue to fill our team with strong and experienced talent.

Diversity and Inclusion

At Tourmaline, diversity means making a conscious effort to reflect the many experiences and identities of the world outside, while treating each other with fairness and without bias. Inclusion is the choice we make every day to foster an

environment where people of all backgrounds not only belong but excel, so that together, as a company, we can succeed. Tourmaline strives to foster an inclusive community, both inside and out of the office.

Compensation and Benefits

An important part of attracting and retaining key talent is competitive pay and benefits. To ensure our compensation programs are competitive, we engage a nationally recognized outside compensation consulting firm to independently evaluate the effectiveness of our programs and to provide benchmarking against our peers within the industry. Our pay for performance philosophy seeks to motivate and reward employees while accomplishing our short and long-term strategic goals. As part of our performance management process, employees are evaluated both on what they accomplished and on their experience managing and mentoring other employees. Annual salary increases and incentive bonuses are based on market data and merit, and include individual and corporate performance factors.

To encourage our employees to think like owners and share in our company's success, all employees are granted stock options. Employees are eligible for health insurance, a retirement plan, and life and accidental death and dismemberment coverage.

Corporate Information

Our common stock is listed on The Nasdaq Global Select Market under the symbol "TRML".

We were incorporated under the laws of the State of Delaware in February 2002. Legacy Tourmaline was incorporated under the laws of the State of Delaware in September 2021. Following the Reverse Merger with Tourmaline Sub, Inc. (formerly Tourmaline Bio, Inc.) on October 19, 2023, we changed our name from Talaris Therapeutics, Inc. to Tourmaline Bio, Inc. Our principal executive offices are located at 27 West 24th Street, Suite 702, New York, New York 10010 and our telephone number is (646) 481-9832.

Available Information

Our website address is www.tourmalinebio.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports which we have filed or may in the future file pursuant to Sections 13(a) and 15(d) of the Exchange Act are made available free of charge on or through our website as soon as reasonably practicable after such reports are filed with, or furnished to, the SEC. The information contained on, or that can be accessed through, our website is not incorporated by reference into this Report or in any other report or document we file with the SEC, and any references to our website are intended to be inactive textual references only.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information contained in this Annual Report on Form 10-K, including our audited consolidated financial statements and related notes hereto, before deciding to invest in our common stock. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties that we are unaware of, or that we currently believe are not material, may also become important factors that affect us. We cannot assure you that any of the events discussed below will not occur. If any of the following risks actually occurs, our business, prospects, operating results and financial condition could suffer materially. In such event, the trading price of our common stock could decline and you might lose all or part of your investment.

SUMMARY OF RISK FACTORS

An investment in our common stock involves various risks, and prospective investors are urged to carefully consider the matters discussed in the section titled "Risk Factors" prior to making an investment in our common stock. These risks include, but are not limited to, the following:

- We have a limited operating history and no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.

- We have incurred net losses every year since our inception and have no source of product revenue. We expect to continue to incur significant operating losses and may never become profitable.

- Our business is highly dependent on the success of pacibekitug (also referred to as TOUR006) as well as any other potential future product candidates. If we are unable to successfully complete clinical development of, obtain regulatory approval for, or commercialize, pacibekitug or any other potential future product candidates, or if we experience delays in doing so, our business will be materially harmed.

- We will need significant additional capital to proceed with the development and commercialization of pacibekitug and any potential future product candidates and our other operations. We may not be able to access sufficient capital on acceptable terms, if at all, and, as a result, we may be required to delay, scale back or discontinue development of such product candidates or other operations.

- We will incur additional costs and increased demands upon management as a result of complying with the laws and regulations applicable to public companies.

- We may not be able to obtain and maintain the relationships with third parties that are necessary to develop, commercialize, and manufacture pacibekitug and any potential future product candidates.

- We rely completely on contract development and manufacturing organizations ("CDMOs") for the manufacture and testing of pacibekitug and any potential future product candidates under current good manufacturing practices ("cGMP"), and we are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of any potential product candidates and any future products. Additionally, any difficulties in the transfer of drug substance or drug product to or from clinical sites or manufacturing facilities could materially adversely affect our business, financial condition, and results of operations.

- As of December 31, 2024, our manufacturing and testing of bulk drug substance for pacibekitug currently takes place in the U.S. through a global CDMO with facilities around the world. Our manufacturing and testing of drug product for pacibekitug occurs in facilities in Austria and the U.S. Our drug product is packaged in Germany and the U.S. A significant disruption in the operation of these manufacturing facilities, a trade war, or political unrest could materially adversely affect our business, financial condition, and results of operations.

- We may seek to establish business development arrangements ("BD Arrangements"), and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.

- Pacibekitug and any other of our future product candidates must undergo rigorous clinical trials before seeking regulatory approvals, and clinical trials may be delayed, suspended, or terminated at any time for many reasons, any of which could delay or prevent regulatory approval and, if approval is granted, commercialization of our product candidates.

- If clinical trials of pacibekitug or any potential future product candidates fail to timely initiate, enroll, complete, or produce positive results, or to demonstrate safety and efficacy to the satisfaction of the U.S. Food and Drug Administration (the "FDA") or comparable health authorities or sufficiently demonstrate differentiation from other approved therapies or therapies in development, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

- If we experience delays or difficulties in the enrollment of patients in clinical trials, development of pacibekitug, or any potential future product candidates, may be delayed or prevented, which would have a material adverse effect on our business.

- Even if we obtain approval to market pacibekitug or other potential future product candidates, these products may become subject to unfavorable pricing regulations, reimbursement practices from third-party payors or healthcare reform initiatives in the U.S. and abroad, which could harm our business.

- Product liability lawsuits against us could cause us to incur substantial liabilities and to limit development and commercialization of any products that we may develop.

- Healthcare reform may negatively impact our ability to profitably sell pacibekitug and any potential future product candidates, if approved.

- Our current and future relationships with investigators, healthcare professionals, customers, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, transparency, and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

- Our ability to use our U.S. net operating loss carryforwards and certain other U.S. tax attributes may be limited.

- Our internal control over financial reporting may not meet the standards required by Section 404 of the Sarbanes-Oxley Act, and failure to achieve and maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business and share price.

- We have previously identified material weaknesses in our internal control over financial reporting. If we identify additional material weaknesses in the future or otherwise fail to maintain effective internal control over financial reporting, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business.

- We expect to expand our clinical development, manufacturing, and regulatory capabilities and potentially implement sales, marketing, and distribution capabilities, including significant growth in the number of our employees, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

- Our international operations may expose us to business, regulatory, political, operational, financial, pricing, and reimbursement risks associated with doing business outside of the U.S.

- Our business could be materially and adversely affected in the future by the effects of disease outbreaks, epidemics, and pandemics.

Risks Related to Our Financial Condition and Capital Needs

We have a limited operating history and no history of commercializing products which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.

We are a biotechnology company with a limited operating history and a single product candidate, pacibekitug, in development to date. Legacy Tourmaline was formed in 2021 and commenced operations in 2022. To date, we have not yet demonstrated our ability to successfully complete pivotal clinical trials, obtain regulatory approvals, manufacture a product on a commercial scale or arrange for a third-party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization, and we may not be successful in doing so in the future. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

In addition, as a business with a limited operating history, we may encounter unforeseen expenses, technical or regulatory challenges, or unanticipated delays in development timelines. We will eventually need to transition from a company with a clinical development focus to a company, if pacibekitug or any potential future product candidates are approved, capable of supporting commercial activities. We may not be successful in such a transition.

We have incurred net losses every year since our inception and have no source of product revenue. We expect to continue to incur significant operating losses and may never become profitable.

We have no products approved for commercial sale and have not generated any revenue from product sales to date. Legacy Tourmaline has incurred losses in each year since it commenced operations.

We expect to continue to incur significant research and development ("R&D") costs and other expenses related to our ongoing operations for the foreseeable future, particularly to fund R&D of, and seek regulatory approvals for, pacibekitug and any potential future product candidates. We also expect to continue to incur significant operating losses over the next several years as our research, development, manufacturing, preclinical study, clinical trial and related activities grow. We expect our accumulated deficit will also increase in future periods. The size of our future net losses will depend, in part, on the amount of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had, and will continue to have, an adverse effect on our stockholders' deficit and working capital.

In addition, we will not be able to generate product revenue unless and until pacibekitug, or any potential future product candidate, successfully completes clinical trials, receives regulatory approval, and is successfully commercialized or generates revenues through business development activities. We do not expect to receive product revenue from our product candidates for a number of years, if ever.

Our ability to generate any product revenue from pacibekitug and any potential future product candidates also depends on a number of additional factors, including our ability, or the ability of any potential future third-party partner, to successfully:

- complete research and clinical development of current and future product candidates and obtain regulatory approval for those product candidates;
- establish and maintain supply and manufacturing relationships, and ensure adequate, scaled-up, and legally compliant manufacturing of bulk drug substances and drug products to maintain sufficient supply;
- launch and commercialize pacibekitug or any potential future product candidates for which marketing approval is obtained, if any, and, if launched independently by us without a partner, successfully establish a sales force and marketing and distribution infrastructure;
- demonstrate the necessary safety data (and, if accelerated approval is obtained, verify the clinical benefit) post-approval to ensure continued regulatory approval;
- obtain coverage and adequate product reimbursement from third-party payors, including government payors, for any approved products;
- achieve market acceptance for any approved products;
- enter into collaboration, partnering, licensing, or other similar arrangements on economically favorable terms;
- establish, maintain, protect and enforce our intellectual property rights; and/or
- attract, hire and retain qualified personnel.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, including that pacibekitug and any potential future product candidates may not advance through development or be approved for commercial sale, we are unable to predict if or when we will generate product revenue or achieve or maintain profitability.

Even if we successfully complete development and obtain health authority approval for commercialization for any product candidates that we take forward, we anticipate incurring significant costs associated with launching and commercializing any products. If we fail to become profitable or do not sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or cease operations.

Our business is highly dependent on the success of pacibekitug as well as any other potential future product candidates. If we are unable to successfully complete clinical development of, obtain regulatory approval for, or commercialize, pacibekitug or any other potential future product candidates, or if we experience delays in doing so, our business will be materially harmed.

Our future success and ability to generate revenue from pacibekitug or any potential future product candidates, which we do not expect will occur for several years, if ever, is dependent on our ability to successfully develop, obtain regulatory approval for and commercialize one or more product candidates. If pacibekitug encounters undesirable safety signals, insufficient efficacy results, development delays, regulatory issues or other problems, our development plans and business would be significantly harmed.

We have identified atherosclerotic cardiovascular disease ("ASCVD") as the lead indication for pacibekitug. As previously announced in January 2024, we reached alignment with the FDA on the ASCVD clinical development program, including a Phase 2 trial evaluating the reduction of high-sensitivity C-reactive protein ("hs-CRP"), a validated biomarker for inflammation, with quarterly and monthly dosing of pacibekitug in patients with elevated cardiovascular risk. The related Investigational New Drug application ("IND") was cleared by the FDA in March 2024, and we initiated a Phase 2 trial of pacibekitug in patients with chronic kidney disease and elevated hs-CRP in April 2024, which we refer to as the TRANQUILITY trial.In December 2024, we announced the over-enrollment of the Phase 2 TRANQUILITY trial. We expect to announce topline data from the Phase 2 TRANQUILITY trial in the second quarter of 2025. Development of pacibekitug for ASCVD will require substantial additional investment for clinical development prior to potentially being submitted for regulatory review and approval in one or more jurisdictions.

Our second indication for pacibekitug is thyroid eye disease ("TED"). We submitted an IND in the U.S. to support initiation of a Phase 2b trial of pacibekitug in first-line TED. This IND was cleared by the FDA in August 2023, and we initiated the aforementioned Phase 2b trial in September 2023, which we refer to as the spiriTED trial. Topline data from the spiriTED trial are expected in the second half of 2025, and initiation of a pivotal Phase 3 trial of pacibekitug in first-line TED will be dependent on those results.

If in either our TRANQUILITY trial or our spiriTED trial, pacibekitug encounters undesirable safety signals, insufficient efficacy results, development delays, regulatory issues or other problems, our development plans and business would be significantly harmed.

We will need significant additional capital to proceed with the development and commercialization of pacibekitug and any potential future product candidates and our other operations. We may not be able to access sufficient capital on acceptable terms, if at all, and, as a result, we may be required to delay, scale back or discontinue development of such product candidates or other operations.

Our operations have consumed substantial amounts of cash since inception, and we will require substantial additional capital to finance our operations and pursue our product development strategy, both in the short- and the long-term, and the amount of funding we will need depends on many factors, including:

- the rate of progress in the development of pacibekitug and our other potential future product candidates;
- the initiation, progress, timing, delays, costs, and results of preclinical studies and clinical trials for pacibekitug and any potential future product candidates;
- the number and development requirements of product candidates that we may pursue;
- the outcome, timing, and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign health authorities, including the potential for such authorities to require that we perform more studies than those that we currently expect;
- the cost to establish, maintain, expand, enforce, and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending, and enforcing any patents or other intellectual property rights;
- the cost and timing of selecting and auditing a manufacturing site for later-stage clinical and commercial-scale manufacturing;
- the cost and timing of performing manufacturing process validation sufficient to meet regulatory expectations and requirements;
- the effect of products that may compete with pacibekitug and any potential future product candidates or other market developments;
- market acceptance of any approved product candidates, including product pricing and product reimbursement by third-party payors;

- the cost of potentially acquiring, licensing, or investing in additional businesses, products, product candidates and technologies; and

- the cost of establishing sales, marketing, and distribution capabilities for pacibekitug and any potential future product candidates for which we may receive regulatory approval and that we decide to commercialize ourselves or in collaboration with partners.

We believe that our working capital will be sufficient to fund our operating expenses and capital expenditure requirements for at least twelve months from the date of issuance of this Annual Report on Form 10-K. More specifically, based on our current development plans and related assumptions, we believe our cash, cash equivalents and investments are sufficient to fund our operations into the second half of 2027. We have based these estimates on plans and assumptions that may prove to be insufficient or inaccurate (for example, with respect to anticipated costs, timing, or success of certain activities), and we could utilize our available capital resources sooner than we currently expect. In addition, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially as a result of a number of factors.

We plan to finance our future cash needs through public or private equity or debt offerings, BD Arrangements, or a combination of these potential financing sources. For example, we may seek BD Arrangements in the future to facilitate clinical development that requires significantly more capital and resources that may otherwise not be available to us on acceptable terms or at all, such as large cardiovascular outcome trials of pacibekitug in patients with ASCVD. Additional capital may not be available in sufficient amounts, on reasonable terms, or when we need it, if at all. In addition, our ability to obtain financing may be adversely impacted by potential worsening global economic conditions and the disruptions to, and volatility in, the credit and financial markets in the U.S. and worldwide resulting from geopolitical tensions, such as the ongoing war in Ukraine and hostilities in the Middle East, global pandemics, inflation, fluctuating interest rates, and liquidity concerns at, and failures of, banks and other financial institutions. The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in economic growth, increases in inflation rates, fluctuating interest rates and uncertainty about economic stability. If the financial market disruptions and economic slowdown deepen or persist, we may not be able to access additional capital on favorable terms, or at all, which could in the future negatively affect our financial condition and our ability to pursue our business strategy.

If adequate funds are not available from public or private equity or debt offerings, or BD Arrangements on acceptable terms when needed, in order to continue the development of pacibekitug or any of our potential future product candidates we may need to:

- seek strategic alliances for R&D programs when we otherwise would not, at an earlier stage than we would otherwise desire or on terms less favorable than might otherwise be available; or

- enter into BD Arrangements that could require us to relinquish, or license, on potentially unfavorable terms, our rights to intellectual property, product candidates, or products that we otherwise would develop or seek to commercialize ourselves.

We may not be able to raise adequate additional capital on a timely basis, on acceptable terms or at all. If we are unable to do so, we may need to significantly delay, scale back or discontinue development of or abandon pacibekitug or any potential future product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects, or we may be required to cease operations altogether.

We will incur additional costs and increased demands upon management as a result of complying with the laws and regulations applicable to public companies.

We will incur significant legal, accounting and other expenses as a public company that we did not incur as a private company, including costs associated with public company reporting obligations under the Exchange Act. Our management team consists of the executive officers of Legacy Tourmaline prior to the Reverse Merger, some of whom have not previously managed and operated a public company. These executive officers and other personnel will need to devote substantial time to gaining expertise related to public company reporting requirements and compliance with applicable laws and regulations to ensure that we comply with all of these requirements. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated

with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on the board of directors or on board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

Once we are no longer an emerging growth company, a smaller reporting company, or otherwise no longer qualify for applicable exemptions, we will be subject to additional laws and regulations affecting public companies that will increase our costs and the demands on management and could harm our operating results.

We are subject to the reporting requirements of the Exchange Act, which requires, among other things, that we file with the SEC, annual, quarterly, and current reports with respect to our business and financial condition as well as other disclosure and corporate governance requirements. However, as an emerging growth company, we may take advantage of exemptions from various requirements, such as an exemption from the requirement to have our independent auditors attest to our internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002, as well as an exemption from the "say on pay" voting requirements pursuant to the Dodd-Frank Act. After we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which may allow us to take advantage of some of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. Even after we no longer qualify as an emerging growth company, we expect to still qualify as a "smaller reporting company," as such term is defined in Rule 12b-2 under the Exchange Act, in at least the near term, which will 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 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in periodic reports and proxy statements. Once we are no longer an emerging growth company, a smaller reporting company, or otherwise qualify for these exemptions, we will be required to comply with these additional legal and regulatory requirements applicable to public companies and will incur significant legal, accounting and other expenses to do so. If we are not able to comply with the requirements in a timely manner or at all, our financial condition or the market price of our common stock may be harmed. For example, if we or our independent auditor identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, we could face additional costs to remedy those deficiencies, the market price of our stock could decline, or we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

Risks Related to Our Dependence on Third Parties

We may not be able to obtain and maintain the relationships with third parties that are necessary to develop, commercialize and manufacture pacibekitug and any potential future product candidates.

We expect to depend on third parties, including contract research organizations ("CROs"), clinical data management organizations, clinical investigators, and CDMOs and other third-party partners and service providers to support our development efforts, to conduct our clinical trials and certain aspects of our research and preclinical studies, to manufacture clinical and commercial-scale quantities of our drug substances and drug products under cGMP and to market, sell and distribute any products we successfully develop and for which we obtain regulatory approval. Any problems we experience with any of these third parties could delay the development, manufacturing or commercialization of pacibekitug or any potential future product candidates, which could harm our results of operations.

We cannot guarantee that we or, as applicable, any of our partners will be able to successfully negotiate agreements for, and maintain relationships with, third-party partners and service providers on favorable terms, if at all. If we or any of our partners are unable to obtain and maintain these agreements, we may not be able to clinically develop, manufacture, obtain regulatory approvals for or commercialize pacibekitug or any potential future product candidates, which will, in turn, adversely affect our business. If we or any of our partners need to enter into alternative arrangements, it could delay our product development and, if applicable, commercialization activities and such alternative arrangements may not be available on terms acceptable to us.

We expect to continue to expend substantial time and effort to enter into relationships with third parties and, if we successfully enter into such relationships, to manage these relationships. In addition, our reliance on these third parties for development activities reduces our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that our clinical trials are conducted in accordance with the general investigational plan and protocols for the trial and we remain responsible for ensuring that manufacturing activities are conducted under cGMP. However, we cannot control the amount or timing of resources our partners will devote to our programs, pacibekitug or

potential future product candidates, and we cannot guarantee that these parties will fulfill their obligations to us under these arrangements in a timely fashion, if at all. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct their clinical trials or other R&D activities in accordance with regulatory requirements, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for pacibekitug or any potential future product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize any approved products. In addition, we base our expense accruals related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf and, if their estimates are not accurate, it could negatively affect the accuracy of our financial statements.

Any agreements we have or may enter into with third-party partners and service providers 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 our programs, the approach for regulatory approvals or commercialization strategy. Any disputes or commercial conflicts could lead to the termination of our 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 and time-consuming arbitration or litigation.

We rely completely on CDMOs for the manufacture and testing of pacibekitug and any potential future product candidates under cGMP, and we are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of any potential product candidates and any future products. Additionally, any difficulties in the transfer of drug substance or drug product to or from clinical sites or manufacturing facilities could materially adversely affect our business, financial condition, and results of operations.

We require the services of third-party CDMOs to provide process development, analytical method development, formulation development, and manufacturing. We do not have, and do not currently plan to acquire or develop, the facilities or capabilities to manufacture and test bulk drug substance or filled drug product for use in clinical trials or commercialization. As a result, we rely completely on CDMOs, which entails risks to which we would not be subject if we manufactured pacibekitug or any potential future product candidates or products ourselves, including risks related to reliance on third parties for availability of drug product to use in our clinical trials and for regulatory compliance and quality assurance with respect to such drug product, the possibility of breach of the manufacturing agreement by third parties because of factors beyond our control (including a failure to manufacture pacibekitug and any potential future product candidates or any products we may eventually commercialize in accordance with our specifications) and the possibility of termination or nonrenewal of agreements by third parties, based on their own business priorities, at a time that is costly or damaging to us.

Pacibekitug is a biologic, and the manufacture and testing of biologic products is complex, highly regulated and requires significant expertise and capital investment, including the development of advanced manufacturing techniques, process controls, and advanced analytical testing capability. As a result, the manufacture and testing of our product candidate is subject to many risks, including the following, some of which we may experience:

- product loss or other negative consequences due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, shortages of qualified personnel or improper delivery or storage conditions;

- difficulties with product yields, quality control release testing, including challenges related to analytical method development and the qualification and implementation of those methods for release testing, which can delay availability of clinical trial materials;

- challenges with long-term stability of our product candidate and products at reasonable and expected storage conditions;

- challenges with comparability of product made following changes in the manufacturing process such as a change in the manufacturing facility, scale-up, changes in the storage container used for drug product, or other changes;

- the negative consequences of failure to comply with strictly enforced federal, state and foreign regulations;

- major deviations from normal manufacturing processes, which may result in reduced production yields, product defects and other supply disruptions;

- the presence of microbial, viral or other contaminants discovered in our product candidate or in the manufacturing facilities in which it is made, which can necessitate closure of facilities for an extended period of time to investigate and eliminate the contamination;

- the negative consequences of our CDMOs' failure to be approved for commercial production following an audit by regulatory authorities, by us or by our partners;

- Our CDMOs' changing strategies and business priorities, which can affect the availability of facilities where we intend to manufacture our product candidate; and

- Our CDMOs' manufacturing facilities being adversely affected by labor, raw material and component shortages, turnover of qualified staff or financial difficulties of their owners or operators, including as a result of natural disasters, power failures, local political unrest or other factors.

We cannot ensure that issues relating to the manufacture or testing of our product candidates, such as those described above, will not occur or continue to occur in the future. If we or our CDMOs experience any such issues there could be a shortage of drug substance or drug product for use in our clinical trials, which could delay clinical and regulatory timelines significantly and have an adverse effect on our business.

In addition, to date, pacibekitug has been manufactured and tested by our drug substance and drug product CDMOs solely for clinical trials. We intend to continue to use CDMOs for these purposes, and also for the supply of larger quantities that may be required to conduct accelerated or expanded early clinical trials or larger, later clinical trials and for commercialization if we advance any of our product candidates through regulatory approval and to commercialization. These manufacturers may not have sufficient manufacturing capacity and may not be able to scale up the production of drug substance or drug product in the quantities we need and at the level of quality required in a timely or effective manner, or at all. In particular, there is increased competition in the biotechnology industry for CDMO manufacturing slots and other capabilities generally, which has had, and may continue to have, a negative impact on the availability of manufacturing capacity and therefore our ability to supply clinical trial materials for planned, ongoing or expanded clinical trials or commercialization.

The scale up and validation of the manufacturing processes in the CDMOs' facilities to manufacture larger quantities or different formats such as a pre-filled syringe involve complex activities and coordination. Scale up and process validation activities entail risks such as process reproducibility and robustness, stability of in-process intermediates, product quality consistency and other technical challenges. We may be unable to scale up or validate our manufacturing processes, which can be expensive and time-consuming and could delay the initiation or completion of our clinical trials.

Similarly, we or our CDMOs may make changes to our manufacturing processes at various points in product development for many reasons, including changing manufacturing facilities, scaling up, facility fit, raw material or component availability, improving process robustness and reproducibility, decreasing processing times, changing the storage container, or others. In some circumstances, we may fail to demonstrate that the product from the new process is comparable to product from the prior process and we may be required to perform additional bridging studies, animal or human studies to demonstrate that the product used in earlier clinical trials are comparable to the product we intend to use in later trials or later stages of an ongoing trial. These efforts are expensive and there is no assurance that they will be successful, which could impact our ability to continue or initiate clinical trials in a timely manner, or at all, and could require the conduct of additional clinical trials.

Any future adverse developments affecting manufacturing operations or the scale up or validation of manufacturing processes for pacibekitug or any of our future product candidates may result in shipment delays, lot failures, clinical trial delays or discontinuations, or, if we are commercializing products, inventory shortages, product withdrawals or recalls or other interruptions in supply. We may also have to record inventory write-offs and incur other charges and expenses for drug substance or drug product that fail to meet specifications or cannot be used before its expiration date. In addition, for out of specification materials, we may need to undertake costly remediation efforts or manufacture new batches at considerable cost and time delays or, in the longer run, seek more expensive manufacturing alternatives.

We currently have a single source of supply for our drug substance and for our drug product. Single sourcing minimizes our leverage with our CDMOs, who may take advantage of our reliance on them to increase the pricing of their manufacturing services or require us to change our intended manufacturing plans based on their strategies and priorities. Single sourcing also imposes a risk of interruption or delays in supply in the event of manufacturing, quality or compliance

difficulties and/or other difficulties in timely supplying us with materials. We do not currently have arrangements in place for redundant supply for drug substance or drug product. If one of our suppliers fails or refuses to supply us for any reason or we otherwise choose to engage a new supplier for pacibekitug or any of our future product candidates, including a second-source supplier to mitigate the risks of single-source supply, it may take a significant amount of time and cost to implement and execute the necessary technology transfer to, and qualification of, a new supplier. The FDA or comparable foreign health authority must approve manufacturers of commercial drug substance and drug product. If there are any delays in qualifying new suppliers or facilities or a new supplier is unable to meet the requirements of the FDA or comparable foreign health authority for approval of production of our commercial supply, there could be a shortage of drug substance or drug product with respect to the affected product candidates.

If our CDMOs are unable to source certain raw materials and components from their supplier and if they must obtain such materials from a different supplier, additional testing, and regulatory approvals, may be required, which may negatively impact manufacturing timelines. Any significant delay in the acquisition or decrease in the availability of these materials, components or other items, or failure to successfully qualify alternative materials or components, could considerably delay the manufacture of our product candidates, which could adversely impact the timing or completion of any ongoing and planned trials or the timing of regulatory approvals, if any, of our product candidates.

In addition, our CDMOs' facilities and operations may be adversely affected by labor, raw material and component shortages, high turnover of staff and difficulties in hiring trained and qualified replacement staff and the operations of our CDMOs may be requisitioned, diverted or allocated by U.S. or foreign government orders such as under emergency, disaster and civil defense declarations. Changes in economic conditions, supply chain constraints, labor, raw material and component shortages and steps taken by governments and central banks could also lead to higher inflation than previously experienced or expected, which could, in turn, lead to an increase in costs.

If any CDMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CDMO, which we may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials supply could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or product candidates may be unique or proprietary to the original CDMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CDMOs for any reason, we will be required to verify that the new CDMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We would also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product candidate according to the specifications previously submitted to the FDA or another regulatory authority. The delays associated with the verification of a new CDMO could negatively affect our ability to develop product candidates or commercialize our products in a timely manner or within budget. Furthermore, a CDMO may possess technology related to the manufacture of our product candidate that such CDMO owns independently. This would increase our reliance on such CDMO or require us to obtain a license from such CDMO in order to have another CDMO manufacture our product candidates.

As of December 31, 2024, our manufacturing and testing of bulk drug substance for pacibekitug currently takes place in the U.S. through a global CDMO with facilities around the world. Our manufacturing and testing of drug product for pacibekitug occurs in facilities in Austria and the U.S. Our drug product is packaged in Germany and the U.S. A significant disruption in the operation of these manufacturing facilities, a trade war or political unrest could materially adversely affect our business, financial condition and results of operations.

We currently contract manufacturing operations to third parties. Pacibekitug bulk drug substance for clinical studies is manufactured and tested within third-party facilities in the U.S. Pacibekitug drug product is manufactured in Austria and the U.S. and packaged in Germany and the U.S. Any disruption in production or inability of our manufacturers in those countries to produce adequate quantities to meet our needs, whether as a result of a natural disaster or other causes, could impair our ability to operate our business on a day-to-day basis and to continue development of our product candidates. Any of these matters could materially and adversely affect our business and results of operations. In addition, manufacturing interruptions or failure to comply with regulatory requirements by any of these manufacturers could significantly delay clinical development of potential products and reduce third-party or clinical researcher interest and support of proposed trials. Furthermore, any recall of the manufacturing lots or similar action regarding our product candidates used in clinical trials could delay the trials or detract from the integrity of the trial data and its potential use in future regulatory filings. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currencies. Future

appreciation of the local currencies could increase our costs. In addition, our labor costs could continue to rise as wage rates increase due to increased demand for skilled laborers and the availability of skilled labor declines in such countries.

Additionally, we have transferred manufacturing and testing of pacibekitug bulk drug substance to a facility in the U.S. that is licensed for commercial production. We intend to use this U.S. facility to produce pacibekitug bulk drug substance for late-stage clinical studies and commercial supply. There may have been, or may be, as yet unknown negative consequences of transferring the manufacture and testing process as described above. Furthermore, our process at the new facility may result in the production of pacibekitug that is not comparable to the current pacibekitug clinical trial material produced at the facility in China, where we previously manufactured pacibekitug bulk drug substance.. Also, we plan to conduct manufacturing and testing of pacibekitug drug product at a facility in Europe that is licensed for commercial production, through a global CDMO. Pacibekitug drug product produced at the commercial facility may not be comparable to the current pacibekitug drug product that is being used in our clinical studies.

We may seek to establish BD Arrangements, and, if we are not able to establish them on commercially reasonable terms, or at all, we may have to alter our development and commercialization plans.

Our product development programs and the potential commercialization of pacibekitug or any of our future product candidates will require substantial additional cash to fund expenses. For pacibekitug or any of our future product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a BD Arrangement will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's own evaluation of a potential collaboration. Such factors a potential collaborator will use to evaluate a BD Arrangement may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a BD Arrangement could be more attractive than one with us for our product candidate. The terms of any additional BD Arrangements or other arrangements that we may establish may not be favorable to us.

We may in the future be restricted under our current BD Arrangements from entering into potential future BD Arrangements on certain terms with potential collaborators. BD Arrangements are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate BD Arrangements on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay our development program or one or more of our other development programs, delay our potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

In addition, any future BD Arrangements that we enter into may not be successful. The success of our BD Arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a BD Arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of the BD Arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. BD Arrangements with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect us financially and could harm our business reputation.

We have no experience in sales, marketing and distribution and may have to enter into agreements with third parties to perform these functions, which could prevent us from successfully commercializing pacibekitug or any potential future product candidates.

We currently have no sales, marketing or distribution capabilities. To commercialize pacibekitug or any potential future product candidates we must either develop our own sales, marketing and distribution capabilities or make arrangements with third parties to perform these services for us. If we decide to market or distribute any of our products on our own, we will have to commit significant resources to developing a marketing and sales force and supporting distribution capabilities. If we decide to enter into arrangements with third parties for performance of these services, we may find that they are not available on terms acceptable to us, or at all. If we are not able to establish and maintain successful arrangements with third parties or build our own sales and marketing infrastructure, we may not be able to commercialize our product candidates, which would adversely affect our business, financial condition, results of operations and prospects.

We, our CROs, our CDMOs, our service providers, our current and potential future partners or other third parties with whom we work, could experience a security incident, system disruption or failure, data loss, cyberattack, or similar event that could compromise our systems and data (or those of the third parties with whom we work), result in material disruptions to our business operations, lead to regulatory investigations or actions, litigation, fines and penalties, affect our reputation, revenue or profits, or otherwise harm our business.

We collect, store, receive, transmit, generate, use, transfer, disclose, make accessible, protect, secure, dispose, share and otherwise process (collectively, process) proprietary, confidential and otherwise sensitive information, including personal information (such as health-related data of clinical trial participants and employee information), in the course of our business. Our technology systems and the information and data processed and stored by us or by third parties with whom we work (e.g., research collaborators, partners, CROs, CDMOs, contractors, consultants and other third parties), are vulnerable to a variety of evolving online and offline threats that could result in security incidents, including unauthorized, unlawful, or accidental loss, damage, corruption, access, use, encryption, acquisition, disclosure, misappropriation, or other compromise of such systems or data. A security incident or other interruption could disrupt our ability (and that of third parties with whom we work) to operate our business (including to conduct our clinical trials) and may have other adverse effects.

We and third parties with whom we work face threats that are constantly evolving and growing in frequency, sophistication, and intensity. These threats include (without limitation) malware (including as a result of advanced persistent threat intrusions), viruses, worms, software vulnerabilities and bugs, software or hardware failures, hacking, denial of service attacks, social engineering attacks (including through deep fakes, which may be increasingly more difficult to identify as fake, and phishing), credential harvesting, ransomware, personnel misconduct or errors, credential stuffing, telecommunications failures, loss or theft of devices, data or other information technology assets, attacks enhanced or facilitated by AI, earthquakes, fires, floods and other similar threats. Threats such as ransomware attacks, for example, are becoming increasingly prevalent and severe, and attackers are increasingly leveraging multiple attack methods to extort payment from victims, such as data theft and disabling systems. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. If a security incident were to materially impact us, our CROs, our CDMOs, our service providers, our current or potential future parties or other third parties with whom we work, there could be material disruptions to our business operations or other significant harm to our business.

Security incidents may result from the actions of a wide variety of actors with a wide range of motives and expertise, including traditional hackers, hacktivists, our personnel, or the personnel of the third parties we work with, sophisticated nation-states, nation-state-supported actors, and organized criminal threat actors. During times of war and other major conflicts, we, the third parties with whom we work, and our customers may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, supply chain, and ability to produce, sell and distribute our goods and services.

Certain functional areas of our workforce work remotely on a full- or part-time basis outside of our corporate network security protection boundaries or otherwise utilize network connections, computers and devices outside of our premises or network, which imposes additional risks to our business, including increased risk of industrial espionage, phishing, and other cybersecurity attacks, and unauthorized dissemination of proprietary or confidential information, including personal information, any of which could have a material adverse effect on our business. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and

technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program.

In addition, we rely on third parties to operate critical business systems and process sensitive data in a variety of contexts, including, without limitation, cloud-based infrastructure, data center facilities, encryption and authentication technology, personnel email, and other functions. We also rely on third parties, including CROs, clinical trial sites and clinical trial vendors, to process sensitive data as part of our research activities. Our ability to monitor these third parties is limited, and these third parties may not have adequate information security measures in place and may expose us to cyberattacks and other security incidents. Supply-chain attacks have also increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or the supply chains of the third parties with whom we work have not been compromised. If the third parties with whom we work experience a security incident or other interruption, we could experience materially adverse consequences. While we may be entitled to damages if the third parties with whom we work fail to satisfy their 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.

We may be required to, or we may choose to, expend significant resources (including financial) or modify our business activities (including our clinical trial activities) in an effort to protect our information systems and data (including against security incidents) or to detect, investigate, mitigate, contain and remediate a security incident, particularly where required by applicable data privacy and security laws or regulations or industry standards. While we have implemented security measures and processes designed to protect against, mitigate and remediate security incidents, we cannot assure you that these security measures that we or our service providers implement will be effective in preventing security incidents, disruptions, cyberattacks, or other similar events. For example, we have been the target of unsuccessful phishing attempts in the past and expect such attempts will continue in the future. We take steps designed to detect, mitigate, and remediate vulnerabilities in our information systems (such as our hardware and/or software, including that of third parties with whom we work). We may not, however, detect and remediate, all such vulnerabilities including on a timely and effective basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities could be exploited and result in a security incident.

Any of the previously identified or similar threats could cause a security incident. A security incident could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to data. If our information systems or data, or that of the third parties with whom we work, are compromised or were perceived to be compromised, it could interrupt our operations, disrupt our development programs and have a material adverse effect on our business, financial condition and results of operations. For example, the loss or corruption of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of pacibekitug, to analyze clinical trial samples and to conduct clinical trials, and security incidents experienced by these third parties could have a material adverse effect on our business. Actual or perceived security incidents affecting us or the third parties with whom we work or partner with could result in substantial remediation costs and expose us to litigation (including class claims), regulatory enforcement action (for example, investigations, fines, penalties, audits and inspections), additional reporting requirements and/or oversight, fines, penalties, indemnification obligations, negative publicity, reputational harm, monetary fund diversions, diversion of management attention, interruptions in our operations (including availability of data or processing of sensitive information), financial loss and other liabilities, and harms. Additionally, such incidents may trigger data privacy and security obligations requiring us to notify relevant stakeholders, such as individuals, regulators, and others, or take other required remedial or corrective actions and may subject us to liability. Such disclosures and remediation efforts may be costly, and related requirements or the failure to comply with them could lead to adverse consequences.

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 claims related to our data privacy and security obligations. Additionally, we cannot be certain that our insurance coverage will be adequate for data security liabilities actually incurred, will continue to be available to us on economically and commercially reasonable terms, or at all, or that any insurer will not deny coverage as to any future claim. The successful assertion of one or more large claims against us that exceed available insurance coverage, or the occurrence of changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could adversely affect our reputation, business, financial condition and results of operations.

In addition to experiencing a security 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. Additionally, sensitive information of the Company could be leaked, disclosed, or revealed as a result of or in connection with our personnel's, or vendors' use of generative AI technologies.

We (and the third parties with whom we work) are subject to rapidly changing and increasingly stringent foreign and domestic laws, regulations, and rules, contractual obligations, industry standards, policies and other obligations relating to privacy, data protection and information security. The restrictions imposed by these requirements or our actual or perceived failure to comply with such obligations (or such failure by the third parties with whom we work) could lead to regulatory investigations or actions, litigation (including class claims) and mass arbitration demands, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits, loss of customers or sales, and other adverse business consequences.

We process proprietary, confidential and sensitive information, including personal information (including health-related data), which subjects us to numerous evolving and complex data privacy and security obligations, including various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contracts and other obligations that govern the processing of such information in connection with our business.

Outside the U.S., an increasing number of laws, regulations, and industry standards govern data privacy and security. For example, the European Union's General Data Protection Regulation, ("EU GDPR") and the United Kingdom's GDPR, ("UK GDPR") and the Swiss Federal Data Protection Act, ("Swiss FADP") impose strict requirements for processing personal information, and may apply to our processing of personal information from clinical trial participants and other individuals located in the European Economic Area ("EEA"), the UK, or Switzerland and, if pacibekitug or any potential future product candidates are approved, our possible commercialization of those products in the EEA, the UK, or Switzerland (as applicable). Companies that violate the GDPR can face private litigation, regulatory investigations and enforcement actions, prohibitions on data processing, other administrative measures, reputational damage and fines of up to the greater of 20 million Euros under the EU GDPR/17.5 million pounds sterling under the UK GDPR, or 4% of their worldwide annual revenue, in either case, whichever is greater. The EU and UK GDPR require us to, among other things: give detailed disclosures about how we collect, use and share personal information; contractually commit to data protection measures in our contracts with vendors; maintain appropriate data security measures; notify regulators and affected individuals of certain personal data breaches; meet privacy governance and documentation requirements; and honor individuals' data protection rights, including their rights to access, correct and delete their personal information.

In the ordinary course of business, we transfer personal data from Europe and other jurisdictions to the U.S or other countries. Certain jurisdictions have enacted data localization restrictions or laws and regulations restricting cross-border transfers of personal information. In particular, regulators and courts in the EEA, the UK, and Switzerland have significantly restricted the transfer of personal information to the U.S. and other countries that have not been declared "adequate" for data protection purposes by a relevant governmental authority. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws. Although there are currently mechanisms that may be used to transfer personal information from the EEA, the UK, or Switzerland to the U.S. in compliance with European data protection laws, such as the EEA 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 to relevant U.S.-based organizations who self-certify compliance and participate in the EU-U.S. Data Privacy Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to transfer personal data to the U.S.

If we are unable to implement a valid compliance mechanism for cross-border transfers of personal information, or if the requirements for a legally-compliant transfer are too onerous, we will face increased exposure to significant adverse consequences, including substantial fines, regulatory actions, as well as injunctions against the export and processing of personal information from the EEA, UK, Switzerland, or other countries that implement cross-border data transfer restrictions. Our inability to import personal information from the EEA, UK or Switzerland or other countries may also restrict or prohibit our clinical trial activities in those countries; limit our ability to collaborate with CROs, service providers, contractors and other companies subject to laws restricting cross-border data transfers; require us to increase our data processing capabilities in other countries at significant expense and may otherwise negatively impact our business operations. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the U.S, are subject to increased scrutiny from regulators, individual litigants, and activist groups. We may also become subject to new laws in the EEA and other jurisdictions that regulate cybersecurity and non-personal data, such as data

collected through the internet of things. Depending on how these laws are interpreted, we may have to make changes to our business practices and products to comply with such obligations.

Additionally, other countries have enacted or are considering enacting similar cross-border data transfer restrictions and laws requiring local data residency, which could increase the cost and complexity of delivering our services and operating our business. Regulators in the U.S. are also increasingly scrutinizing certain personal data transfers and may impose personal data localization requirements.

Privacy and data security laws in the U.S. at the federal, state and local level are increasingly complex and changing rapidly. For example, at the federal level, HIPAA, as amended by HITECH, imposes specific requirements relating to the privacy, security and transmission of individually identifiable health information. Additionally, at the state level, the privacy and data protection landscape is changing rapidly. Many states have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. As applicable, such rights may include the right to access, correct, or delete certain personal data, and to opt-out of certain data processing activities, such as targeted advertising, profiling, and automated decision-making. Certain state laws also impose stricter requirements for processing sensitive personal information such as obligating covered businesses to conduct data privacy impact assessments. These state laws allow for statutory fines for noncompliance. For example, the California Consumer Privacy Act ("CCPA"), applies to personal data of consumers, business representatives, and employees who are California residents, and requires certain businesses to provide specific disclosures in privacy notices and honor requests of such individuals to exercise certain privacy rights. The CCPA provides for fines for noncompliance and a limited private right of action in connection with certain data breaches. While the CCPA and other comprehensive state privacy laws contain exemptions for certain personal information processed in connection with clinical trials, the evolving patchwork of differing state and federal privacy and data security laws increases the cost and complexity of operating our business and increases our exposure to liability, including from third-party litigation and regulatory investigations, enforcement, fines, and penalties.

We are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful.

We publish privacy policies and provide notices regarding data privacy and security. Regulators are increasingly scrutinizing these statements, and if these policies or notices are found to be deficient, lacking in transparency, deceptive, unfair, misleading, or not representative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences.

Our personnel and others with whom we work 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 lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages.

Our obligations related to data privacy and security (and individuals' data privacy expectations) are quickly changing in an increasingly stringent fashion and creating uncertainty. These obligations may be subject to differing applications and interpretations, which may be inconsistent or in conflict among jurisdictions. Monitoring, preparing for and complying with these obligations requires us to devote significant resources (including, without limitation, financial and time-related resources). These obligations may necessitate changes to our information technologies, systems and practices and to those of any third parties that process personal information on our behalf. In addition, these obligations may require us to change aspects of our business model (such as where we conduct clinical trials). Although we endeavor to comply with applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. Moreover, despite our efforts, our personnel or third parties with whom we work may fail to comply with such obligations, which could negatively impact our business operations.

If we (or third parties with whom we work) fail, or are perceived to have failed, to address or comply with data privacy, protection and security obligations, we could face significant consequences, including (without limitation): government enforcement actions (e.g., investigations, fines, penalties, audits, inspections and similar); litigation (including class-related claims) and mass arbitration demands; additional reporting requirements and/or oversight; bans on processing personal information; orders to destroy or not use personal information; and/or imprisonment of company officials. 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 monumental 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; interruptions or stoppages in our business operations (including clinical trials); inability to process personal information or to operate in certain jurisdictions; limited ability to develop or commercialize our products; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or revision or restructuring of our operations.

Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates

Pacibekitug and any other of our future product candidates must undergo rigorous clinical trials before seeking regulatory approvals, and clinical trials may be delayed, suspended or terminated at any time for many reasons, any of which could delay or prevent regulatory approval and, if approval is granted, commercialization of our product candidates.

Pacibekitug and any other product candidates we might develop are subject to rigorous and extensive clinical trials before we can seek regulatory approval from the FDA and comparable foreign health authorities such as the European Medicines Authority. Clinical trials may be delayed, altered, suspended or terminated at any time for reasons including but not limited to:

- ongoing discussions with the FDA or comparable foreign health authorities regarding the scope or design of our clinical trials;
- delays in obtaining, or the inability to obtain, required approvals from institutional review boards ("IRBs") and ethics committees or other governing entities at clinical trial sites selected for participation in our clinical trials;
- delays in reaching agreement on acceptable terms with clinical trial sites on clinical budgets and/or clinical trial agreements;
- lack and/or loss of personnel at clinical trial sites to conduct our trials, including patient screening, patient visits and/or assessments, data entry of patient data into the clinical database and/or processing of patient samples;
- institutional policies related to in-person patient visits resulting in delays to treatments or assessments being conducted, CRO and/or sponsor visits to conduct monitoring visits to verify data and/or site adherence to regulatory requirements;
- delays in patient enrollment and other key trial activities;
- delays in reaching agreement on acceptable terms with prospective CROs;
- the failure of CROs, testing laboratories and other third parties to satisfy their contractual duties to us or meet expected deadlines;
- deviations from the trial protocol by clinical trial sites and investigators, or failures to conduct the trial in accordance with regulatory requirements;
- alterations in the size and scope of the trial;
- lower than anticipated retention rates of participants in clinical trials, including patients dropping out due to protocol non-compliance, side effects or disease progression;
- missing or incomplete data;
- failure of enrolled patients to complete treatment or to return for post-treatment follow-up;
- for clinical trials in selected patient populations, delays in identification and auditing of central or other laboratories and the transfer and validation of assays or tests to be used to identify selected patients and test any patient samples;

- implementation of new, or changes to, guidance or interpretations from the FDA or comparable foreign health authorities with respect to approval pathways for pacibekitug and any potential future product candidates we are pursuing;

- the need to repeat or conduct additional clinical trials as a result of inconclusive or negative results, poorly executed testing or changes in required endpoints or other changes to the trial or analysis;

- insufficient supply or deficient quality of drug substance, drug product or other clinical trial material necessary to conduct our clinical trials, as well as delays in the testing, validation, manufacturing and delivery to clinical trial sites of such material;

- withdrawal of clinical trial sites or investigators from our clinical trials for any reason, including as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials;

- unfavorable FDA or comparable foreign health authority inspection or review of a clinical trial site or records of any clinical or preclinical investigation;

- drug-related adverse effects or tolerability issues experienced by participants in our clinical trials;

- changes in government regulations or administrative actions;

- lack of adequate funding to continue the clinical trials;

- ability to hire and retain key R&D and other personnel; or

- the placement of a clinical hold on a trial by the FDA or comparable foreign health authorities.

We cannot guarantee that we will be able to successfully obtain FDA or other global health authority clearance to proceed with any planned clinical investigations of pacibekitug or any potential future product candidates or to accomplish required regulatory and/or manufacturing activities or all of the other activities necessary to initiate and complete clinical trials in a timely fashion, if at all. As a result, our preclinical studies and clinical trials may be extended, delayed or terminated, and we may be unable to obtain regulatory approvals or successfully commercialize our products. In addition, we have only limited experience in conducting late-stage clinical trials required to obtain regulatory approval. In any event, we do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all.

Our product development costs will increase if we experience delays in clinical testing. Significant clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects. We or our partners' inability to timely complete clinical development could result in additional costs to us or impair our ability to generate product revenue or development, regulatory, commercialization and sales milestone payments and royalties on product sales.

If clinical trials of pacibekitug or any potential future product candidates fail to timely initiate, enroll, complete, or produce positive results or to demonstrate safety and efficacy to the satisfaction of the FDA or comparable health authorities or sufficiently demonstrate differentiation from other approved therapies or therapies in development, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from health authorities for the sale of pacibekitug or any potential future product candidates, we or our partners must conduct extensive preclinical studies and clinical trials to demonstrate its safety and efficacy in humans. Preclinical studies and clinical trials are expensive, take several years to complete and may not yield results that support further clinical development or product approvals. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. There is a high failure rate for drugs and biologic products proceeding through clinical trials and failure can occur at any stage of testing. Because we have limited experience designing clinical trials, we may be unable to design and execute a clinical trial to support regulatory approval.

We may also not be successful in generating clinical data sufficient to differentiate pacibekitug from other products in the same therapeutic area. If our competitors' products are, or are perceived to be, more effective, more convenient, less costly or safer than pacibekitug, or we are unable to demonstrate differentiation in any of those factors, we may not be able to achieve a competitive position in the market.

In addition, data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In any event, it is impossible to predict when or if any of our product candidates will prove safe and effective in humans or will receive regulatory approval. If we are unable to successfully discover, develop or enable our partners to develop drugs that regulatory authorities deem effective and safe in humans, we will not have a viable business.

We may not be able to file INDs, IND amendments, or clinical trial applications ("CTAs") to commence clinical trials on the timelines we expect, and even if we are able to, the FDA or comparable health authorities may not permit us to proceed.

We may not be able to file INDs or CTAs for pacibekitug or any future product candidates on the timelines we expect, if at all. For example, we may experience, or our partners may experience, manufacturing delays or other delays with IND-enabling studies. Moreover, we cannot be sure that submission of an IND or CTA will result in the FDA or comparable health authority allowing initial or later-stage clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate clinical trials. Additionally, even if such regulatory authorities agree with the design and implementation of the clinical trials set forth in an IND or CTA, 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 CTAs. Any failure to file INDs and CTAs on the timelines we expect or to obtain regulatory approvals for our trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

If we experience delays or difficulties in the enrollment of patients in clinical trials, development of pacibekitug, or any potential future product candidates, may be delayed or prevented, which would have a material adverse effect on our business.

We may not be able to initiate or continue clinical trials for our product candidate if we, or a potential future sponsor, are unable to locate and enroll a sufficient number of eligible patients to participate in these continuing trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials.

Patient enrollment may be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, at clinical trial sites participating in our clinical trials, or at clinical trial sites not participating in our clinical trials and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment may also be affected by other factors, including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability of approved therapies, other medicines, surgical procedures, or other therapies or interventions that would lead a patient to opt for that treatment or care approach instead of enrolling in our trial;
- patient eligibility criteria for the trial in question;
- nature of the trial protocol;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- perceived risks and benefits of the product candidate under study;
- the occurrence of adverse events attributable to our lead product candidate;

- efforts to facilitate timely enrollment in clinical trials;
- the number and nature of competing products or product candidates and ongoing clinical trials of competing product candidates for the same indication at clinical trial sites participating in our clinical trials, or at clinical trial sites not participating in our clinical trials;
- patient referral practices of physicians;
- risk that enrolled subjects will drop out or die before completion;
- competition for patients from other clinical trials at clinical trial sites participating in our clinical trials, or at clinical trial sites not participating in our clinical trials;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- continued enrollment of prospective patients by clinical trial sites.

Even if we are able to enroll a sufficient number of patients in our clinical trials, if the pace of enrollment is slower than expected, the development costs for our product candidates may increase and the completion of our trials may be delayed or our trials could become too expensive to complete. Any delays in completing our clinical trials will increase costs, delay or prevent product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. Any delays in completing our clinical studies for our product candidates may also decrease the period of commercial exclusivity. Any of these occurrences may significantly harm our business, financial condition, results of operations, and prospects.

Success in preclinical studies or earlier-stage clinical trials for pacibekitug, or evidence from published observations, clinical studies, or other literature for other anti-IL-6 or anti-IL-6 receptor agents, may not be indicative of such results in future or ongoing clinical trials for pacibekitug.

To date, the data supporting our drug discovery and development programs are derived in part from laboratory and preclinical studies and earlier-stage clinical trials conducted by Pfizer. Owing in part to the complexity of biological pathways, when used to treat human patients, as well as differences in the design or conduct of clinical trials, pacibekitug might not demonstrate the biochemical and pharmacological properties we anticipate based on laboratory studies or earlier-stage clinical trials, and it may interact with human biological systems or other drugs in unforeseen, ineffective or harmful ways. Success in preclinical studies and earlier-stage clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate or positive data to demonstrate the effectiveness and safety of our current and potential future product candidates. In this regard, the data supporting our drug discovery and development programs are derived from laboratory and preclinical studies, and future clinical trials in humans may show that one or more of our product candidates are not safe and effective, in which event we may need to abandon development of such product candidates. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical studies and earlier-stage clinical trials. Similarly, preliminary data and interim results from clinical trials may not be predictive of final results. As a general matter, there is also a substantial risk that Phase 3 trials with larger numbers of patients and/or longer durations of therapy will fail to replicate efficacy and safety results observed in earlier clinical trials. The impact of such differences may lead to a clinical trial(s) of pacibekitug failing to reproduce any positive efficacy, safety, or other findings from laboratory and preclinical studies and earlier-stage clinical trials for pacibekitug.

In addition, the rationale supporting our drug discovery and development programs is also based upon published articles describing positive results from clinical trial(s) and/or the clinical experience of physicians using tocilizumab (and other inhibitors of IL-6 or IL-6 receptor) in various diseases. For example, part of the rationale supporting the development and investigation for pacibekitug in TED is from published articles describing the off-label use of tocilizumab in TED, which report observations of positive efficacy and safety results.

Results from our future or ongoing clinical trials of pacibekitug may differ significantly from those from published articles in the literature of other molecules in the anti-IL-6 or anti-IL-6R class. For example, differences in clinical results may arise from differences between drug targets or between molecules that inhibit the same drug target. In addition, there may

be substantial differences, even if the same disease or indication, between clinical trial(s) of pacibekitug and published literature (e.g., case series or reports, clinical trials, etc.) for other molecules in the anti-IL-6 or anti-IL-6R class based upon factors such as the clinical use setting, patient population being treated or investigated, assessments (e.g., efficacy, safety, pharmacodynamics, etc.), data collection and handling, analysis, study conduct, or other factors. Bias may have also been introduced in the published clinical reports that led to an incorrect determination or overestimate of the efficacy and safety results for pacibekitug because of the open-label nature and lack of controls or other robustness measures in these case series and uncontrolled clinical studies. There also can be publication bias, if only examples of successful cases of the clinical use of an anti-IL-6 or anti-IL-6R molecule (e.g., tocilizumab, satralizumab, sarilumab, siltuximab, ziltivekimab, etc.) may have been published, while treatment experiences for such molecules that were unsuccessful and/or associated with adverse safety outcomes were not published.

The impact of such differences may lead to a clinical trial(s) of pacibekitug failing to reproduce any positive efficacy, safety, or other findings in relation to inhibition of IL-6 or the IL-6 receptor that were reported in publications of other molecules. If such an event was to occur, there is a risk that the pacibekitug development program in a particular indication(s) or all indications is terminated, longer or more expensive development programs (including larger, longer, and/or costlier clinical trials) may be required to investigate pacibekitug, pacibekitug is not approved by the FDA or other regulatory authorities, pacibekitug is not reimbursed by payors or other similar bodies, or there is limited or no success achieved in the commercialization of pacibekitug.

Preliminary, initial, or interim results from clinical trials that we announce, present, or publish from time to time may change as more data and information become available (or are updated based upon audit, validation and verification procedures of the data/information commonly performed for clinical trials) that could result in material changes in the final trial results.

From time to time, we may announce, present or publish preliminary, initial, or interim data or other information from our clinical trials. Any such data and other results from our clinical trials may materially change as more patient data and information become available. Such data and information may also undergo significant change following subsequent auditing, validation and/or verification procedures that are commonly conducted in clinical trials. Thus, any preliminary, initial, or interim data or other information may not be predictive of final results from the clinical trial and should be viewed with caution until the final data are available. We may also arrive at different conclusions, or other determinations that may qualify such results, once we have received and fully evaluated the additional data. Differences between preliminary, initial or interim results and final results could lead to significantly different interpretations or conclusions of the trial outcomes.

Further, others, including regulatory authorities and collaboration or regional partners, 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 pacibekitug, the approvability or commercialization of pacibekitug or any future product candidates, and us in general. In addition, the information we choose to publicly disclose regarding a particular clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If the preliminary, initial or interim data that our reports differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, pacibekitug may be harmed, which could significantly harm our business, financial condition, results of operations and prospects.

Pacibekitug may cause undesirable side effects or adverse events or have other properties or safety risks, which could terminate further development of this product candidate, result in a lack of product approval by the FDA or other regulatory authorities, delay the timing (and/or increase the cost) of a product approval by the FDA or other regulatory authorities, lead to a restrictive product label that significantly limits prescribing of an approved product, delay or preclude reimbursement by payors, or significantly limit or preclude the commercialization of pacibekitug.

A concerning safety signal (such as that involving serious adverse events, life-threatening adverse events, or deaths, or a nonserious adverse event that may occur at a high or concerning frequency and/or severity or if rare, leads to a significant safety concern), tolerability concern (e.g., undesirable side effects that cannot be tolerated by patients, require suboptimal dosing alterations require additional monitoring and/or lead to patients missing or delaying doses) or other safety issue caused by pacibekitug may be observed in any future or ongoing clinical trial of pacibekitug. For example, dosing in the 200 mg arm of the prior Pfizer Phase 2 trial of pacibekitug in systemic lupus erythematosus was stopped for safety concerns based on an unblinded data review and recommendation from the internal review committee for that study. Prior safety (clinical and nonclinical) data for pacibekitug, safety data and observations for other molecules in the anti-IL-6 and anti-IL-6R classes, and published safety data and observations for other molecules in the anti-IL-6 and anti-IL-6R classes used in the same disease or indication as that being investigated in pacibekitug clinical trial(s) may not be indicative of similar safety and tolerability results or profile for pacibekitug in future or ongoing clinical trials. For example, some potential therapeutics developed in the biopharmaceutical industry that initially showed therapeutic promise in early-stage trials have later been found to have a problematic safety or tolerability profile that prevented their further development.

In addition, pacibekitug is a recombinant protein. Recombinant proteins can sometimes induce host immune responses that can cause the production of anti-drug antibodies ("ADAs"). ADAs may neutralize the effectiveness of the product candidate, can require that higher doses be used to obtain a therapeutic effect or can cross react with substances naturally occurring in a subject's body, which can cause unintended effects, including potential impacts on efficacy and adverse events. For example, the ADAs may prevent the drug from offering a therapeutic benefit or lead to a less efficacious effect. ADAs may also cause hypersensitivity reactions (including anaphylaxis) that may require patients to stop taking that drug or can, in some cases, be serious, life-threatening, or fatal. If we determine that ADAs are causing safety or efficacy concerns for pacibekitug, we may need to delay, halt, or terminate our clinical trials and the affected product candidates. pacibekitug may never obtain regulatory approval by the FDA or other regulatory authorities. We cannot provide assurance that the detection of ADAs will not occur at a higher rate than what we have observed historically or that ADA will not lead to meaningful impacts upon efficacy or safety, or that the detection of ADAs will not otherwise result in pacibekitug not being approved by the FDA or other regulatory authorities.

If a safety signal, tolerability concern, ADA concern, or other safety issue emerges from any future or ongoing clinical trial for pacibekitug, or any other IL-6 inhibitor product candidate, this could result in:

- slowing of patient enrollment in our clinical trials or inability to enroll the trials;
- a meaningful rate of patients dropping out of trials (which could lead to a delay in completing the clinical trial or adversely impact the trial's probability of success in observing a positive efficacy result);
- a meaningful rate of patients missing or postponing their trial procedures (including but not limited to dosing, study visits and efficacy assessments) which in turn could lead to a delay in completing the clinical trial or adversely impact the trial's probability of success in observing a positive efficacy result;
- an inability to use a dose that offers efficacy or necessitating the use of a lower dose that may offer only low or partial efficacy;
- suspension of the clinical trial by us, the FDA or other regulatory authority, or local IRB or ethics committee;
- termination of the clinical trial;
- need for additional and/or larger clinical trial(s) to further evaluate the safety profile of pacibekitug;
- abandonment of the development of pacibekitug for that particular indication being evaluated by the clinical trial or for other indications or as a program altogether;
- refusal by the FDA or other regulatory authority to grant product approval;

- restrictions on the product labeling (such as a black boxed warning, warnings and precautions, limitations of use, and/or narrowed and limited indication) that may significantly limit the prescribing and usage of pacibekitug;
- requirement to develop a Risk Evaluation and Mitigation Strategy ("REMS") for pacibekitug in the U.S. or a similar strategy as required by a comparable foreign regulatory authority;
- a view by healthcare professionals that pacibekitug presents an unfavorable benefit-risk profile which in turn may significantly limit the prescribing and usage of pacibekitug;
- a meaningful rate of patients either choosing to not start pacibekitug treatment or to prematurely discontinue usage of pacibekitug;
- use of additional monitoring by healthcare professionals, either on their own or due to the recommendations of expert panels or treatment guidelines, in the use of pacibekitug that in turn may significantly limit the prescribing and usage of pacibekitug;
- a view by payors that pacibekitug presents an unfavorable benefit-risk profile which in turn may significantly limit the reimbursement of pacibekitug;
- a requirement to conduct additional post-market studies, including clinical trials;
- lawsuit(s) that results in us being held liable for harm caused to trial participants or other patients; and/or
- reputational injury to us.

Any of these occurrences could materially and adversely affect our business, financial condition, results of operations and prospects.

Pacibekitug is a product candidate within the IL-6 inhibitor and IL-6R inhibitor class and may be adversely impacted by results for other members in the class, which could delay, terminate or increase the cost of development of pacibekitug, delay or prevent approval by the FDA or other regulatory authorities, lead to a restrictive product label that significantly limits prescribing, delay or preclude reimbursement by payors, or significantly limit or preclude the commercialization of pacibekitug.

Pacibekitug is a member of the IL-6 inhibitor and IL-6R inhibitor class. There are other products and product candidates within this class that are being developed or commercialized by third parties over which we have no control and for which we do not have any information beyond what is publicly available. It is possible that negative data or information may emerge from one or more of these other products or product candidates related to a limitation or failure of efficacy, safety concern, negative publicity or other issue. Such an occurrence may adversely impact pacibekitug or its perceived product profile and could terminate further development of pacibekitug, result in a lack of product approval by the FDA or other regulatory authorities, delay the timing (and/or increase the cost) of a product approval, lead to a restrictive product label that significantly limits prescribing, delay or preclude reimbursement by payors, or significantly limit or preclude the commercialization of pacibekitug.

We face significant competition from other biotechnology and pharmaceutical companies targeting immune and inflammatory disease indications. Our operating results will suffer if we fail to compete effectively.

The markets for immune and inflammatory disease therapies are competitive and are characterized by significant technological development and new product introduction. For example, there are several large and small pharmaceutical companies focused on delivering therapeutics for ASCVD and TED. We anticipate that, if we obtain regulatory approval of pacibekitug, we will face significant competition from other approved therapies or drugs that become available in the future for the treatment of our target indications. If approved, pacibekitug may also compete with unregulated, unapproved and off-label treatments. Pacibekitug may also face biosimilar competition following loss of regulatory exclusivity and/or patent expiry. Even if an approved biosimilar product is less effective than pacibekitug, a less effective biosimilar may be more quickly adopted by physicians and patients than our competing product candidate based upon cost. Pacibekitug will have to compete with existing therapies, some of which are widely known and accepted by physicians and patients. To compete successfully in this market, we will have to demonstrate that the relative cost, safety and efficacy of our product, if approved, provides an attractive alternative to existing and other new therapies to gain a share of some patients'

discretionary budgets and to gain physicians' attention within their clinical practices. Some of the companies that may offer competing products also have a broad range of other product offerings, large direct sales forces and long-term customer relationships with our target physicians, which could inhibit our market penetration efforts. Such competition could lead to reduced market share for our product candidate and contribute to downward pressure on the pricing of our product candidate, which could harm our business, financial condition, results of operations and prospects.

We expect to face competition from agents with various mechanisms of action in both ASCVD and TED. For example, in January 2020, the FDA approved Amgen Inc.'s (formerly Horizon Therapeutics Public Limited Company) TEPEZZA (teprotumumab), an anti-IGF-1R antibody, for the treatment of TED. In addition, there are multiple other agents in various stages of development for the treatment of TED, including Roche's satralizumab, an anti-IL-6R monoclonal antibody. The first line of treatment for patients with TED is generally immunosuppressive therapy, including high doses of corticosteroids. For ASCVD, several classes of therapies are routinely used, including statins, beta-blockers, ACE inhibitors, ARBs, aspirin, and other anti-platelet agents. Additionally, we are aware of two IL-6 blockers currently being developed for the treatment of ASCVD.

Many of our existing or potential competitors have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, as well as in obtaining regulatory approvals of those product candidates in the U.S. and in foreign countries. Many of our current and potential future competitors also have significantly more experience commercializing drugs that have been approved for marketing. Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a smaller number of our competitors. Competition may reduce the number and types of patients available to us to participate in clinical trials because 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.

Due to varying regulatory requirements in certain foreign countries, there are many more products and procedures available for use to treat immune and inflammatory diseases in some international markets than are approved for use in the U.S. In certain international markets, there are also fewer limitations on the claims that our competitors can make about the effectiveness of their products and the manner in which they can market their products.

Our ability to compete successfully will depend largely on our ability to:

- develop and commercialize therapies in our target indications that are competitive with other products in the market;
- demonstrate through our clinical trials that pacibekitug or any potential future product candidates is differentiated from existing and future therapies;
- attract and retain qualified scientific, product development, manufacturing and commercial personnel;
- obtain patent or other proprietary protection for pacibekitug and any potential future product candidates;
- obtain required regulatory approvals, including approvals to market pacibekitug or any potential future product candidates we develop;
- have commercial quantities of any approved product manufactured at acceptable cost and quality levels and in compliance with FDA and other regulatory requirements;
- successfully commercialize pacibekitug or any potential future product candidates, if approved;
- obtain coverage and adequate reimbursement from, and negotiate competitive pricing with, third-party payors; and
- avoid regulatory exclusivities or patents held by competitors that may inhibit our products' entry to the market.

The availability of our competitors' products could limit the demand and the price we are able to charge for any product candidate we develop. The inability to compete with existing or subsequently introduced treatments would have an adverse impact on our business, financial condition, results of operations and prospects.

If the market opportunities for pacibekitug and any potential future product candidates are smaller than we estimate or if any approval that we obtain is based on a narrower definition of the patient population, then our revenue potential and ability to achieve profitability will be adversely affected.

The total addressable market opportunity for pacibekitug and any other potential future product candidates we may develop will ultimately depend upon, among other things, the proportion of patients identified as sensitive to our treatments, acceptance by the medical community, patient access, drug and any related companion diagnostic pricing and their reimbursement.

We intend to initially seek regulatory approval of pacibekitug as therapies for patients with ASCVD, abdominal aortic aneurysm ("AAA") and TED. The number of patients in our targeted commercial markets and elsewhere may turn out to be lower than expected, patients may not be otherwise amenable to treatment with our drugs or new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business. In addition, we may not be successful in our efforts to identify additional product candidates. Due to our limited resources and access to capital, we must prioritize development of certain product candidates, which may prove to be the wrong choice and may adversely affect our business, financial condition, results of operations and prospects.

We may not successfully identify new product candidates to expand our development pipeline.

The success of our business over the longer term depends upon our ability to identify and validate new potential therapeutics. Efforts to identify new product candidates require substantial technical, financial and human resources, and our methodology may not successfully identify medically relevant potential therapeutics to be developed as product candidates. Moreover, our research and business development efforts may identify molecules that initially show promise yet fail to yield product candidates for clinical development for multiple reasons. For example, potential product candidates may, on further study, be shown to have inadequate efficacy, harmful side effects, suboptimal drug profiles, suboptimal manufacturability or stability, or other characteristics suggesting that they are unlikely to be commercially viable products. Our inability to successfully identify additional new product candidates to advance into clinical trials could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to the Marketing and Commercialization of Our Product Candidates

Even if any of our current or future product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If pacibekitug or any of our potential future product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our current or potential future candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy, safety and potential advantages compared to alternative treatments, including pharmaceutical and nonpharmaceutical interventions;
- the acceptance of our product candidates as front-line treatments for various indications;
- the prevalence and severity of any side effects, in particular compared to alternative treatments;
- limitations or warnings contained in the labeling approved by the FDA or other regulatory authorities;
- the size of the target patient population;
- the willingness and ability of the target patient population to try new therapies and adhere or comply with taking such therapy as prescribed and of physicians to prescribe these therapies;
- our ability to offer our products for sale at competitive prices;

- our ability to protect our approved products from generic or biosimilar competition through the use of regulatory exclusivity or patents;
- the convenience and ease of administration compared to alternative treatments;
- the amount of clinical burden upon healthcare professionals or patients related to any additional monitoring or other measures needed in order for patients to initiate and/or continue receiving such products;
- the strength of marketing, sales and distribution support;
- publicity for our product candidates and competing products and treatments;
- the availability of third-party payor coverage and adequate reimbursement;
- the timing of any marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on the use of our products together with other medications.

Even if we obtain approval to market pacibekitug or other potential future product candidates, these products may become subject to unfavorable pricing regulations, reimbursement practices from third-party payors or healthcare reform initiatives in the U.S. and abroad, which could harm our business.

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. In many regions, including the European Union ("EU"), Japan and Canada, the pricing of prescription drugs is controlled by the government and 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 regulatory approval for the product is granted. Regulatory agencies in those countries could determine that the pricing for our products should be based on prices of other commercially available drugs for the same disease, rather than allowing us to market our products 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 its 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. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our commercial success also depends on coverage and adequate reimbursement of our product candidates by third-party payors, including government payors, private health insurers, health maintenance organizations and other organizations, 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 U.S. and markets in other countries, governments and private insurers closely examine medical products to determine whether they should be covered by reimbursement and, if so, the level of reimbursement that will apply. In the U.S., the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services ("CMS"), an agency within the U.S. Department of Health and Human Services ("HHS"). CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drugs. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drug products. We cannot be sure that coverage and reimbursement will be available for any product that we or our partners commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we or our partners obtain regulatory 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 product 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 health 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 costs of 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 private 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 U.S. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs. 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, ability to raise capital needed to commercialize products and overall financial condition.

Even if we are able to obtain regulatory approval for pacibekitug or any of our future product candidates, we may receive an undesirable label, including, but not limited to, a black boxed warning, which could impede our ability to successfully commercialize pacibekitug or any of our future product candidates or compete successfully.

Even if we receive regulatory approval for any of our product candidates, the FDA may determine that labels for our product candidates may require safety restrictions such as a black boxed warning, warnings and precautions, limitations of use, and/or narrowed and limited indication that may significantly limit the prescribing and usage of pacibekitug. Safety restrictions such as a black boxed warning may impede our ability to successfully market and commercialize our product candidates and our ability to compete successfully against our competitors.

Two approved therapies in the IL-6 class, tocilizumab (Actemra®) and sarilumab (Kevzara®) have received black boxed warning for risks of serious infections. Two approved therapies in the IL-6 class, satralizumab (Enspryng®) and siltuximab (Sylvant®) have not. We cannot guarantee or ensure that pacibekitug will not get a black boxed warning or significant safety restrictions on its product labels, if approved.

Our estimates of market opportunity and forecasts of market growth may prove to be inaccurate, and even if the markets in which we compete achieve the forecasted growth, our business may not grow at similar rates, or at all.

Our market opportunity estimates and growth forecasts are subject to significant uncertainty and are based on assumptions and estimates which may not prove to be accurate. Our estimates and forecasts relating to size and expected growth of our target market may prove to be inaccurate. Even if the markets in which we compete meet our size estimates and growth forecasts, our business may not grow at similar rates, or at all. Our growth is subject to many factors, including our success in implementing our business strategy, which is subject to many risks and uncertainties.

Our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to obtain coverage and reimbursement, the ability to gain market share and whether we own the commercial rights for that territory. If the number of our addressable patients is not as significant as our estimates, the indication approved by regulatory authorities is narrower than we expect or the treatment population is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit development and commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we or our partner commercializes any resulting products. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidates or products that we may develop caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for any product candidates or products that we may develop;

- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial subjects or patients;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize any products that we may develop.

Our clinical trial liability insurance coverage may not adequately cover all liabilities that we may incur. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Our inability to obtain product liability insurance at an acceptable cost or to otherwise protect against potential product liability claims could prevent or delay the commercialization of any products or product candidates that we develop. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for pacibekitug or any potential future product candidates, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. If we are sued for any injury caused by our products, product candidates or processes, our liability could exceed our product liability insurance coverage and our total assets. Claims against us, regardless of their merit or potential outcome, may also generate negative publicity or hurt our ability to obtain physician endorsement of our products or expand our business.

Risks Related to Government Regulation

The regulatory approval processes of the FDA and comparable foreign health authorities are lengthy and inherently unpredictable. Our inability to obtain regulatory approval for pacibekitug would substantially harm our business.

Currently, we have no product candidate that has received regulatory approval and pacibekitug or any potential future product candidates is not expected to be commercially available for several years, if at all. The time required to obtain approval from the FDA and comparable foreign health authorities is unpredictable but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the health authorities. In addition, approval policies, regulations or the type and amount of preclinical and clinical data necessary to gain approval may change during the course of a product candidate's development and may vary among jurisdictions. It is possible that none of our existing or future product candidates will ever obtain regulatory approval.

Pacibekitug or any of our future product candidates could fail to receive regulatory approval from the FDA or a comparable foreign health authority for many reasons, including:

- disagreement with the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of results of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- the insufficiency of data collected from clinical trials to support the submission and filing of a Biologics License Application ("BLA") or other submission or to obtain regulatory approval;

- failure to obtain approval of the manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies;

- unfavorable quality review or audit/inspection findings; or

- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or a comparable foreign health authority may require more information, including additional preclinical or clinical data, to support approval, which may delay or prevent approval and commercialization, or we may decide to abandon the development program for other reasons. If we obtain approval, regulatory authorities may approve pacibekitug or any potential future product candidates for fewer or more limited indications than we request, may grant accelerated approval or conditional marketing authorization based on a surrogate endpoint and contingent on the successful outcome of costly and time-consuming post-marketing confirmatory clinical trials or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate.

We may seek fast track and/or breakthrough therapy designations or priority review for one or more of our product candidates, but we might not receive such designation or priority review, and even if we do, such designation or priority review may not lead to a faster development or regulatory review or approval process, and does not assure FDA approval of our product candidates. Even if a product qualifies for such designation or priority review, the FDA may later decide that the product no longer meets the conditions for qualification or may decide that the time period for FDA review or approval will not be shortened.

We may seek fast track and/or breakthrough therapy designations for one or more of our product candidates.

The FDA may issue a fast track designation to a product candidate if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biologic may request that the FDA designate the biologic as a fast track product at any time during the clinical development of the product. For fast track products, sponsors may have greater interactions with the FDA during product development. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. However, the FDA's PDUFA goal for reviewing a BLA fast track application under the Prescription Drug User Fee Act ("PDUFA") does not begin until the last section of the application is submitted. Fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate 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 product candidates that have been designated as breakthrough therapies, interaction 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. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the BLA.

Fast track designation and breakthrough therapy designation are within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for any such designation, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of such designation may expedite the development or approval process, but does not change the standards for approval. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the BLA is eligible only for standard review.

In the EU, 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 similar to the breakthrough therapy designation in the U.S.

Sponsors that benefit from PRIME designation are potentially eligible for accelerated assessment of their marketing authorization applications, although this is not guaranteed. If a product for which PRIME designation was granted is the subject of an accelerated assessment, the product may be placed on the market in the EU before our product candidate with a similar therapeutic indication.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shutdowns, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. 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 business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operation.

Our failure to obtain health authority approval in foreign jurisdictions would prevent us from marketing pacibekitug or any potential future product candidates outside the U.S.

If we or our partners succeed in developing any products, we intend to market them in the EU and other foreign jurisdictions in addition to the U.S. In order to market and sell our products in other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the U.S. generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the U.S., we must secure product pricing and reimbursement approvals before health authorities will approve the product for sale in that country. 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 our products in certain countries. Further, clinical trials conducted in one country may not be accepted by health authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. If we fail to obtain approval of pacibekitug or any potential future product candidates by health authorities in another country, we will be unable to commercialize our product in that country, and the commercial prospects of that product candidate and our business prospects could decline. In addition, failure to obtain regulatory approval in one country or region could adversely affect future regulatory approvals in other countries.

Even if pacibekitug and any potential future product candidates receive regulatory approval, they will still face extensive ongoing regulatory requirements, which may result in significant expenses, and may still face future development and regulatory difficulties.

Even if we obtain regulatory approval for a product candidate, it would be subject to ongoing requirements by the FDA and comparable foreign health authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. We will be subject to ongoing requirements, including submissions of safety and other post-marketing information, reports, establishment registration and product listing requirements, requirements relating to current cGMP, applicable product tracking and tracing requirements, quality control, quality assurance and corresponding maintenance of records and documents, and recordkeeping. We will also need to ensure continued compliance by it and/or any future contract manufacturing organizations and CROs for any post-approval clinical trials that we conduct. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to conditions of approval, or contain requirements for costly post-

marketing testing and surveillance to monitor the safety or efficacy of the product. Additionally, under the Food and Drug Omnibus Reform Act of 2022, sponsors of approved drugs and biologics must provide 6 months' notice to the FDA of any changes in marketing status, such as the withdrawal of a drug, and failure to do so could result in the FDA placing the product on a list of discontinued products, which would revoke the product's ability to be marketed.

Even after approval, the FDA and comparable foreign health authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA or comparable foreign health authorities become aware of new safety information after approval of pacibekitug and any potential future product candidates, they may require labeling changes or establishment of a REMS, or similar strategy, impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. Failure to comply with any related obligations may result in the suspension or withdrawal of an obtained approval and in civil and/or criminal penalties. Receipt of approval for narrower indications than sought, restrictions on marketing through a REMS or similar strategy imposed by the FDA or in an EU member state or other foreign country, or significant labeling restrictions or requirements in an approved label such as a black boxed warning could have a negative impact on our ability to recoup our R&D costs and to successfully commercialize that product, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects. In any event, if we are unable to comply with our post-marketing obligations imposed as part of the marketing approvals in the U.S., the EU, or other countries, our approval may be varied, suspended or revoked, product supply may be delayed and our sales of our products could be materially adversely affected.

In addition, manufacturers of drug substance and drug product and their facilities are subject to continual review and periodic inspections by the FDA and comparable foreign health authorities for compliance with cGMP regulations. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency 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. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the U.S. If we or the manufacturing facilities for pacibekitug or any potential future product candidates fail to comply with applicable regulatory requirements, or if pacibekitug or any potential future product candidates are found to cause undesirable or unacceptable side effects, a regulatory agency may:

- issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product;
- issue warning letters or untitled letters;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners, or require other restrictions on the labelling or marketing of such products;
- require that we conduct and complete post-marketing studies;
- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend marketing of, withdraw or modify regulatory approval of or initiate a recall of such product;
- suspend or modify any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or refuse to permit the import or export of products.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue.

Advertising and promotion of any product candidate that obtains approval in the U.S. will be heavily scrutinized by the FDA, DOJ, HHS, OIG, state attorneys general, members of Congress and the public. Violations, including promotion of our products for unapproved (or off-label) uses, are subject to enforcement letters, inquiries and investigations and civil and criminal sanctions by the government. Any actual or alleged failure to comply with labeling and promotion requirements may result in fines, warning letters, mandates to corrective information to healthcare practitioners, injunctions, or civil or criminal penalties. Additionally, comparable foreign health authorities, public prosecutors, industry associations, healthcare professionals and other members of the public will heavily scrutinize advertising and promotion of any product candidate outside of the U.S.

In the U.S., engaging in the impermissible promotion of our products for off-label uses can subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. These false claims statutes include the federal FCA, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these FCA lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements regarding certain sales practices promoting off-label drug uses involving fines in excess of $1 billion. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations and be excluded from Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition and results of operations.

The FDA's policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of pacibekitug or any potential future product candidates. For example, the U.S. Supreme Court's June 2024 decision in Loper Bright Enterprises v. Raimondo ("Loper") overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper decision could result in additional legal challenges to regulations and decisions issued by federal agencies, including the FDA, on which we rely. Any such legal challenges, if successful, could have a material impact on our business. Additionally, the Loper decision may result in increased regulatory uncertainty, inconsistent judicial interpretations, and other impacts to the agency rulemaking process, any of which could adversely impact our business and operations. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. Certain policies of any administration may impact our business and industry. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

In the EU, the advertising and promotion of medicinal products are subject to both EU and EU member state 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 directives, the details are governed by regulations in each member state 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 a marketing authorization. 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.

Failure to comply with EU, EU member state, and other country laws that apply to the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and marketing of such products, both before and after grant of a marketing authorization, or with other applicable regulatory requirements, may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the

marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties. In addition, directives adopted at the EU level may be implemented differently by individual member states. These directives, and their differing implementations in member states, increase our legal and financial compliance costs and may make some activities more time-consuming and expensive.

Healthcare reform may negatively impact our ability to profitably sell pacibekitug and any potential future product candidates, if approved.

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

For example, on August 16, 2022, the Inflation Reduction Act of 2022 (the "IRA") was signed into law, which among other things, (1) directs the HHS, to negotiate the price of certain single-source biologics that have been on the market for at least 11 years covered under Medicare (the "Medicare Drug Price Negotiation Program") and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA includes certain exemptions to the price negotiation program, including a limited exemption for products with orphan drug designation. This exemption applies only to products with one orphan drug designation that is (i) for a rare disease or condition and (ii) is approved for indication(s) for such rare disease or condition. By limiting price negotiation exemption to products with only one orphan drug designation, the IRA may decrease our interest in pursuing orphan drug designation for our product candidates in multiple indications. The IRA also, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025 and eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. These provisions began to take effect progressively starting in fiscal year 2023. On August 15, 2024, HHS announced the agreed-upon reimbursement price of the first ten drugs that were subject to price negotiations, although the Medicare Drug Price Negotiation Program is currently subject to legal challenges. On January 17, 2025, HHS selected fifteen additional products covered under Part D for price negotiation in 2025. Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. Further, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively referred to as the ACA, was enacted, which includes measures that have significantly changed the way health care is financed by both governmental and private insurers. There have been amendments to and executive, judicial and congressional challenges to certain aspects of the ACA. While Congress has not passed comprehensive legislation repealing the ACA, such legislation may be reintroduced, particularly given recent U.S. elections. It is possible that the ACA and IRA may be subject to judicial or Congressional challenges in the future. It is unclear how any additional healthcare reform measures may impact the ACA or IRA, increase the pressure on drug pricing or limit the availability of coverage and adequate reimbursement for pacibekitug and any potential future product candidates, which would adversely affect our business.

There has also been increasing executive, legislative and enforcement interest in the U.S. with respect to drug pricing practices. There have been U.S. congressional inquiries, presidential executive orders and proposed and enacted legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. For example, on December 7, 2023, an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act was announced. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. We expect that the healthcare reform measures that have been adopted and may be adopted in the future may result in more rigorous coverage criteria and additional downward pressure on the price that we receive for any approved product and could seriously harm its future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare, particularly given recent U.S. Presidential and Congressional elections. The current administration is pursuing policies to reduce regulations and expenditures across government including at HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. These actions may include, for example, directives to reduce agency workforce, rescinding a Biden administration executive order tasking the Center for Medicare and Medicaid Innovation ("CMMI") to consider new payment and healthcare models to limit drug spending and eliminating the Biden administration's executive order that directed HHS to establishing an AI task force and developing a strategic plan. Additionally, in the June 2024 Loper decision, the U.S. Supreme Court overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper decision could result in additional legal challenges to current regulations and guidance issued by federal agencies applicable to our operations, including those issued by the FDA. Finally, Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program created under the IRA. We cannot predict which additional measures may be adopted or the impact of current and additional measures on the marketing, pricing and demand for pacibekitug. Such reforms could have an adverse effect on anticipated revenue from pacibekitug and any potential future product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

In many countries outside the U.S., government-sponsored healthcare systems are the primary payors for drugs. With increasing budgetary constraints and/or difficulty in understanding the value of medicines, governments and payors in many countries are applying a variety of measures to exert downward price pressure and we expect that legislators, policy makers and healthcare insurance funds in the EU Member States will continue to propose and implement cost cutting measures. These measures include mandatory price controls, price referencing, therapeutic-reference pricing, increases in mandates, incentives for generic substitution and biosimilar usage, government-mandated price cuts, limitations on coverage of target population and introduction of volume caps.

Many countries implement health technology assessment ("HTA"), procedures that use formal economic metrics such as cost-effectiveness to determine prices, coverage and reimbursement of new therapies. These assessments are increasingly implemented in established and emerging markets. In the EU, Regulation (EU) 2021/2282 on Health Technology Assessment, which will become effective on January 12, 2025, will allow EU member states to use common HTA tools, methodologies and procedures to conduct joint clinical assessments and joint scientific consultations whereby HTA authorities may provide advice to health technology developers. Each EU member state will, however, remain exclusively competent for assessing the relative effectiveness of health technologies and making pricing and reimbursement decisions. Given that the extent to which pricing and reimbursement decisions are influenced by the HTA process currently varies between EU member states, it is possible that our products may be subject to favorable pricing and reimbursement status only in certain EU countries. If we are unable to maintain favorable pricing and reimbursement status in EU member states that represent significant markets, including following periodic review, our anticipated revenue from and growth prospects for our products in the EU could be negatively affected. Moreover, in order to obtain reimbursement for our products in some EU member states, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. Efforts to generate additional data for the HTA process will involve additional expenses which may substantially increase the cost of commercializing and marketing our products in certain EU member states.

We cannot predict the likelihood, nature or extent of healthcare reform initiatives that may arise from future legislation or administrative action. However, it is possible that countries will continue taking aggressive actions to seek to reduce expenditures on drugs. Similarly, fiscal constraints may also affect the extent to which countries are willing to approve new and innovative therapies and/or allow access to new technologies.

If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

Our current and future relationships with investigators, healthcare professionals, customers, and third-party payors will be subject to applicable anti-kickback, fraud and abuse, transparency, and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens, and diminished profits and future earnings.

Healthcare professionals, including physicians and healthcare institutions, and third-party payors, will play a primary role in the recommendation and prescription of any product candidates for which we or our partner obtains marketing approval. Our existing and future arrangements with healthcare professionals and institutions, and any arrangements we enter into with third-party payors and customers, may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we currently research, and in the future, market, sell and distribute products for which we or our partner obtain marketing approval. Restrictions under federal and state healthcare laws and regulations that are or may be applicable to us, include, without limitation, the following:

- the federal Anti-Kickback Statute, which is a criminal law, prohibits, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, the referral of an individual for the furnishing or arranging for the furnishing, or the purchase, lease or order, or arranging for or recommending the purchase, lease or order, of any good or service for which payment may be made under a federal healthcare program, such as Medicare and Medicaid or other federally financed healthcare programs. The term "remuneration" is not defined in the federal Anti-Kickback Statute and has been broadly interpreted by the federal government to include anything of value, for example, cash payments, gifts, discounts, coupons, and the furnishing of free or discounted services or supplies, and other items or services of value to the recipient. This statute has been broadly interpreted to apply to manufacturer arrangements with prescribers, purchasers, formulary managers and patients, among others. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for such exceptions or safe harbors. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that 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 FCA or federal civil monetary penalties;

- the FCA imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. The FCA also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;

- the federal Civil Monetary Penalties Law, which authorizes the imposition of substantial civil monetary penalties against an entity that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal health care programs to provide items or services reimbursable by a federal health care program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment;

- other federal healthcare fraud-related laws also impose criminal liability for violations. For example, the Criminal Healthcare Fraud Statute (18 U.S.C. §1347) prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payors. Federal criminal law also prohibits knowingly and willfully falsifying, concealing or covering up 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;

- a number of states also have statutes or regulations similar to the federal Anti-Kickback Statute and FCA that apply to items and services reimbursed under Medicaid and other state programs. Some state anti-kickback statutes apply not just to government payors, but to all payors, including commercial payors and patients;

- the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), as amended by the Health Information Technology for Economic and Clinical Health Act, imposes obligations on "covered entities," including health plans and healthcare providers, and their business associates with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, as well as their covered subcontractors. Although we are not directly subject to HIPAA as a covered entity or business associate, we could be subject to criminal or civil penalties if we knowingly obtain individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. We are also subject to state, federal and international privacy and security laws governing the processing and security of personal identifiable information. HIPAA also imposes criminal liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense or knowingly and willfully making false statements relating to healthcare matters. 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;

- the federal Physician Payments Sunshine Act requirements under the Affordable Care Act, as amended, and its implementing regulations, require manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the HHS information related to certain direct and indirect "payments or other transfers of value" made to covered recipients (defined to include physicians, dentists, optometrists, podiatrists and chiropractors), other health care professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance requirements promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and local laws requiring the registration of pharmaceutical sales representatives; state and foreign 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 pricing; federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and state and foreign laws that govern the privacy and security and other processing of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Failure to comply with these laws and requirements could result in significant civil penalties and other adverse consequences.

Efforts to ensure that our current and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental 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 our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, disgorgement, additional regulatory oversight, litigation, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Even the mere issuance of a subpoena, civil investigative demand or the fact of an investigation alone, regardless of the merit, may result in negative publicity, a drop in our share price and other harm to our business, financial condition and our results of operations. Other pharmaceutical companies have settled alleged or admitted violations of these fraud and abuse laws with state and federal authorities in recent years and in some cases these settlements have amounted to hundreds of millions, or even billions, of dollars in damages, fines, and penalties, as well as the imposition of compliance program obligations through Corporate Integrity Agreements and other means. Lawsuits, or enforcement actions brought under fraud and abuse laws, can be extremely costly to defend, even if a company has strong defenses and ultimately succeeds in getting the allegations or enforcement action dismissed. If any of the physicians or other healthcare professionals or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Outside the U.S., interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti-bribery laws of EU member states, 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.

Changes in tax laws or regulations could adversely affect our business and financial condition.

New tax laws, statutes, rules, regulations, or ordinances could be enacted at any time. For instance, the IRA imposes, among other rules, a 15% minimum tax on the book income of certain large corporations and a 1% excise tax on certain corporate stock repurchases. Further, existing tax laws, statutes, rules, regulations, or ordinances could be interpreted differently, changed, repealed, or modified at any time. Any such enactment, interpretation, change, repeal, or modification could adversely affect us, possibly with retroactive effect. In particular, changes in corporate tax rates, the realization of our net deferred tax assets, the taxation of foreign earnings, and the deductibility of expenses under the 2017 Tax Act, as amended by the Coronavirus Aid, Relief, and Economic Security Act or any future tax reform legislation, could have a material impact on the value of our deferred tax assets, result in significant one-time charges, and increase our future tax expenses.

Our ability to use our U.S. net operating loss carryforwards and certain other U.S. tax attributes may be limited.

As of December 31, 2024, we had U.S. federal net operating loss carryforwards of approximately $50.6 million. Under current law, U.S. federal net operating loss carryforwards generated in taxable periods beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such net operating loss carryforwards is limited to 80% of taxable income. In addition, our U.S. federal net operating loss carryforwards and tax credits may be subject to limitations under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if we have undergone or undergo an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a rolling three-year period. We may have experienced such ownership changes in the past and may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. Our net operating loss carryforwards and tax credits may also be impaired or restricted under state law. If we earn taxable income, such limitations could result in increased future income tax liability and our future cash flows could be adversely affected. We have recorded a valuation allowance related to our net operating loss carryforwards and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

Future changes in financial accounting standards or practices may cause adverse and unexpected revenue fluctuations and adversely affect our reported results of operations.

Future changes in financial accounting standards may cause adverse, unexpected revenue fluctuations and affect our reported financial position or results of operations. Financial accounting standards in the U.S. are constantly under review and new pronouncements and varying interpretations of pronouncements have occurred frequently in the past and are expected to occur again in the future. As a result, we may be required to make changes in our accounting policies. Those changes could affect our financial condition and results of operations or the way in which such financial condition and results of operations are reported. Compliance with new accounting standards may also result in additional expenses. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from business activities to compliance activities.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

Our internal control over financial reporting may not meet the standards required by Section 404 of the Sarbanes-Oxley Act, and failure to achieve and maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act, could have a material adverse effect on our business and share price.

Our management is required to establish and maintain an adequate internal control structure and procedures for financial reporting. The rules governing the standards that must be met for our management to assess our internal control over financial reporting are complex and require significant documentation, testing and possible remediation.

Any failure to maintain effective internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins our reporting on internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

We have previously identified material weaknesses in our internal control over financial reporting. If we identify additional material weaknesses in the future or otherwise fail to maintain effective internal control over financial reporting, we may not be able to accurately or timely report our financial condition or results of operations, which may adversely affect our business.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements would not be prevented or detected on a timely basis.

Effective internal control over financial reporting is necessary for us to provide reliable financial reports in a timely manner commensurate with the financial reporting requirements of an SEC registrant. Prior to the completion of the Reverse Merger, we were a private company and therefore had not designed or maintained internal controls over financial reporting commensurate with the financial reporting requirements of an SEC registrant.

Our management identified material weaknesses in our internal control over financial reporting primarily related to limited staffing levels within the finance and accounting departments that were not commensurate with our financial accounting and reporting requirements. We had to rely increasingly on outsourced service providers and specialists, without adequate resources to monitor such work and did not maintain appropriate segregation of duties. Based on this, we did not fully implement components of the COSO framework, resulting in material weaknesses either individually, or in the aggregate, in the control environment, risk assessment, control activities, information and communication, and monitoring components.

We determined the material weaknesses previously identified have been remediated as of December 31, 2024 through effective implementation of our remediation plan, which included hiring additional accounting personnel with expertise commensurate with our financial accounting and reporting requirements and that have the requisite experience to oversee outsourced service providers and specialists, upgrading our financial systems and implementing information technology general controls, establishing controls to identify, assess, and respond to the risks of material misstatements, and establishing controls to identify and account for certain non-routine, unusual or complex transactions in a timely fashion.

While we have remediated the previously identified material weaknesses in our internal control over financial reporting, we may in the future identify additional material weaknesses which may adversely affect our business and could result in a future misstatement of one or more account balances or disclosures that would result in a material misstatement to the annual or interim consolidated financial statements that would not be prevented or detected.

We expect to expand our clinical development, manufacturing and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, including significant growth in the number of our employees, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of March 7, 2025, we had 74 full-time employees, including 54 who are engaged in research and development activities, and no part-time employees. As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical product development, business development, regulatory affairs and, if pacibekitug or any potential future product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. Our choice to focus on multiple therapeutic areas may negatively affect our ability to develop adequately the specialized capability and expertise necessary for operations. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

We must attract and retain highly skilled employees in order to succeed. If we are not able to retain our current management team or to continue to attract and retain qualified scientific, technical and business personnel, our business may suffer.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel and we face significant competition for experienced personnel. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm

our operating results. An important element of our strategy is to take advantage of the R&D and other expertise of our current management. The loss of any one of our executive officers, other senior members of the leadership team, or other key personnel could result in a significant loss in the knowledge and experience that we, as an organization, possess and could cause significant delays, or outright failure, in the development and further commercialization of pacibekitug and any potential future product candidates.

There is intense competition for qualified personnel, including management, in the technical fields in which we operate and we may not be able to attract and retain qualified personnel necessary for the successful research, development and future commercialization, if any, of pacibekitug and any potential future product candidates.

Our Executive Severance and Change in Control Plan with certain of our executive officers may require us to pay severance benefits to any of those persons who are terminated in connection with a change in control of us or otherwise, which could harm our financial condition or results.

Certain of our executive officers are parties to our Executive Severance and Change in Control Plan that contains change in control and severance provisions providing for aggregate cash payments for (i) severance and other benefits and (ii) acceleration of vesting of stock options, in the event of a termination of employment in connection with a change in control of us. The accelerated vesting of options could result in dilution to our existing stockholders and harm the market price of our common stock. The payment of these severance benefits could harm our financial condition and results. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

Our international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement risks associated with doing business outside of the U.S.

Our business is subject to risks associated with conducting business internationally. Some of our manufacturing and clinical trial sites are located outside of the U.S. Furthermore, if we or any future partner succeeds in developing pacibekitug or any of our potential future product candidates, we intend to market them in the EU and other jurisdictions in addition to the U.S. If approved, we or any future partner may hire sales representatives and conduct physician and patient association outreach activities outside of the U.S. Doing business internationally involves a number of challenges and risks, including but not limited to:

- multiple, conflicting and changing laws and regulations, such as privacy and data protection regulations, tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- rejection or qualification of foreign clinical trial data by the competent authorities of other countries;
- delays or interruptions in the supply of clinical trial material resulting from any events affecting raw material or component supply or manufacturing capabilities abroad;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining, maintaining, protecting and enforcing our intellectual property rights;
- difficulties in staffing and managing foreign operations;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;
- limits on our ability to penetrate international markets;
- financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of inflation and local and regional financial crises on demand and payment for our products and exposure to foreign currency exchange rate fluctuations;

- natural disasters, political, global geopolitical and economic instability, including geopolitical conflicts such as the ongoing war in Ukraine and hostilities in the Middle East, terrorism and political unrest, disease outbreaks, epidemics and pandemics;

- export control and economic sanctions restrictions, which may restrict or prohibit altogether the sale or supply of certain of our product candidates to certain governments, persons, entities, countries and territories, including those that are the target of comprehensive sanctions, unless there are license exceptions that apply or specific licenses are obtained; and

- regulatory and compliance risks that relate to anti-corruption compliance and record-keeping that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its accounting provisions or its anti-bribery provisions or provisions of anti-corruption or anti-bribery laws in other countries.

Any of these factors could harm our ongoing international clinical operations and supply chain, as well as any future international expansion and operations and, consequently, our business, financial condition, prospects and results of operations.

Our business could be materially and adversely affected in the future by the effects of disease outbreaks, epidemics, and pandemics.

Disease outbreaks, epidemics and pandemics in regions where we may have clinical trial sites or other business operations could adversely affect our business, including by causing significant disruptions in our operations and/or in the operations of third-party manufacturers and CROs upon whom we rely. Disease outbreaks, epidemics and pandemics have negative impacts on our ability to initiate new clinical trial sites, to enroll new patients and to maintain existing patients who are participating in our clinical trials, which may include increased clinical trial costs, longer timelines and delay in our ability to obtain regulatory approvals of pacibekitug and any potential future product candidates, if at all. Disease outbreaks, epidemics and pandemics also could adversely impact clinical trial results for pacibekitug or other future potential product candidates, such as by diminishing or eliminating their efficacy or by producing a safety concern, either through direct biological effects or through confounding of the data collection and analysis. This adverse impact could terminate further development of pacibekitug, result in a lack of product approval by the FDA or other regulatory authorities, delay the timing (and/or increase the cost) of a product approval by the FDA or other regulatory authorities, lead to a restrictive product label that significantly limits prescribing of an approved product, delay or preclude reimbursement by payors, or significantly limit or preclude the commercialization of pacibekitug.

General supply chain issues may be exacerbated during disease outbreaks, epidemics and pandemics and may also impact the ability of our clinical trial sites to obtain basic medical supplies used in our trials in a timely fashion, if at all. If our CDMOs are required to obtain an alternative source of certain raw materials and components, for example, additional testing, validation activities and regulatory approvals may be required which can also have a negative impact on timelines. Any associated delays in the manufacturing and supply of drug substance and drug product for our clinical trials could adversely affect our ability to conduct ongoing and future clinical trials of pacibekitug on our anticipated development timelines. Likewise, the operations of our third-party manufacturers may be requisitioned, diverted or allocated by U.S. or foreign government orders. If any of our CDMOs or raw materials or components suppliers become subject to acts or orders of U.S. or foreign government entities to allocate or prioritize manufacturing capacity, raw materials or components to the manufacture or distribution of vaccines or medical supplies needed to test or treat patients in a disease outbreak, epidemic or pandemic, this could delay our clinical trials, perhaps substantially, which could materially and adversely affect our business.

Unfavorable domestic or global economic conditions could adversely affect our business, financial condition, results of operations, or cash flows.

Our results of operations could be adversely affected by general conditions in the domestic or global economy and in the domestic or global financial markets. Political developments impacting government spending and international trade, including current or potential government-imposed sanctions, potential government shutdowns and trade disputes and tariffs, may negatively impact markets and cause weaker macro-economic conditions. A severe or prolonged economic downturn could result in a variety of risks to our business, including, weakened demand for our current and future potential product candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers to delay

making payments for our services. 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.

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

Our facilities may experience electrical blackouts as a result of a shortage of available electrical power. Future blackouts, which may be implemented by the local electricity provider in the face of high winds and dry conditions, could disrupt our operations. 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 comprehensive 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.

We and the third parties with whom we contract use and generate materials that may expose us to material liability.

Our clinical development activities require the use of hazardous materials, chemicals, and radioactive and biological materials. We contract with CDMOs, laboratories and other vendors that are subject to foreign, federal, state and local environmental and health and safety laws and regulations related to such hazardous materials and byproducts. We cannot completely eliminate the risks associated with the use, manufacture, handling, storage and disposal of hazardous materials and waste products, which could cause personal injuries or illnesses, accidental contamination of our raw materials, drug substance, and/or drug product, interruption of our development or manufacturing efforts, environmental damage resulting in costly cleanup, or liabilities under domestic or foreign laws and regulations. Also, we may incur significant costs to ensure our CDMOs, laboratories and other vendors comply with these current or future environmental and health and safety laws and regulations. In the event of an accident, an injured party may seek to hold us liable for any damages that result. Any liability could exceed the limits or fall outside the coverage of our applicable insurance, and we may not be able to maintain insurance on acceptable terms, if at all. We currently carry no insurance specifically covering environmental claims.

We may be exposed to litigation, including stockholder litigation, which could have an adverse effect on our business and operations.

We may be exposed to litigation from stockholders, suppliers and other third parties from time to time. Such litigation may have an adverse impact on our business and results of operations or may cause disruptions to our operations. In addition, in the past, stockholders have initiated class action lawsuits against biotechnology companies following periods of volatility in the market prices of these companies' common stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty and breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Risks Related to Our Intellectual Property

Our success depends in significant part upon our ability to obtain and maintain intellectual property protection for our products and technologies.

Our success depends in significant part on our ability and the ability of our current or future licensors, licensees, partners and collaborators to establish and maintain adequate intellectual property rights covering the product candidates, products

and technologies that we plan to develop. In addition to taking other steps designed to protect our intellectual property, we have applied for, and intend to continue applying for, patents with claims covering our technologies, processes and product candidates when and where we deem it appropriate to do so. However, the patent prosecution process is expensive and time-consuming, and we and our current or future licensors, licensees, partners or collaborators may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current or future licensors, licensees, partners or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Pending and future patent applications filed by us or our current or future licensors', licensees', partners' or collaborators' may not result in patents being issued that protect our technology or product candidates, or products resulting therefrom, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products.

We have filed twelve provisional patent applications (one of which has expired in favor of a new provisional patent application and eight of which have been converted to non-provisional or Patent Cooperation Treaty ("PCT") applications) and four non-provisional patent applications in the U.S., as well as seven PCT patent applications and four non-PCT applications related to the U.S. applications, to obtain patent rights to our inventions, with claims directed to methods of use, combination therapy and other technologies relating to our product candidates. There can be no assurance that any of these patent applications will issue as patents or, for those applications that do mature into patents, whether the claims of the patents will exclude others from making, using or selling our product or product candidates, or products or product candidates that are substantially similar to us for the same or similar uses. In countries where we have not and do not seek patent protection, third parties may be able to manufacture and sell products that are substantially similar or identical to our products or product candidates without our permission, and we may not be able to stop them from doing so.

Similar to other biotechnology companies, our patent position is highly uncertain and involves complex legal and factual questions. In this regard, we cannot be certain that we or our current or future licensors, licensees, partners or collaborators were the first to make an invention, or the first inventors to file a patent application claiming an invention in our owned or licensed patents or pending patent applications. In addition, even if patents are issued, given the amount of time required for the development, testing and regulatory review of our product candidates, any patents protecting such candidates might expire before or shortly after the resulting products are commercialized. Moreover, the laws and regulations governing patents could change in unpredictable ways that could weaken the ability of us and our current or future licensors, licensees, partners or collaborators to obtain new patents or to enforce existing patents and patents we may obtain in the future. In any event, our patent rights and those of our current or future licensors, licensees, partners or collaborators may not effectively prevent others from commercializing competitive technologies and products.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from or license to third parties and may be reliant on our current or future licensors, licensees, partners or collaborators to perform these activities, which means that these patent applications may not be prosecuted or maintained, and these patents may not be enforced, in a manner consistent with the best interests of our business. If our current or future licensors, licensees, partners or collaborators fail to establish, maintain, protect or enforce such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current or future licensors, licensees, partners or collaborators are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

In addition, the legal protection afforded to inventors and owners of intellectual property in countries outside of the U.S. may not be as broad or effective as that in the U.S. and we may be unable to acquire and enforce intellectual property rights outside the U.S. to the same extent as in the U.S., if at all. Accordingly, our efforts, and those of our licensors, licensees, partners and collaborators, to enforce intellectual property rights around the world may be inadequate to obtain a commercial advantage from the intellectual property that we own or license.

We do not currently own or have a license to any issued patents that cover pacibekitug, although this product candidate is disclosed and its use claimed in our pending U.S. provisional applications, U.S. non-provisional applications, and PCT applications. The patent landscape surrounding pacibekitug is crowded, and there can be no assurance that we will be able to secure patent protection that would adequately cover the use of such product candidate, that we will obtain sufficiently broad claims to be able to prevent others from selling competing products for the same or similar uses, or that we will be able to protect and maintain any patent protection that we initially secure.

Any changes we make to pacibekitug to cause it to have what we view as more advantageous properties may not be covered by its existing patent applications, and we may be required to file new patent applications and/or seek other forms of protection for any such altered product candidate.

We are dependent on patents, know-how and technology, both our own and licensed from others. In particular, we are dependent on our license agreements with Pfizer and Lonza. Any termination, or reduction or narrowing, of these licenses could result in the loss of significant rights and could harm our ability to commercialize pacibekitug and any potential future product candidates.

Disputes may also arise between us and our current licensors and future licensors regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our product candidates and technologies infringe intellectual property rights of the licensor that are not subject to the licensing agreement;
- our right to sublicense patent rights and other rights to third parties under collaborative development relationships;
- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of pacibekitug and any potential future product candidates, and the activities that are deemed to satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- our payment obligations with respect to licensed intellectual property.

Additionally, with regard to the Pfizer License Agreement, if we fail to cure a material breach, Pfizer has customary rights to terminate the Pfizer License Agreement. With regard to the Lonza License Agreement, Lonza has the right to terminate the Lonza License Agreement in the event of a change of control or if we contest the secret or substantial nature of the licensed know-how.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current or future licensing arrangements on acceptable terms, or if Pfizer or Lonza terminates their respective license agreement, we may be unable to successfully develop and commercialize the affected product candidates and technologies.

We are generally also subject to all of the same risks with respect to protection of intellectual property that we license, as it is for intellectual property that we own, which are described herein. If we, Pfizer, Lonza or any other current or future licensors fail to adequately protect any licensed intellectual property, our ability to commercialize products could suffer.

We may be unable to obtain intellectual property rights or technologies necessary to develop and commercialize pacibekitug or any potential future product candidates.

Several third parties are actively researching and seeking and obtaining patent protection in the fields of TED and Cardiovascular Disease, and there are issued third-party patents and published third-party patent applications in these fields. The patent landscape around our product candidate is complex, and we are aware of several third-party patents and patent applications containing claims directed to compositions-of-matter, methods of use and related subject matter, some of which pertain, at least in part, to subject matter that might be relevant to our product candidate. However, we may not be aware of all third-party intellectual property rights potentially relating to our product candidate and technologies, since patent applications are not published until eighteen months after their initial filing date. Therefore, we cannot know whether certain unpublished patent applications, if ultimately issued, may recover relevant uses of pacibekitug or other products of ours.

Depending on what patent claims ultimately issue and how courts construe the issued patent claims, as well as the ultimate formulation and methods of use of our product candidate, we may need to obtain a license to practice the technology claimed in such patents. There can be no assurance that such licenses will be available on commercially reasonable terms, or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the

existing rights to third-party intellectual property rights we have, we might be unable to develop and commercialize pacibekitug or any potential future product candidates, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We could lose the ability to continue the development, manufacture, and commercialization of pacibekitug or any potential future product candidates if we breach any license agreement with service providers and vendors related to those product candidates.

Our commercial success depends upon our ability, and the ability of our current and future licensors, licensees, partners and collaborators, to develop, manufacture, market and sell our products and product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. A third-party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our product candidates and products. As a result, we are a party to a number of technology and patent licenses that are important to our business, and we expect to enter into additional licenses in the future. If we fail to comply with the obligations under these agreements, including payment and diligence obligations, our licensors may have the right to terminate these agreements. In the event of a termination of these agreements, we may not be able to develop, manufacture, market or sell any product that is covered by the intellectual property rights that are the subject of these agreements or to engage in any other activities necessary to our business that require the freedom-to-operate afforded by the agreements, or we may face other penalties under the agreements. For example, in addition to the license agreements with Pfizer and Lonza described above we are party to license agreements with multiple vendors, under which we license technology used to produce pacibekitug. We are required to obtain prior consent from some of these vendors to grant sub-licenses under these agreements. Therefore, these vendors may prevent us from granting sub-licenses to third parties, which could affect our ability to use certain desired manufacturers in order to manufacture our current and future product candidates. In the event of a termination of any of our license agreements, our ability to manufacture or develop any product candidates covered by these agreements may be limited or halted unless we can develop or obtain the rights to technology necessary to produce these product candidates.

Any of the foregoing could materially adversely affect the value of the product or product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in having to negotiate new or amended agreements, which may not be available to us on equally favorable terms, or at all, or cause us to lose our rights under these agreements, including our rights to intellectual property or technology important to our development programs.

We may become involved in lawsuits or other proceedings to protect or enforce our intellectual property rights, which could be expensive, time-consuming and unsuccessful, and have a material adverse effect on the success of our business.

Third parties may infringe patents or misappropriate or otherwise violate intellectual property rights owned or controlled by us or our current or future licensors, licensees, partners or collaborators. In the future, it may be necessary to initiate legal proceedings to enforce or defend these intellectual property rights, to protect trade secrets or to determine the validity or scope of intellectual property rights that are owned or controlled by us or our current or future licensors, licensees, partners or collaborators. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results.

If we or our current or future licensors, licensees, partners or collaborators initiate legal proceedings against a third party to enforce a patent covering a product candidate, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement during prosecution. In an infringement or declaratory judgment proceeding, a court may decide that a patent owned by or licensed to us or our current or future licensors, licensees, partners or collaborators is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that the patent does not cover the technology in question. An adverse result in any litigation proceeding could put one or more of the patents at risk of being invalidated, narrowed, held unenforceable or interpreted in such a manner that would not preclude third parties from entering the market with competing products.

Third parties may initiate legal proceedings against us or our current or future licensors, licensees, partners or collaborators to challenge the validity or scope of intellectual property rights we own or control. For example, generic or biosimilar drug

manufacturers or other competitors or third parties may challenge the scope, validity or enforceability of patents owned or controlled by us or our current or future licensors, licensees, partners or collaborators. These proceedings can be expensive and time-consuming, and many of our adversaries may have the ability to dedicate substantially greater resources to prosecuting these legal actions than us. Accordingly, despite our efforts, we or our current or future licensors, licensees, partners or collaborators may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own, control or have rights to, particularly in countries where the laws may not protect those rights as fully as in the U.S.

There is a risk that some of our confidential information could be compromised by disclosure during litigation because of the substantial amount of discovery required. Additionally, many foreign jurisdictions have rules of discovery that are different than those in the U.S. and that may make defending or enforcing our patents extremely difficult. There also could 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 common stock.

Third-party pre-issuance submission of prior art to the USPTO, opposition, derivation, revocation, reexamination, inter partes review or interference proceedings, or other pre-issuance or post-grant proceedings, as well as other patent office proceedings or litigation in the U.S. or other jurisdictions brought by third parties against patents or patent applications owned or controlled by us or our current or future licensors, licensees, partners or collaborators, may affect the inventorship, priority, patentability or validity of these patents or patent applications. An unfavorable outcome could leave our technology or current and future product candidates without patent protection and allow third parties to commercialize its technology or product candidates without payment to us. Additionally, potential licensees, partners or collaborators could be dissuaded from collaborating with us to license, develop or commercialize current or future product candidates if the breadth or strength of protection provided by our patents and patent applications is threatened. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and we may distract our management and other employees.

Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of the third-party intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Third parties may initiate legal proceedings against us or our current or future licensors, licensees, partners or collaborators alleging that we infringe their intellectual property rights. Alternatively, we may initiate legal proceedings to challenge the validity or scope of intellectual property rights controlled by third parties, including in oppositions, interferences, revocations, reexaminations, inter partes review or derivation proceedings before the USPTO or its counterparts in other jurisdictions. In this regard, we are aware of several third-party patents and patent applications containing claims directed to compositions-of-matter, methods of use and related subject matter, some of which pertain, at least in part, to subject matter that might be relevant to pacibekitug. These proceedings can be expensive and time-consuming, and many of our adversaries may have the ability to dedicate substantially greater resources to prosecuting these legal actions than us.

In addition, we may be subject to claims that we or our employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer, or that third parties have an interest in our patents as an inventor or co-inventor. Likewise, we and our current and future licensors, licensees, partners and collaborators may be subject to claims that former employees, partners, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor or an owner of rights via assignment from such an inventor or co-inventor. Litigation may be necessary to defend against these claims.

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, enforceability or priority. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity in favor of the granted third-party patent. This is a high burden, requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim.

An unfavorable outcome in any such proceeding could require us and our current or future licensors, licensees, partners or collaborators to cease using the related intellectual property or developing or commercializing the product or product candidate, or to attempt to license rights to us from the prevailing party, which may not be available on commercially

reasonable terms, or at all. Additionally, 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 pacibekitug or any potential future product candidates or force us to cease some of our business operations, which could materially harm our business.

Reliance on third parties requires us to share our proprietary information, which increases the possibility that such information will be misappropriated or disclosed.

Because we rely on third parties for aspects of development, manufacture, or commercialization of pacibekitug and our technologies, or if we collaborate with third parties for the development or commercialization of our future product candidates and technologies, we must, at times, share proprietary information with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. Despite the contractual provisions employed when working with third parties, the need to share confidential information increases the risk that such information become known by our competitors, is inadvertently incorporated into the technology of others, or is disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how, a competitor's discovery of our know-how or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors, and consultants to publish data potentially relating to our know-how. Despite our efforts to protect our know-how, we may not be able to prevent the unauthorized disclosure or use of our technical know-how by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors, and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third-party illegally obtained and is using our proprietary information, like patent litigation, is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the U.S. are sometimes less willing to protect proprietary information.

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

Filing, prosecuting and defending patents in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S., even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our or our licensors' inventions in all countries outside the U.S., even in jurisdictions where we or our licensors pursue patent protection. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop its own competing products and, further, may export otherwise infringing products to territories where it has patent protection, but enforcement is not as strong as that in the U.S.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies 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.

In Europe, starting from June 1, 2023, European applications have the option, upon grant of a patent, of becoming a Unitary Patent which is subject to the jurisdiction of the Unified Patent Court (the "UPC"). This is a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. It is our initial belief that the UPC, while offering a cheaper streamlined process, has potential disadvantages to patent holders, such as making a single European patent vulnerable in all jurisdictions when challenged in a single jurisdiction.

Risks Related to Our Common Stock

The market price of our common stock is expected to be volatile, and the market price of the common stock may drop.

The market price of our common stock could be subject to significant fluctuations. Some of the factors that may cause the market price of our common stock to fluctuate include:

- results of clinical trials and preclinical studies of our current and future potential product candidates, or those of our competitors or our existing or future collaborators;
- failure to meet or exceed financial and development projections we may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- actions taken by regulatory agencies with respect to our current and future potential product candidates, clinical studies, manufacturing process or sales and marketing terms;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if we issue adverse or misleading opinions regarding our business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions or market conditions in the pharmaceutical and biotechnology sectors;
- sales of securities by us or our securityholders in the future;
- if we fail to raise an adequate amount of capital to fund our operations and continued development of our current and future potential product candidates;
- trading volume of our common stock;
- announcements by competitors of new commercial products, clinical progress or lack thereof, significant contracts, commercial relationships or capital commitments;
- adverse publicity relating to IL-6 inhibitor and IL-6R inhibitor product candidates, including with respect to other such products on the market;
- the introduction of technological innovations or new therapies that compete with the products and services of ours; and
- period-to-period fluctuations in our financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock. In addition, a recession, depression or other sustained adverse market event resulting from fluctuating interest rates, inflation, global geopolitical conflict, or other macroeconomic conditions could materially and adversely affect our business and the value of our common stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against such companies. Furthermore, market volatility may lead to increased shareholder activism if we experience a market valuation that activists

believe is not reflective of our intrinsic value. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on our operating results and financial condition.

Provisions in our charter documents and under Delaware law could make an acquisition of us more difficult and may discourage any takeover attempts stockholders may consider favorable, and may lead to entrenchment of management.

Provisions of our amended and restated certificate of incorporation, as amended, and amended and restated bylaws could delay or prevent changes in control or changes in management without the consent of the board of directors. These provisions will include the following:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board;
- a requirement that no member of our board may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our charter; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial.

We will also be subject to the anti-takeover provisions contained in Section 203 of the DGCL. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Our bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum 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 other employees.

Our bylaws provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to any provisions of the DGCL, our certificate of incorporation or bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. The exclusive forum provision does not apply to actions arising under the Exchange Act. The amended and restated bylaws will also provide that the federal district courts of the U.S will be the exclusive forum for the resolution of any complaint asserting a cause of action under the Securities Act. The provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in the certificate of incorporation and bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially and adversely affect our business, financial condition and results of operations.

We do not anticipate that we will pay any cash dividends in the foreseeable future.

The current expectation is that we will retain our future earnings, if any, to fund the growth of our business as opposed to paying dividends. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 1C. Cybersecurity.

Risk Management and Strategy

We have implemented and maintain various information security processes designed to identify, assess, and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our data, including intellectual property, confidential information that is proprietary, strategic, or competitive in nature, data related to our manufacturing, clinical development and clinical trials, and personal data (collectively, "Information Systems and Data").

The cybersecurity function within the Company, which comprises, in part, our internal information technology ("IT") and legal personnel who work with external service providers (including an external chief information security officer ("CISO") and certain information security vendors) helps identify, assess and manage the Company's cybersecurity threats and risks. Together with, and under the direction of, our Head of IT, our cybersecurity function identifies and assesses risks from cybersecurity threats by monitoring and evaluating our threat environment using various methods. These methods include, for example, manual and automated tools, subscriptions to services that identify cybersecurity threats and actors, evaluations of our and our industry's risk profile, evaluations of threats reported against us, work with third parties who conduct threat assessments, and conducting vulnerability assessments.

Depending on the environment and data, we implement and maintain various technical, physical, and organizational measures, processes, standards, and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: strategies related to incident detection, incident response, disaster recovery and business continuity; assessing security risk and the results of gap assessments conducted by third parties of certain Company systems; encrypting certain data; maintaining certain access and physical security controls; engaging in asset, system, and vendor management; conducting personnel training on cybersecurity risks; and maintaining cybersecurity insurance.

Our assessment and management of material risks from cybersecurity threats are integrated into the Company's overall risk management processes. For example, (1) our Head of IT works with the Chief Business Officer and General Counsel, and other Company management as appropriate to prioritize our risk management processes and mitigate cybersecurity threats that may be more likely to lead to a material impact to our business; and (2) our executive leadership team evaluates material risks from cybersecurity threats against our overall business objectives and reports to the Audit Committee of the Tourmaline Board of Directors, which evaluates our overall enterprise risk.

We use third-party service providers to assist us from time to time to identify, assess, and manage material risks from cybersecurity threats, including for example, our external CISO, professional services firms (including legal counsel), threat intelligence service providers, cybersecurity consultants, cybersecurity software providers, and managed cybersecurity service providers.

We use third-party service providers to perform a variety of functions throughout our business, such as application providers, hosting companies, contract research organizations, contract development and manufacturing organizations, supply chain resources, laboratories, and clinical database and data management providers and consultants. We have vendor security assessment processes such as assessing cybersecurity risks associated with our use of certain vendors for our clinical trials, manufacturing, and related operations. Our vendor risk management processes, depending upon the type of vendor, include conducting vendor risk assessments, submitting security questionnaires, conducting audits, and imposing contractual obligations related to information security and data protection. Depending on the nature of the services provided, the sensitivity of the Information Systems and Data at issue, and the identity of the provider, our vendor management processes involve different levels of assessment designed to help identify cybersecurity risks associated with a provider.

For a description of the risks from cybersecurity threats that may materially affect the Company and how they may do so, see our risk factors under Part 1. Item 1A. Risk Factors in this Annual Report on Form 10-K, including *Risks Related to Government Regulation, Risks Related to Intellectual Property,* and risk factors entitled *"We, our CROs, our CDMOs, service providers, our current and potential future partners or other third parties with whom we work, could experience a*

security incident, system disruption or failure, data loss, cyberattack, or similar event that could compromise our systems and data (or those of the third parties with whom we work), result in material disruptions to our business operations, lead to regulatory investigations or actions, litigation, fines and penalties, affect our reputation, revenue or profits, or otherwise harm our business" and *"We (and the third parties with whom we work) are subject to rapidly changing and increasingly stringent foreign and domestic laws, regulations, and rules, contractual obligations, industry standards, policies and other obligations relating to privacy, data protection and information security. The restrictions imposed by these requirements or our actual or perceived failure to comply with such obligations (or such failure by the third parties with whom we work) could lead to regulatory investigations or actions, litigation (including class claims) and mass arbitration demands, fines and penalties, disruptions of our business operations, reputational harm, loss of revenue or profits, loss of customers or sales, and other adverse business consequences*."

Governance

Our board of directors addresses the Company's cybersecurity risk management as part of its general oversight function. The Audit Committee of the Tourmaline Board of Directors is responsible for overseeing the Company's cybersecurity risk management processes, including oversight of mitigating risks from cybersecurity threats.

Our cybersecurity risk assessment and management processes are implemented and maintained by certain Company management, including our: (1) Chief Business Officer and General Counsel, who reports to the Chief Executive Officer; (2) Head of IT, who reports to the Chief Business Officer and General Counsel; and (3) Assistant General Counsel, who also reports to the Chief Business Officer and General Counsel.

Our Head of IT is responsible for engaging and managing external consultants and vendors related to cybersecurity, hiring appropriate personnel, helping to integrate cybersecurity risk considerations into the Company's overall risk management strategy, developing an information and cybersecurity strategy roadmap, and communicating key priorities to relevant personnel. Our Head of IT works with our Chief Business Officer and General Counsel, along with our Chief Financial Officer and Assistant General Counsel, to prepare appropriate budgets, prepare for cybersecurity incidents, review and approve cybersecurity processes, and review security assessments and other security-related reports. Our Head of IT has over 20 years of experience in IT and information security functions. Our external CISO has over 25 years of experience in IT and information security functions, as well as advanced degrees and certain certificates pertaining to information security.

Our cybersecurity incident response strategy is designed to escalate certain cybersecurity incidents to members of management depending on the circumstances, including Head of IT and/or Chief Business Officer and General Counsel. Our Head of IT works with our external CISO, managed risk detection and response vendors, the Company's legal team and external counsel, and other third-party consultants and vendors to help the Company mitigate and remediate cybersecurity incidents of which they are notified. In addition, the Company's incident response strategy includes reporting to the Audit Committee of the Board of Directors for certain cybersecurity incidents.

The Audit Committee receives reports from, as appropriate depending upon given circumstances, the Head of IT, the Chief Business Officer and General Counsel, or their designees concerning the Company's significant cybersecurity threats and risk and the processes the Company has implemented to address them. The Audit Committee also has access to various reports, summaries or presentations related to cybersecurity threats, risk and mitigation.

Item 2. Properties.

We lease approximately 3,274 square feet of office space at 27 West 24th Street, Suite 702, New York, New York, 10010, which serves as our corporate headquarters. The lease expires on February 28, 2026. We believe that our current facilities are adequate to meet our ongoing needs, and that, if we require additional space, we will be able to obtain additional facilities on commercially reasonable terms.

Item 3. Legal Proceedings.

From time to time, we may become involved in legal proceedings arising from the ordinary course of business. For additional information regarding legal proceedings, see Note 13 "Commitments and Contingencies—Litigation" to our audited financial statements included elsewhere in this Report. We believe there are currently no pending legal proceedings to which we or our property are subject that could have a material adverse effect on our financial position, results of operations 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.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently 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 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. Our future ability to pay cash dividends on our capital stock may also be limited by the terms of any future debt or preferred securities or future credit facility.

Stockholders

Our common stock is listed on The Nasdaq Global Select Market under the symbol "TRML". As of March 7, 2025, there were 27 stockholders of record of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Recent Sales of Unregistered Securities

Not applicable.

Purchases of Equity Securities by the Issuer and Affiliated Parties

The following table provides information about purchases we made during the three months ended December 31, 2024 of equity securities that are registered by us pursuant to Section 12 of the Exchange Act:

Period	Total Number of Shares Purchased[1]	Average Price Paid Per Share	Shares Purchased as Part of Publicly Announced Plans or Programs[2]	Approximate Dollar Value of Shares That May Yet be Purchased Under the Plans or Programs
October 1 through October 31, 2024	—	$ —	—	$ —
November 1 through November 30, 2024	26,051	$ 0.13	—	—
December 1 through December 31, 2024	—	$ —	—	—
Three Months Ended December 31, 2024	26,051	$ 0.13	—	$ —

(1) We repurchased 26,051 shares of common stock from a former employee, originally issued upon the early exercise of stock options, which were unvested as of the employee's separation date. This repurchase was made at the original exercise price.

(2) We did not have a repurchase program in place during the three months ended December 31, 2024.

Item 6. Reserved.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and other financial information included elsewhere in this Report. Some of the information contained in this discussion and analysis or set forth elsewhere in this Report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" section of this Report for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

In this section, we discuss our financial condition, changes in financial condition and results of our operations for the year ended December 31, 2024 compared to the year ended December 31, 2023. For a discussion and analysis comparing our results for the year ended December 31, 2023 to the year ended December 31, 2022, please refer to Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the year ended December 31, 2023. References to "we", "our" and "the Company" refer to Legacy Tourmaline for periods prior to the closing of the Reverse Merger, and to Tourmaline Bio, Inc. (formerly Talaris Therapeutics, Inc.) for all other periods, as the context requires.

Overview

We are a late-stage clinical biotechnology company focused on developing transformative medicines that dramatically improve the lives of patients with life-altering immune and inflammatory diseases. In doing so, we seek to identify and develop medicines that have the potential to establish new standards-of-care in areas of high unmet medical need.

Our initial product candidate is pacibekitug (also known as TOUR006), a fully human monoclonal antibody that selectively binds to interleukin-6 ("IL-6"), a key proinflammatory cytokine involved in the pathogenesis of many autoimmune and inflammatory disorders. The anti-IL-6 and anti-IL-6 receptor ("IL-6R") antibody class ("IL-6 class") has over two decades of clinical and commercial experience treating over a million patients with a variety of autoimmune and inflammatory diseases. To date, four anti-IL-6 or anti-IL-6R antibodies have been approved in the United States ("U.S."). These four anti-IL-6 or anti-IL-6R antibodies together generated more than $3.5 billion in global sales in 2024.

Pacibekitug is a long-acting anti-IL-6 antibody which we believe has best-in-class properties including a high binding affinity to IL-6, long half-life, and low observed immunogenicity. These characteristics may allow pacibekitug to achieve substantial IL-6 pathway suppression with relatively low amounts of drug exposure, potentially enabling delivery in a convenient, low volume, infrequently administered, subcutaneous injection.

We are pursuing two strategic paths for pacibekitug, the first of which is cardiovascular inflammation. We believe pacibekitug has the potential to transform the standard of care for patients living with high risk of cardiovascular disease by targeting key inflammatory pathways driving cardiovascular disease. Atherosclerotic cardiovascular disease ("ASCVD") is a leading cause of death globally. Preventing major adverse cardiovascular events ("MACE"), such as death, nonfatal myocardial infarction or nonfatal stroke, has the potential to significantly reduce global cardiovascular disease burden. IL-6 has been identified as a promising drug target for addressing the risk of MACE in ASCVD, and multiple external Phase 3 cardiovascular outcome trials investigating IL-6 blockade are ongoing. We believe that pacibekitug potentially offers a meaningfully enhanced product profile to these competitor programs with a potential for subcutaneous dosing once every three months.

As previously announced in January 2024, we have reached alignment with the U.S. Food and Drug Administration ("FDA") on our ASCVD clinical development program, including our Phase 2 TRANQUILITY trial evaluating the reduction of high sensitivity C-reactive protein ("hs-CRP"), a validated biomarker for inflammation, with quarterly and monthly dosing of pacibekitug in patients with elevated hs-CRP and chronic kidney disease. In March 2024, the FDA cleared our Investigational New Drug application ("IND") related to our ASCVD clinical development program. The Phase 2 TRANQUILITY trial commenced in April 2024 and completed over-enrollment in December 2024. We expect to report topline data in the second quarter of 2025. Pending successful completion of the study, we expect that positive results from the Phase 2 TRANQUILITY trial will position pacibekitug to be Phase 3-ready for ASCVD.

Additionally we have nominated abdominal aortic aneurysm ("AAA") as an additional indication within our cardiovascular inflammation disease focus. We expect to provide additional details on a planned Phase 2 proof-of-concept trial in AAA after topline results from the Phase 2 TRANQUILITY trial are reported in the second quarter of 2025.

Our second strategic path is thyroid eye disease ("TED"). TED is an autoimmune disease characterized by autoantibody-mediated activation of the tissues surrounding the eye, causing inflammation and disfigurement which can be sight-threatening in severe cases. We have identified a substantial body of published clinical observations characterizing the beneficial off-label use of currently marketed IL-6 pathway inhibitors, namely Actemra® (tocilizumab), an anti-IL-6R monoclonal antibody, in reducing inflammation, eye-bulging, and levels of autoantibodies in patients with TED. However, no formal, industry-sponsored development effort studying the IL-6 class for the treatment of TED has been completed to date. We are currently evaluating pacibekitug in a pivotal Phase 2b trial in first-line TED, which we refer to as the spiriTED trial. We initiated the spiriTED trial in September 2023 and expect to report topline data in the second half of 2025.

We continue to identify additional indication opportunities for pacibekitug and evaluate new in-licensing and acquisition opportunities for assets that we believe have standard-of-care changing potential for patients with immune and inflammatory diseases.

Since our inception, we have funded our operations primarily through the sale of convertible preferred stock, the Reverse Merger and Pre-Merger Financing Transaction, each as defined and outlined further below, and the January 2024 Offering as defined and described below. As of December 31, 2024, we had total cash, cash equivalents and investments of $294.9 million.

Due to our significant research and development expenditures, we have accumulated substantial losses since our inception, including net losses of $73.2 million and $42.1 million for the years ended December 31, 2024 and 2023, respectively. In addition, we had an accumulated deficit of $135.3 million as of December 31, 2024. We expect to incur additional losses in the future as we expand our research and development activities.

Recent Developments

November 2024 ATM Sales Agreement

In November 2024, we entered into a Sales Agreement (the "ATM Sales Agreement") with Leerink Partners LLC ("Leerink"), as sales agent, under which we may offer and sell, from time to time, shares of our common stock (the "ATM Shares"), through Leerink (the "ATM Offering"). In November 2024, we filed a registration statement on Form S-3 (the "Shelf Registration Statement"), including a base prospectus and sales agreement prospectus, with the Securities and Exchange Commission (the "SEC"), for the issuance and sale of up to $100.0 million of shares of our common stock under the ATM Sales Agreement. Under the ATM Sales Agreement, Leerink may sell the ATM Shares by methods deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Exchange Act of 1934, as amended. We may sell the ATM Shares in amounts and at times to be determined by us from time to time subject to the terms and conditions of the ATM Sales Agreement, but we have no obligation to sell any of the ATM Shares in the ATM Offering.

As of December 31, 2024, we have not sold any shares of our common stock pursuant to the ATM Offering. We may offer and sell ATM shares at an aggregate offering price of up to the remaining $100.0 million available under the ATM Offering.

January 2024 Equity Offering

On January 25, 2024, we entered into an underwriting agreement with Jefferies LLC, Piper Sandler & Co., Guggenheim Securities, LLC and Truist Securities, Inc. (collectively, the "Underwriters") relating to the public offering of 4,615,384 shares of our common stock at a public offering price of $32.50 per share (the "January 2024 Offering"). We granted the Underwriters a 30-day option to purchase up to 692,307 shares of common stock at the public offering price, less underwriting discounts and commissions, which was exercised by the Underwriters in full on January 25, 2024. The January 2024 Offering closed on January 29, 2024, and we issued and sold a total of 5,307,691 shares of common stock to the Underwriters for net proceeds of $161.4 million after deducting underwriting discounts and offering costs.

Reverse Merger with Talaris and Pre-Merger Financing Transaction

On June 22, 2023, privately-held Tourmaline Sub, Inc. (formerly Tourmaline Bio, Inc., "Legacy Tourmaline") entered into an Agreement and Plan of Merger (the "Merger Agreement") with Talaris Therapeutics, Inc. ("Talaris"), a publicly traded company, and Terrain Merger Sub, Inc., a direct, wholly owned subsidiary of Talaris ("Merger Sub"). On October 19,

2023, Legacy Tourmaline completed the merger with Talaris in accordance with the terms of the Merger Agreement, pursuant to which, among other matters, Merger Sub merged with and into Legacy Tourmaline, with Legacy Tourmaline surviving as a wholly owned subsidiary of Talaris (such transaction, the "Reverse Merger"). The Reverse Merger was intended to qualify for federal income tax purposes as a tax-free reorganization under the provisions of Section 368(a) of the Internal Revenue Code of 1986, as amended.

Immediately prior to the effective time of the Reverse Merger, Talaris effected a 1-for-10 reverse stock split of its common stock (the "Reverse Stock Split").

Pursuant to the terms of the Merger Agreement, immediately prior to the effective time of the Reverse Merger, each share of Legacy Tourmaline's Series A convertible preferred stock was converted into a share of Legacy Tourmaline common stock. At the effective time of the Reverse Merger, Talaris issued an aggregate of approximately 15,877,090 shares of common stock to Legacy Tourmaline's stockholders, based on an exchange ratio of 0.07977 shares of common stock for each share of Legacy Tourmaline's capital stock, including those shares of Legacy Tourmaline's common stock issued upon the conversion of the Series A convertible preferred stock and those shares of Legacy Tourmaline's common stock issued in the Pre-Merger Financing Transaction (as described below), resulting in approximately 20,336,741 shares of common stock of the combined company being issued and outstanding immediately following the effective time of the Reverse Merger. In connection with the Reverse Merger, the Amended and Restated Investor Rights Agreement, dated May 2, 2023, between Tourmaline and certain of its stockholders and the Amended and Restated Investors' Rights Agreement, dated September 22, 2020, between Talaris and certain of its stockholders, were terminated.

Immediately prior to the completion of the Reverse Merger, pursuant to a securities purchase agreement, Legacy Tourmaline issued 4,092,035 shares (as effected by the exchange ratio described above) of Legacy Tourmaline's common stock in a private placement for gross proceeds of $75.0 million (the "Pre-Merger Financing Transaction").

In connection with the completion of the Reverse Merger, Talaris changed its name from "Talaris Therapeutics, Inc." to "Tourmaline Bio, Inc.," Legacy Tourmaline changed its name to "Tourmaline Sub, Inc.," and we began conducting the business conducted by Legacy Tourmaline. On June 30, 2024, Tourmaline Sub, Inc. was merged with and into Tourmaline Bio, Inc., with Tourmaline Bio, Inc. as the surviving entity.

License Agreements

Pfizer License Agreement

On May 3, 2022, we entered into a License Agreement (the "Pfizer License Agreement") with Pfizer Inc. ("Pfizer"), pursuant to which we obtained an exclusive, sublicensable, royalty-bearing, worldwide right to use and license under certain know-how for the development, commercialization and manufacture of PF-04236921 (now known as pacibekitug) and any pharmaceutical or biopharmaceutical product incorporating such compound for the treatment, diagnosis, or prevention of any and all diseases, disorders, illnesses and conditions in humans and animals. In consideration for the license and other rights we received under the Pfizer License Agreement, we paid Pfizer an upfront payment of $5.0 million and granted Pfizer 7,125,000 Series A preferred units of Tourmaline Bio, LLC, the predecessor of Legacy Tourmaline (which subsequently converted to 7,125,000 shares of our Series A preferred stock) at $1.00 per share for aggregate consideration of approximately $7.1 million, with such shares representing 15% of all of our capital stock on a fully-diluted basis at the time of issuance.

As additional consideration for the license, we are obligated to pay Pfizer up to $128.0 million upon the achievement of specific development and regulatory milestones. We are also obligated to pay Pfizer up to $525.0 million upon the first achievement of specific sales milestones. We are obligated to pay Pfizer a marginal royalty rate in the low double digits (less than 15%), subject to specified royalty reductions. The royalty term, on a Product-by-Product and country-by-country basis, begins on the first commercial sale of such Product and expires upon the later of twelve years following the date of the first commercial sale or the expiration of regulatory exclusivity protecting such Product. In the event we complete a Significant Transaction (as defined in the Pfizer License Agreement), we will be obligated to pay Pfizer a one-time payment in the low-eight digits (up to $20.0 million); the amount of such payment is based on the timing of the transaction.

The Pfizer License Agreement originally contained an anti-dilution provision that allowed Pfizer to maintain a 15% interest in us on a fully-diluted basis unless and until certain thresholds are met, whereupon the anti-dilution provision would no longer apply. Upon consummation of a Series A convertible preferred stock financing (the "Series A Extension") on May 4, 2023, we issued 8,823,529 shares of our Series A convertible preferred stock to Pfizer pursuant to this anti-dilution

provision. Subsequent to the issuance of these additional shares of Series A convertible preferred stock, the anti-dilution provision is no longer in force and effect. Such shares of Series A convertible preferred stock were converted into 1,272,214 aggregate shares of our common stock upon consummation of the Reverse Merger outlined above.

The Pfizer License Agreement expires, unless earlier terminated, upon the last to expire royalty term, and at such time our license will become fully paid-up, irrevocable and perpetual. Each party has the right to terminate the Pfizer License Agreement in its entirety in the event of a material breach if the breaching party fails to cure such breach within a specified cure period after written notice. Pfizer may terminate the Pfizer License Agreement on a Product-by-Product and country-by-country basis if we have materially breached our diligence obligations. Each party has the right to terminate the Pfizer License Agreement in the event of a bankruptcy event. We have the right to terminate the Pfizer License Agreement at our convenience in its entirety or on a country-by-country basis (except with respect to the major market countries identified therein) upon a specified notice period based on the time of the termination.

As of December 31, 2024, we do not owe any amounts under the Pfizer License Agreement and no royalties or milestone payments have been paid to date under the Pfizer License Agreement.

Lonza License Agreement

In May 2022, we entered into the Lonza License Agreement with Lonza Sales AG ("Lonza"), pursuant to which we obtained a worldwide, non-exclusive, sublicensable (subject to certain conditions) license under certain know-how to market, sell, offer for sale, distribute, import and export products containing pacibekitug ("Product"). We also obtained a non-exclusive, sublicensable (subject to certain conditions) license under certain licensed know-how to use, develop, and manufacture (including have manufactured in accordance with the terms of the Lonza License Agreement) the Product at premises approved by Lonza.

In consideration for the licenses and other rights we received under the Lonza License Agreement, we are obligated to pay Lonza a royalty in the low-single digits on the Net Sales (as defined in the Lonza License Agreement) of Product, and the royalty rate shall be based on the entity manufacturing the drug substance contained in the Product. Royalties are payable on a Product-by-Product basis and a country-by-country basis for ten years following the first commercial sale of a Product in a certain country. In addition, we may owe Lonza a low six figure annual fee following the occurrence of a specified event depending on which entity manufactures the drug substance, all as specified in the Lonza License Agreement.

The Lonza License Agreement shall continue in full force and effect unless terminated in accordance with the terms of the Lonza License Agreement. Each party shall have the right to terminate the Lonza License Agreement in its entirety in the event of a breach by the other party if the breach is irremediable or the breaching party fails to cure such breach within a specified cure period after written notice. Each party shall have the right to terminate the Lonza License Agreement in the event of a bankruptcy event of the other party. We shall have the right to terminate the Lonza License Agreement at its convenience upon a specified notice period. Lonza shall have the right to terminate the Lonza License Agreement in the event of a change of control of our company or we contest the secret or substantial nature of the licensed know-how.

As of December 31, 2024, we do not owe any amounts under the Lonza License Agreement, and no royalty payments or other fees have been paid to date under the Lonza License Agreement.

Macroeconomic Considerations

Worldwide economic conditions remain uncertain and we continue to monitor the impact of macroeconomic conditions, including those related to global health crises, global geopolitical conflicts such as the war in Ukraine and hostilities in the Middle East and fluctuating inflation rates. The effect of macroeconomic conditions may not be fully reflected in our results of operations until future periods. If, however, economic uncertainty increases or the global economy worsens, our business, financial condition and results of operations may be harmed.

Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may experience increases in the near future on our operating costs, including our labor costs and research and development costs, due to supply chain constraints, consequences associated with global geopolitical conflicts, and employee availability and wage increases, which may result in additional stress on our working capital resources.

Financial Operations Overview

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the near future, if at all. If our development efforts are successful and result in commercialization of pacibekitug or any future product candidates or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from product sales, payments from such collaboration or license agreements or a combination thereof.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs related to our clinical trials, costs related to manufacturing material for clinical and preclinical studies, and other costs incurred for the development of our product candidate, pacibekitug. Research and development expenses include:

- personnel-related costs, including salaries, bonuses, benefits and stock-based compensation expenses for employees engaged in research and development functions;

- payments to third parties in connection with the research and development of pacibekitug and any future product candidates, including agreements with third parties such as contract research organizations ("CROs"), clinical trial sites and consultants;

- the cost of manufacturing products for use in our clinical and preclinical studies, including payments to contract development and manufacturing organizations ("CDMOs") and consultants; and

- payments to third parties in connection with the preclinical development of pacibekitug and any future product candidates, including for outsourced professional scientific development services, consulting research and collaborative research.

Research and development expenses also include the cost of in-process research and development ("IPR&D") assets purchased in asset acquisition transactions. IPR&D assets are expensed as incurred if the asset has not yet received regulatory approval and does not have an alternative future use. Acquired IPR&D payments are immediately expensed in the period in which they are incurred and have historically included upfront payments as well as shares of our capital stock. Research and development costs incurred after the acquisition of IPR&D assets are expensed as incurred.

We recognize research and development expenses in the periods in which they are incurred. Our internal resources, employees and infrastructure are not directly tied to any one research or drug discovery program and are typically deployed across multiple programs. External expenses are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our service providers or our estimate of the level of service that has been performed at each reporting date. We utilize CROs for research and development activities and CDMOs for manufacturing activities and we do not have our own laboratory or manufacturing facilities. Therefore, we have no material facilities expenses attributed to research and development.

Product candidates in later stages of development generally have higher development costs than those in earlier stages. As a result, management expects that our research and development expenses will increase substantially over the next several years as we advance our product candidate, pacibekitug, and any future product candidates into larger and later-stage clinical trials, work to discover and develop additional product candidates, seek to expand, maintain, protect and enforce our intellectual property portfolio, and hire additional research and development personnel.

The successful development of pacibekitug and any future product candidates is highly uncertain, and management does not believe it is possible at this time to accurately project the nature, timing and estimated costs of the efforts necessary to complete the development of, and obtain regulatory approval for, pacibekitug and any future product candidates. To the extent pacibekitug and any future product candidates continue to advance into larger and later-stage clinical trials, our expenses will increase substantially and may become more variable. The duration, costs and timing of development of

pacibekitug and any future product candidates are subject to numerous uncertainties and will depend on a variety of factors, including:

- per patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to activate clinical sites and recruit, screen, and enroll eligible patients;
- the number of patients that participate in the trials;
- the length of hospitalization of patients in clinical trials;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing pacibekitug and any future product candidates;
- the phase of development of pacibekitug and any future product candidates;
- the efficacy and safety profile of pacibekitug and any future product candidates;
- the timing and progress of nonclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- raising necessary additional funds;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current development program and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of drug substance and drug product for use in production of pacibekitug and any future product candidates;
- the development of commercial scale manufacturing and distribution processes for pacibekitug and any future product candidates;
- establishing and maintaining agreements with third-party manufacturers for commercial manufacturing, if we pursue a third party manufacturing strategy outside of the U.S, and if pacibekitug and any future product candidates are approved;
- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the U.S and internationally;

- our ability to protect our rights in our intellectual property portfolio;
- our ability to successfully recruit and retain employees;
- the commercialization of pacibekitug and any future product candidates, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of pacibekitug and any future product candidates, if approved, by patients, the medical community and third-party payors;
- evolving standards of care in target indications;
- competition with other marketed or development-stage products; and
- a continued acceptable safety profile of our therapies following approval, if and when approved.

A change in the outcome of any of these variables with respect to the development of pacibekitug or any future product candidates could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for our product candidate or any future product candidates.

General and Administrative Expenses

General and administrative expenses primarily consist of salaries, bonuses, benefits, and stock-based compensation expense for personnel in operational, finance, and administrative functions; professional fees for legal, consulting, accounting, and audit services; recruiting costs; travel expenses; technology costs; and insurance premiums. General and administrative expenses also include corporate facility costs, including rent, utilities, depreciation, and maintenance. We recognize general and administrative expenses in the periods in which they are incurred.

We expect that our general and administrative expenses will increase in the future to support our continued research and development activities, pre-commercial preparation activities for our product candidate and any future product candidates and, if any product candidate receives marketing approval, commercialization activities. Going forward, we expect to continue to incur expenses associated with being a public company, including expenses related to accounting, audit, legal, public company reporting and compliance, director and officer insurance, investor and public relations, and other administrative and professional services.

Other Income, Net

Other income, net is primarily comprised of interest and investment income on our cash equivalents and investments.

Results of Operations

Comparison of Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for years ended December 31, 2024 and 2023:

	Year Ended December 31,		
(in thousands)	**2024**	**2023**	**$ Change**
Operating expenses:			
Research and development	$ 66,985	$ 32,368	$ 34,617
General and administrative	22,747	13,041	9,706
Total operating expenses	89,732	45,409	44,323
Loss from operations	(89,732)	(45,409)	(44,323)
Other income, net	16,522	3,285	13,237
Net loss	$ (73,210)	$ (42,124)	$ (31,086)

Research and Development Expenses

Research and development expenses increased by $34.6 million from $32.4 million for the year ended December 31, 2023 to $67.0 million for the year ended December 31, 2024. The increase in research and development expenses was primarily attributable to the following:

- $10.9 million of increased payroll-related costs, including $0.3 million of increased stock-based compensation expense, attributable to an increase in headcount;
- $18.1 million of increased clinical trial expenses related to our TRANQUILITY and spiriTED trials;
- $7.7 million of increased chemistry, manufacturing, and controls costs associated with the production of drug substance and drug product for use in our clinical trials;
- $2.5 million of increased medical affairs expenses;
- $2.1 million of increased research and development consulting expenses;
- $1.5 million of increased toxicology expenses; and
- $0.7 million of increased other operating expenses, including information technology ("IT") expenses and facilities expenses.

We recognized $8.8 million of non-cash research and development expense during the year ended December 31, 2023 related to the issuance of additional shares to Pfizer under the anti-dilution provision outlined above; no such research and development expense was recognized during the year ended December 31, 2024.

General and Administrative Expenses

General and administrative expenses increased by $9.7 million from $13.0 million for the year ended December 31, 2023 to $22.7 million for the year ended December 31, 2024. The increase in general and administrative expenses was primarily attributable to the following:

- $4.3 million of increased payroll-related costs, including $0.5 million of increased stock-based compensation expense, attributable to an increase in headcount;
- $2.4 million of increased consulting expenses, including recruiting, commercial planning and other services;
- $1.1 million of increased other operating expenses, including costs associated with being a public company and employee business expenses;
- $1.1 million of increased insurance expenses; and
- $0.9 million of increased IT expenses.

Other Income, Net

Other income, net increased by $13.2 million from $3.3 million for the year ended December 31, 2023 to $16.5 million for the year ended December 31, 2024. The increase in other income, net was primarily attributable to a $7.7 million increase in investment income and a $5.6 million increase in interest income.

Liquidity and Capital Resources

Sources of Liquidity

Since inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our product candidate and any future product candidates. We

expect that our research and development and general and administrative costs will continue to increase significantly, including in connection with conducting clinical trials and potentially manufacturing for our product candidate and any future product candidates to support commercialization and providing general and administrative support for our operations, including the cost associated with operating as a public company. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements or other sources.

Since our inception, we have funded our operations primarily with outside capital, including proceeds from the sale of Series A convertible preferred stock, the Pre-Merger Financing Transaction and the January 2024 Offering, having raised aggregate gross proceeds of approximately $359.7 million as of the date hereof. However, we have incurred significant recurring losses, including net losses of $73.2 million and $42.1 million for the years ended December 31, 2024 and 2023, respectively. In addition, we have an accumulated deficit of $135.3 million as of December 31, 2024.

As of December 31, 2024, we had $294.9 million in cash, cash equivalents and investments. Based upon our current operating plan, we believe that our working capital will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2027. We have based this estimate on assumptions that may prove to be incorrect, and we may use all of our available capital resources sooner than we expect.

Future Capital Requirements

Since inception, we have not generated any revenue from product sales. Management does not expect to generate any meaningful product revenue unless and until we obtain regulatory approval of and commercialize our product candidate and any future product candidates, and management does not know when, or if, that will occur. Until we can generate significant revenue from product sales, if ever, we will continue to require substantial additional capital to develop our product candidate and any future product candidates and fund operations for the foreseeable future. Management expects our expenses to increase in connection with our ongoing activities as described in greater detail below. We are subject to all the risks incident in the development of new biopharmaceutical products, and we may encounter unforeseen expenses, difficulties, complications, delays, and other unknown factors that may harm our business.

In order to complete the development of pacibekitug and any future product candidates and to build the sales, marketing and distribution infrastructure that management believes will be necessary to commercialize product candidates, if approved, we will require substantial additional capital. Accordingly, until such time that we can generate a sufficient amount of revenue from product sales or other sources, if ever, management expects to seek to raise any necessary additional capital through private or public equity or debt financings, loans or other capital sources, which could include income from collaborations, partnerships or other marketing, distribution, licensing or other strategic arrangements with third parties, or from grants. To the extent that we raise additional capital through equity financings or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, including restricting our operations and limiting our ability to incur liens, issue additional debt, pay dividends, repurchase our own common stock, make certain investments or engage in merger, consolidation, licensing, or asset sale transactions. If we raise capital through collaborations, partnerships, and other similar arrangements with third parties, we may be required to grant rights to develop and market product candidates that we would otherwise prefer to develop and market themselves. We may be unable to raise additional capital from these sources on favorable terms, or at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the U.S and worldwide resulting from recent bank failures, other general macroeconomic conditions and otherwise. The failure to obtain sufficient capital on acceptable terms when needed could have a material adverse effect on our business, results of operations or financial condition, including requiring us to delay, reduce or curtail our research, product development or future commercialization efforts. We may also be required to license rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. Management cannot provide assurance that we will ever generate positive cash flow from operating activities.

Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount and timing of our capital requirements. Our future funding requirements will depend on many factors, including:

- the scope, timing, progress, results, and costs of researching and developing pacibekitug, and conducting larger and later-stage clinical trials;
- the scope, timing, progress, results, and costs of researching and developing other product candidates that we may pursue;
- the costs, timing, and outcome of regulatory review of pacibekitug and any future product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for pacibekitug and any future product candidates for which we receive marketing approval;
- the costs of manufacturing commercial-grade products and sufficient inventory to support commercial launch;
- the revenue, if any, received from commercial sale of our products, should any of our product candidate and any future product candidates receive marketing approval;
- the cost and timing of attracting, hiring, and retaining skilled personnel to support our operations and continued growth;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish, maintain, and derive value from collaborations, partnerships or other marketing, distribution, licensing, or other strategic arrangements with third parties on favorable terms, if at all;
- the extent to which the profile of marketed or development stage competing products affects the clinical and commercial potential of our products;
- the extent to which we acquire or in-licenses other product candidates and technologies, if any; and
- the costs associated with operating as a public company.

A change in the outcome of any of these or other factors with respect to the development of pacibekitug and any of our future product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we may need additional capital to meet the capital requirements associated with such operating plans.

As described above, if we progress pacibekitug through clinical development and, if approved, commercialize it, we may be required to pay Pfizer up to $128.0 million upon the achievement of specific development and regulatory milestones and up to $525.0 million upon the first achievement of specific sales milestones. Upon commercialization, we would also be obligated to pay Pfizer and Lonza royalties on product sales, as outlined in more detail above.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2024 and 2023:

	Year Ended December 31,	
(in thousands)	**2024**	**2023**
Net cash (used in) provided by:		
Operating activities	$ (77,263)	$ (28,081)
Investing activities	(194,305)	3,840
Financing activities	161,348	156,720
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (110,220)	$ 132,479

Cash Used in Operating Activities

Net cash used in operating activities for the year ended December 31, 2024 was $77.3 million, compared to net cash used in operating activities of $28.1 million for the year ended December 31, 2023. Net cash used in operating activities increased by $49.2 million primarily due to the overall growth in our operations, including headcount.

Cash (Used in) Provided by Investing Activities

Net cash used in investing activities for the year ended December 31, 2024 was $194.3 million, compared to net cash provided by investing activities of $3.8 million for the year ended December 31, 2023. This net change of $198.1 million was primarily due to net purchases of investments in excess of maturities during the year ended December 31, 2024.

Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2024 was $161.3 million, compared to net cash provided by financing activities of $156.7 million for the year ended December 31, 2023. Net cash provided by financing activities during the year ended December 31, 2024 was primarily comprised of net proceeds received from the January 2024 Offering whereas net cash provided by financing activities during the year ended December 31, 2023 was primarily comprised of net proceeds from the Series A Extension financing and the Pre-Merger Financing Transaction.

Contractual Obligations and Commitments

Research and Development and Manufacturing Agreements

We enter into agreements with certain vendors for the provision of goods and services, which includes manufacturing services with CDMOs and development and clinical trial services with CROs. These agreements may include certain provisions for purchase obligations and termination obligations that could require payments for the cancellation of committed purchase obligations or for early termination of the agreements. The amount of the cancellation or termination payments vary and are based on the timing of the cancellation or termination and the specific terms of the agreement. These obligations and commitments are not separately presented.

Pfizer License Agreement

In May 2022, we entered into the Pfizer License Agreement. We have not included milestone or royalty payments or other contractual payment obligations under the Pfizer License Agreement as the timing and amount of such obligations are unknown or uncertain and are contingent upon the initiation and successful completion of future activities. See "*—License Agreements—Pfizer License Agreement*" included above for further details on the Pfizer License Agreement.

Critical Accounting Policies and Critical Accounting Estimates

Our financial statements are prepared in accordance with U.S. generally accepted accounting principles. The preparation of the financial statements and related disclosures requires management to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that management believes are reasonable under the circumstances, the results of which form the basis for making

judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Management evaluates estimates and assumptions on a periodic basis. Our actual results may differ from these estimates.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Research and Development Expenses

Expenditures relating to research and development are expensed as incurred. Research and development expenses include external expenses incurred under arrangements with third parties; consulting costs; salaries and personnel-related costs, including non-cash stock-based compensation expense; license fees to acquire in-process research and development that does not have an alternative future use and other expenses. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made. Where contingent milestone payments are due to third parties under research and development or license agreements, the milestone payment obligations are expensed when the related milestone events are achieved.

As part of the process of preparing the consolidated financial statements, we are required to estimate our accrued research and development expenses as of each balance sheet date. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. This process involves reviewing open contracts, communicating with internal 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 the actual cost. We periodically confirm the accuracy of our estimates with our service providers and make adjustments if necessary. The majority of our service providers invoice monthly in arrears for services performed or when contractual milestones are met. The financial terms of agreements with these service providers are subject to negotiation, vary from contract-to-contract and may result in uneven payment flows. In circumstances where amounts have been paid in excess of costs incurred, we record a prepaid expense.

Stock-Based Compensation

We account for stock-based payments in accordance with ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). This guidance requires all stock-based payments, including grants of stock options and restricted common units, to be recognized as expense in the consolidated statements of operations and comprehensive loss based on their grant date fair values. For stock options granted to employees, non-employees and members of our Board of Directors for their services on the Board of Directors, we estimate the grant date fair value of each stock option using the Black-Scholes option-pricing model. For stock-based payments subject to service-based vesting conditions, we recognize stock-based compensation expense equal to the grant date fair value of stock-based payment on a straight-line basis over the requisite service period.

Prior to being publicly-traded, we estimated the grant date fair value of our common stock using an appropriate valuation methodology, in accordance with the framework of the American Institute of Certified Public Accountants' Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*. Each valuation methodology included estimates and assumptions that required our judgment. These estimates and assumptions included a number of objective and subjective factors, including external market conditions, guideline public company information, the prices at which we sold convertible preferred stock to third parties in arms' length transactions, the rights and preferences of securities senior to our common stock at the time and the likelihood of achieving a liquidity event such as an initial public offering or sale. Significant changes to the assumptions used in the valuations could result in different fair values at each valuation date.

In addition to the grant date fair value of our common stock, the Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the calculation of expected term of the stock-based payment, (ii) the risk-free interest rate, (iii) the expected stock price volatility and (iv) the expected dividend yield. We use the simplified method as prescribed by SEC Staff Accounting Bulletin No. 107 to calculate the expected term for stock options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. We determine the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. Because we have only been publicly-traded for a short period of time, there is a lack of company-specific historical and implied volatility data. Accordingly, we base our estimates of expected volatility on the historical volatility of a group of publicly-traded companies with similar characteristics to ourself, including stage of

product development and therapeutic focus within the life sciences industry. Historical volatility is calculated over a period of time commensurate with the expected term of the stock-based payment. We use an assumed dividend yield of zero as we have never paid dividends on our common stock, nor do we expect to pay dividends on our common stock in the foreseeable future.

We account for forfeitures of all stock-based payments when such forfeitures occur.

Recently Adopted Accounting Pronouncements

In November 2023, the FASB issued Accounting Standards Update ("ASU") 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures. This guidance is intended to improve reportable segment disclosure requirements through enhanced disclosures as well as clarify that entities with a single reportable segment are subject to new and existing segment reporting requirements. This guidance is effective for annual periods in fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. Entities must apply this guidance on a retrospective basis. Accordingly, we adopted this new standard for the fiscal year ended December 31, 2024. The adoption of ASU 2023-07 resulted in the inclusion of disclosures in Note 17 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Recent Accounting Pronouncements - Yet to be Adopted

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*. The amendments in ASU 2023-09 address investor requests for enhanced income tax information primarily through changes to disclosure regarding rate reconciliation and income taxes paid both in the United States and in foreign jurisdictions. This guidance is effective for fiscal years beginning after December 15, 2024 on a prospective basis, with the option to apply the standard retrospectively, and early adoption is permitted. We are currently evaluating this guidance to determine the impact it may have on our consolidated financial statements.

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*. The amendments in ASU 2024-03 address investor requests for more detailed expense information and require additional disaggregated disclosures in the notes to financial statements for certain categories of expenses that are included on the face of the income statement. This guidance is effective for fiscal years beginning after December 15, 2026, and interim periods within fiscal years beginning after December 15, 2027, with early adoption permitted. We are currently evaluating this guidance to determine the impact it may have on our consolidated financial statements.

Emerging Growth Company and Smaller Reporting Company Status

In April 2012, the Jumpstart Our Business Startups Act of 2012 ("JOBS Act") was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" ("EGC") can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended ("Securities Act"), for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to use the extended transition period for new or revised accounting standards during the period in which we remain an emerging growth company; however, it may adopt certain new or revised accounting standards early to the extent allowed by the standard.

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) the last day of the fiscal year ending after the fifth anniversary of our initial public offering.

We are also a "smaller reporting company" meaning that the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue was less than $100.0 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 $250.0 million or (ii) our annual revenue was less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 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.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

We are a smaller reporting company as defined by Item 10 of Regulation S-K and are not required to provide the information otherwise required under this item.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Report. An index of those financial statements is found in Item 15, Exhibits and Financial Statement Schedules, of this Report.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation and supervision of our Chief Executive Officer and our Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2024, the end of the period covered by this Report. Disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) are designed to provide reasonable assurance that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to a company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Based on their evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of December 31, 2024.

Remediation of Previously-Identified Material Weaknesses

As previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2023 and as discussed in subsequent filings, we identified material weaknesses in the design and operating effectiveness of our internal control over financial reporting. Through implementation of our remediation plan, we have addressed the previously-identified material weaknesses as follows:

- By hiring additional accounting personnel with expertise commensurate with our financial accounting and reporting requirements and that have the requisite experience to oversee outsourced service providers and specialists, upgrading our financial systems and implementing information technology general controls, we addressed the impact of the material weaknesses on the control environment.

- By establishing controls to identify, assess, and respond to the risks of material misstatement, and by establishing controls to identify and account for certain non-routine, unusual, or complex transactions in a timely fashion, we addressed the impact of the material weaknesses on control activities.

- By performing a risk assessment over all areas of financial reporting, we addressed the impact of the material weakness on risk assessment.

- By documenting our control procedures and communicating the results of control testing to relevant personnel, we addressed the impact of the material weakness on information and communication.

- By engaging a third-party to perform testing on behalf of management, we addressed the impact of the material weakness on monitoring activities.

Through these activities, management determined that, as of December 31, 2024, the previously-identified material weaknesses have been remediated.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining an adequate system of internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-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 U.S. generally accepted accounting principles.

Under the supervision of and with the participation of our Chief Executive Officer and Chief Financial Officer, our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2024 based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control—Integrated Framework (2013). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2024.

This Report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting as required by Section 404(c) of the Sarbanes Oxley Act of 2002 because we qualify for an exemption as an emerging growth company under the JOBS Act.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting that occurred during the quarter ended December 31, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Management recognizes that a control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud or error, if any, have been detected. These inherent limitations include the realities that judgments in decision making can be faulty, and that breakdowns can occur because of a simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the controls. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Item 9B. Other Information.

Not applicable.

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 to the information set forth in the sections titled "Information Regarding the Board of Directors and Corporate Governance," "Election of Directors," and "Executive Officers" appearing in the 2025 Proxy Statement that we will file in connection with our 2025 Annual Meeting of Stockholders and is incorporated by reference herein.

Information regarding our Code of Conduct (the "Code of Conduct") required by this item will be contained in our 2025 Proxy Statement under the caption "Information Regarding the Board of Directors and Corporate Governance – Code of Conduct," and is hereby incorporated by reference. We have adopted the Code of Conduct applicable to all of our employees, officers and directors. The audit committee of our board of directors is responsible for overseeing the Code of Conduct and must approve any waivers of the Code of Conduct for executive officers and directors. If we make any substantive amendments to the Code of Conduct or grant any waiver from a provision of the Code of Conduct to any executive officer or director, we will promptly disclose the amendment or waiver on our website. The Code of Conduct is available on our website at www.tourmalinebio.com. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this Report.

We have adopted an Insider Trading Policy governing the purchase, sale and/or other dispositions of our securities by our directors, officers and employees. A copy of the Insider Trading Policy is filed as an exhibit to this Report. In addition, it is the Company's practice to comply with the applicable laws and regulations relating to insider trading.

Item 11. Executive Compensation.

The information required by this Item 11 will be contained in the sections entitled "Executive Compensation" and "Non-Employee Director Compensation" appearing in the 2025 Proxy Statement that we will file in connection with our 2025 Annual Meeting of Stockholders and is incorporated by reference herein.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The information required by this Item 12 will be contained in the sections entitled "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance under Equity Compensation Plans" appearing in the 2025 Proxy Statement that we will file in connection with our 2025 Annual Meeting of Stockholders and is incorporated by reference herein.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The information required by this Item 13 will be contained in the sections entitled "Transactions with Related Persons" and "Independence of the Board of Directors" appearing in the 2025 Proxy Statement that we will file in connection with our 2025 Annual Meeting of Stockholders and is incorporated by reference herein.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be contained in the section entitled "Ratification of Selection of Independent Registered Public Accounting Firm" appearing in the 2025 Proxy Statement that we will file in connection with our 2025 Annual Meeting of Stockholders and is incorporated by reference herein.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) Financial Statements.

See Index to Consolidated Financial Statements on page F-1 of this Annual Report on Form 10-K, which is incorporated into this item by reference.

(a)(2) Financial Statement Schedules.

All schedules have been omitted because they are not required or because the required information is given in the Consolidated Financial Statements or Notes thereto.

(a)(3) Exhibits.

The exhibits required to be filed as part of this Annual Report on Form 10-K are listed in the Exhibit Index attached hereto and are incorporated herein by reference.

Item 16. Form 10-K Summary

None.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
2.1	Agreement and Plan of Merger and Reorganization, dated as of June 22, 2023, by and among Talaris Therapeutics, Inc., Terrain Merger Sub, Inc. and Tourmaline Bio, Inc. (incorporated by reference to Exhibit 2.1 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on June 22, 2023).
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant, as amended through October 19, 2023 (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-40384), filed with the SEC on November 14, 2023).
3.2	Third Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on September 11, 2024).
4.1	Form of Specimen Common Stock Certificate of Tourmaline Bio, Inc. (incorporated by reference to Exhibit 4.1 to the Registrant's Annual Report on Form 10-K (File No. 001-40384), filed with the SEC on March 19, 2024).
4.2	Description of Securities (incorporated by reference to Exhibit 4.2 to the Registrant's Annual Report on Form 10-K (File No. 001-40384), filed with the SEC on March 19, 2024).
10.1+	Tourmaline Bio, Inc. Executive Severance and Change in Control Plan and Form of Participation Agreement (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 27, 2023).
10.2+	Amended Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-40384), filed with the SEC on May 13, 2024).
10.3+	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form S-4 (File No. 333-273335), filed with the SEC on July 20, 2023).
10.4+	Offer Letter, dated as of October 18, 2023, by and between the Registrant and Sandeep Kulkarni, M.D. (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 20, 2023).
10.5+	Offer Letter, dated as of October 18, 2023, by and between the Registrant and Brad Middlekauff, J.D. (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 20, 2023).
10.6+	Offer Letter, dated as of October 18, 2023, by and between the Registrant and Susan Dana Jones, Ph.D. (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 20, 2023).

10.7+	Offer Letter, dated as of June 7, 2023, by and between the Registrant and Ryan Robinson (incorporated by reference to Exhibit 10.5 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 20, 2023).
10.8+	Tourmaline Bio, Inc. 2022 Equity Incentive Plan and forms of award agreements thereunder (incorporated by reference to Exhibit 10.1 to the Registrant's Registration Statement on Form S-4 (File No. 333-273335), filed with the SEC on July 20, 2023).
10.9+	Tourmaline Bio, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.7 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 20, 2023).
10.10+	Forms of Option Grant Notice, Option Agreement and Notice of Exercise under Tourmaline Bio, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 20, 2023).
10.11+	Forms of Restricted Stock Unit Grant Notice and Award Agreement under Tourmaline Bio, Inc. 2023 Equity Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 20, 2023).
10.12+	Tourmaline Bio, Inc. 2023 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.10 to the Registrant's Current Report on Form 8-K (File No. 001-40384), filed with the SEC on October 20, 2023).
10.13+	Side Letter, dated as of November 10, 2023, by and between the Registrant and Ryan Robinson (incorporated by reference to Exhibit 10.14 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-40384), filed with the SEC on November 14, 2023).
10.14††	License Agreement by and between Tourmaline Bio, LLC and Pfizer Inc., dated May 3, 2022 (incorporated by reference to Exhibit 10.4 to the Registrant's Registration Statement on Form S-4 (File No. 333-273335), filed with the SEC on July 20, 2023).
10.15††	License Agreement by and between Tourmaline Bio, LLC and Lonza Sales AG, dated May 16, 2022 (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-4 (File No. 333-273335), filed with the SEC on July 20, 2023).
10.16+	Confirmatory Offer Letter, by and between the Registrant and Ryan Robinson, dated June 25, 2024 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-40384), filed with the SEC on August 8, 2024).
10.17	Sales Agreement, by and between the Registrant and Leerink Partners, LLC, dated November 7, 2024 (incorporated by reference to Exhibit 1.2 to the Registrant's Registration Statement on Form S-3 (File No. 333-283078), filed with the SEC on November 7, 2024).
19.1*††	Insider Trading Policy.
21.1*	Subsidiaries of the Registrant.
23.1*	Consent of Deloitte & Touche LLP, independent registered public accounting firm.
24.1*	Power of Attorney (incorporated by reference to the signature page of this Annual Report on Form 10-K).
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.
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.
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 2002.
97	Incentive Compensation Recoupment Policy of Tourmaline Bio, Inc. (incorporated by reference to Exhibit 97 to the Registrant's Annual Report on Form 10-K (File No. 001-40384), filed with the SEC on March 19, 2024).
101.INS	Inline XBRL Instance Document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

* Filed herewith.

** This certification is being furnished solely to accompany this Report pursuant to 18 U.S.C. Section 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any

filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

†† Certain confidential portions of this Exhibit were omitted by means of marking such portions with brackets ("[*****]") because the identified confidential portions (i) are not material and (ii) is the type of information that the Company treats as private or confidential.

+ Indicates management contract or compensatory plan.

The agreements and other documents filed as exhibits to this Report are not intended to provide factual information or other disclosure other than with respect to the terms of the agreements or other documents themselves, and you should not rely on them for that purpose. In particular, any representations and warranties made by us in these agreements or other documents were made solely within the specific context of the relevant agreement or document and may not describe the actual state of affairs as of the date they were made or at any other time.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Tourmaline Bio, Inc.

Date: March 13, 2025

By: /s/ Sandeep Kulkarni
Sandeep Kulkarni
Chief Executive Officer

Power of Attorney

KNOW BY ALL THESE PRESENTS, that each person whose signature appears below constitutes and appoints Sandeep Kulkarni, M.D., Ryan Robinson and Brad Middlekauff, and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments to this registration statement (including post-effective amendments), and to sign any registration statement for the same offering covered by this registration statement that is to be effective upon filing pursuant to Rule 462(b) promulgated under the Securities Act, and all post-effective amendments thereto, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as she or he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their, his or her substitute or substitutes, 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/ Sandeep Kulkarni, M.D. Sandeep Kulkarni, M.D.	Chief Executive Officer and Director (*Principal Executive Officer*)	March 13, 2025
/s/ Ryan Robinson Ryan Robinson	Chief Financial Officer (*Principal Financial and Accounting Officer)*	March 13, 2025
/s/ Clay Siegall, Ph.D. Clay Siegall, Ph.D.	Chairman of the Board	March 13, 2025
/s/ Caley Castelein, M.D. Caley Castelein, M.D.	Director	March 13, 2025
/s/ Aaron Kantoff Aaron Kantoff	Director	March 13, 2025
/s/ Mark McDade Mark McDade	Director	March 13, 2025
/s/ Sapna Srivastava, Ph.D. Sapna Srivastava, Ph.D.	Director	March 13, 2025
/s/ Parvinder Thiara Parvinder Thiara	Director	March 13, 2025

Tourmaline Bio, Inc.
Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the stockholders and the Board of Directors of Tourmaline Bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Tourmaline Bio, Inc. and subsidiaries (the "Company") as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' (deficit) equity, and cash flows, for each of the two years in the period ended December 31, 2024, and the related notes (collectively referred to as 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, 2024 and 2023, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2024, in conformity with accounting principles generally accepted in the United States of America.

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

Morristown, New Jersey
March 13, 2025

We have served as the Company's auditor since 2022.

Tourmaline Bio, Inc.
Consolidated Balance Sheets
(amounts in thousands, except share and par value amounts)

	December 31,	
	2024	**2023**
Assets		
Current assets		
Cash and cash equivalents	$ 30,506	$ 140,726
Short-term investments	227,797	62,225
Prepaid expenses and other current assets	10,539	5,923
Total current assets	268,842	208,874
Property and equipment, net	55	85
Long-term investments	36,633	—
Restricted cash	227	227
Operating lease right-of-use asset	212	362
Other non-current assets	3,032	747
Total assets	$ 309,001	$ 210,295
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable	$ 3,583	$ 1,071
Accrued expenses and other current liabilities	5,099	3,710
Operating lease liability, current portion	227	221
Total current liabilities	8,909	5,002
Operating lease liability, net of current portion	17	194
Other liabilities	23	57
Total liabilities	8,949	5,253
Commitments and Contingencies (Note 13)		
Stockholders' equity		
Undesignated preferred stock, $0.0001 par value – 10,000,000 shares authorized as of December 31, 2024 and December 31, 2023, no shares issued or outstanding as of December 31, 2024 or December 31, 2023	—	—
Common stock, $0.0001 par value – 140,000,000 voting shares authorized as of December 31, 2024 and December 31, 2023, 25,617,805 and 20,337,571 voting shares issued and outstanding as of December 31, 2024 and December 31, 2023, respectively; 10,000,000 non-voting shares authorized as of December 31, 2024 and December 31, 2023, no non-voting shares issued or outstanding as of December 31, 2024 or December 31, 2023	3	2
Additional paid-in capital	435,014	267,024
Accumulated other comprehensive income	296	67
Accumulated deficit	(135,261)	(62,051)
Total stockholders' equity	300,052	205,042
Total liabilities and stockholders' equity	$ 309,001	$ 210,295

The accompanying notes are an integral part of these consolidated financial statements.

Tourmaline Bio, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(amounts in thousands, except per share amounts)

	Year Ended December 31,	
	2024	**2023**
Operating expenses:		
Research and development	$ 66,985	$ 32,368
General and administrative	22,747	13,041
Total operating expenses	89,732	45,409
Loss from operations	(89,732)	(45,409)
Other income, net	16,522	3,285
Net loss	$ (73,210)	$ (42,124)
Net loss per share, basic and diluted	$ (2.89)	$ (8.87)
Weighted-average common shares outstanding, basic and diluted	25,348	4,747
Comprehensive loss:		
Net loss	$ (73,210)	$ (42,124)
Other comprehensive income		
Unrealized gain on investments	229	67
Comprehensive loss	$ (72,981)	$ (42,057)

The accompanying notes are an integral part of these consolidated financial statements.

Tourmaline Bio, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' (Deficit) Equity
(amounts in thousands, except share amounts)

	Series A Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares*	Amount				
Balance at December 31, 2022	27,125,000	$ 27,125	867,499	$ —	$ 195	$ —	$ (19,927)	$ (19,732)
Issuance of Series A convertible preferred stock, net of issuance costs	92,200,000	91,823	—	—	—	—	—	—
Issuance of Series A convertible preferred stock pursuant to anti-dilution provision of license agreement with Pfizer, Inc.	8,823,529	8,824	—	—	—	—	—	—
Conversion of convertible preferred stock to common stock in connection with reverse merger	(128,148,529)	(127,772)	10,222,414	1	127,771	—	—	127,772
Issuance of common stock in the pre-closing financing, net of issuance costs	—	—	4,092,035	—	70,468	—	—	70,468
Issuance of common stock to former stockholders of Talaris Therapeutics, Inc. in connection with reverse merger	—	—	4,459,651	1	68,891	—	—	68,892
Reverse Merger transaction costs	—	—	—	—	(6,112)	—	—	(6,112)
Stock-based compensation expense, including acceleration and settlement of former Talaris Therapeutics, Inc. stock-based awards in connection with reverse merger	—	—	—	—	5,769	—	—	5,769
Issuance of common stock from exercise of stock options, including early exercises	—	—	695,142	—	7	—	—	7
Vesting of early exercised stock options	—	—	—	—	35	—	—	35
Issuance of common stock upon vesting of restricted stock units	—	—	830	—	—	—	—	—
Unrealized gain on investments	—	—	—	—	—	67	—	67
Net loss	—	—	—	—	—	—	(42,124)	(42,124)
Balance as of December 31, 2023	—	—	20,337,571	2	267,024	67	(62,051)	205,042
Issuance of common stock from public offering, net of issuance costs	—	—	5,307,691	1	161,352	—	—	161,353
Stock-based compensation expense	—	—	—	—	6,593	—	—	6,593
Vesting of early exercised stock options	—	—	—	—	45	—	—	45
Repurchase of common stock originally issued upon early exercise of stock options	—	—	(32,443)	—	—	—	—	—
Issuance of common stock upon vesting of restricted stock units	—	—	4,986	—	—	—	—	—
Unrealized gain on investments	—	—	—	—	—	229	—	229
Net loss	—	—	—	—	—	—	(73,210)	(73,210)
Balance as of December 31, 2024	—	$ —	**25,617,805**	**$ 3**	**$ 435,014**	**$ 296**	**$ (135,261)**	**$ 300,052**

* Amounts have been restated for the impact of the reverse merger outlined further within Notes 1 and 3.

The accompanying notes are an integral part of these consolidated financial statements.

Tourmaline Bio, Inc.
Consolidated Statements of Cash Flows
(amounts in thousands)

	Year Ended December 31,	
	2024	**2023**
Operating activities:		
Net loss	$ (73,210)	$ (42,124)
Adjustments to reconcile net loss to net cash used in operating activities:		
In-process research and development expense	—	8,824
Stock-based compensation	6,593	5,769
Non-cash lease expense	150	126
Depreciation on property and equipment	39	33
Accretion of discount on investments	(7,594)	(522)
Realized gain on investments	(87)	(17)
Other non-cash items	—	(2)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(4,617)	(1,615)
Other non-current assets	(2,205)	(747)
Accounts payable	2,437	(44)
Accrued expenses and other current liabilities	1,402	2,325
Operating lease liabilities	(171)	(87)
Net cash used in operating activities	(77,263)	(28,081)
Investing activities:		
Purchases of property and equipment	(9)	(56)
Purchases of investments	(366,136)	(16,604)
Maturities of investments	171,840	20,500
Net cash (used in) provided by investing activities	(194,305)	3,840
Financing activities:		
Proceeds from public offering of common stock, net of issuance costs	161,352	—
Repurchase of common stock originally issued upon early exercise of stock options	(4)	—
Proceeds from issuance of Series A convertible preferred stock, net of issuance costs	—	91,823
Proceeds from exercises of stock options	—	144
Payment of reverse merger costs	—	(6,107)
Proceeds from pre-merger financing, net of issuance costs	—	70,468
Cash acquired in connection with reverse merger	—	392
Net cash provided by financing activities	161,348	156,720
Net (decrease) increase in cash, cash equivalents and restricted cash	(110,220)	132,479
Cash, cash equivalents and restricted cash—Beginning of period	140,953	8,474
Cash, cash equivalents and restricted cash—End of period	$ 30,733	$ 140,953
Reconciliation of cash, cash equivalents and restricted cash:		
Cash and cash equivalents	$ 30,506	$ 140,726
Restricted cash	227	227
Total cash, cash equivalents and restricted cash	$ 30,733	$ 140,953
Non-cash investing and financing activities:		
Issuance of Series A convertible preferred stock in exchange for acquired in-process research and development	$ —	$ 8,824
Unpaid reverse merger costs included in accounts payable	$ —	$ 5
Unpaid deferred offering costs included in accounts payable and accrued expenses	$ 80	$ —

The accompanying notes are an integral part of these consolidated financial statements.

Tourmaline Bio, Inc.
Notes to Consolidated Financial Statements

1. Nature of Business

Overview

Tourmaline Bio, Inc. (the "Company") is a late-stage clinical biotechnology company focused on developing transformative medicines that dramatically improve the lives of patients with life-altering immune and inflammatory diseases. The Company is developing pacibekitug, a fully human monoclonal antibody that selectively binds to interleukin-6, a key proinflammatory cytokine involved in the pathogenesis of many autoimmune and inflammatory disorders. The Company's corporate headquarters are in New York, New York.

The Company is subject to risks common to companies in the biotechnology industry including, but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive clinical testing and regulatory approval, prior to commercialization. These efforts will require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

Reverse Merger and Pre-Merger Financing Transaction

On October 19, 2023, the Company completed its reverse merger with Tourmaline Sub, Inc. (formerly Tourmaline Bio, Inc.) ("Legacy Tourmaline") in accordance with the terms of the Agreement and Plan of Merger, dated as of June 22, 2023 (the "Merger Agreement"), by and among the Company, Terrain Merger Sub, Inc., a Delaware corporation and a wholly owned subsidiary of the Company ("Merger Sub"), and Legacy Tourmaline, pursuant to which, among other matters, Merger Sub merged with and into Legacy Tourmaline, with Legacy Tourmaline surviving as a wholly owned subsidiary of the Company (the "Reverse Merger"). In connection with the completion of the Reverse Merger, the Company changed its name from "Talaris Therapeutics, Inc." to "Tourmaline Bio, Inc.," and the business conducted by the Company became primarily the business conducted by Legacy Tourmaline. References to "the Company" refer to Legacy Tourmaline for periods prior to the closing of the Reverse Merger, and to Tourmaline Bio, Inc. (formerly Talaris Therapeutics, Inc., or "Talaris") for all other periods, as the context requires.

Immediately prior to the effective time of the Reverse Merger, Talaris effected a 1-for-10 reverse stock split of its common stock (the "Reverse Stock Split").

At the effective time of the Reverse Merger, the Company issued an aggregate of 15,877,090 shares of Company common stock to the Legacy Tourmaline stockholders, based on the exchange ratio of approximately 0.07977 shares of Company common stock for each share of Legacy Tourmaline common stock, including those shares of Legacy Tourmaline common stock issued upon the conversion of Legacy Tourmaline Series A convertible preferred stock and those shares of the Legacy Tourmaline common stock issued in the Pre-Merger Financing Transaction (as defined below), resulting in 20,336,741 shares of Company common stock being issued and outstanding following the effective time of the Reverse Merger.

At the effective time of the Reverse Merger, Legacy Tourmaline's 2022 Equity Incentive Plan was assumed by the Company, and each outstanding and unexercised option to purchase shares of Legacy Tourmaline common stock immediately prior to the effective time of the Reverse Merger was assumed by the Company and converted into an option to purchase shares of Company common stock, with necessary adjustments to the number of shares and exercise price to reflect the exchange ratio.

The Reverse Merger was accounted for as a reverse recapitalization in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP"). Under this method of accounting, Legacy Tourmaline was deemed to be the accounting acquirer for financial reporting purposes. This determination was primarily based on the expectation that, immediately following the Reverse Merger: (i) Legacy Tourmaline's stockholders own a substantial majority of the voting rights in the combined company; (ii) Legacy Tourmaline's largest stockholders retain the largest interest in the combined company; (iii) Legacy Tourmaline designated a majority (five of seven) of the initial members of the board of directors of the combined company; and (iv) Legacy Tourmaline's executive management team became the

management team of the combined company. Accordingly, for accounting purposes: (i) the Reverse Merger was treated as the equivalent of Legacy Tourmaline issuing stock to acquire the net assets of Talaris; (ii) the net assets of Talaris are recorded at their acquisition-date fair value in the consolidated financial statements of Legacy Tourmaline and (iii) the reported historical operating results of the combined company prior to the Reverse Merger are those of Legacy Tourmaline. Historical common share figures of Legacy Tourmaline have been retroactively restated based on the exchange ratio of 0.07977. Additional information regarding the accounting for the Reverse Merger is included in Note 3, "Reverse Merger".

Concurrently with the execution and delivery of the Merger Agreement, and in order to provide Legacy Tourmaline with additional capital for its development programs, Legacy Tourmaline entered into a Securities Purchase Agreement (the "Private Placement Agreement"), with certain investors named therein (the "Private Placement Investors"), pursuant to which, subject to the terms and conditions of the Private Placement Agreement, immediately prior to the effective time of the Reverse Merger, Legacy Tourmaline issued and sold, and the Private Placement Investors purchased 4,092,035 shares (as effected by the exchange ratio described above) of Legacy Tourmaline common stock for gross proceeds of approximately $75.0 million (the "Pre-Merger Financing Transaction").

Following the completion of the Reverse Merger, on June 30, 2024, Tourmaline Sub, Inc. merged with and into Tourmaline Bio, Inc., with Tourmaline Bio, Inc. as the surviving entity (the "Roll-Up Merger").

Liquidity

As of December 31, 2024, the Company had cash, cash equivalents, and investments of $294.9 million. The Company expects that its existing cash, cash equivalents and investments, will enable it to fund its expected operating expenses and capital expenditure requirements for at least 12 months from March 13, 2025, the filing date of this Annual Report on Form 10-K. The Company expects to finance its future cash needs through a combination of equity or debt financings, collaborations, licensing arrangements and strategic alliances.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (the "SEC") and US GAAP, as found in the Accounting Standards Codification ("ASC") of the Financial Accounting Standards Board ("FASB").

The consolidated financial statements include the accounts of Tourmaline Bio, Inc. and its former wholly owned subsidiary, Tourmaline Sub, Inc. As outlined within Note 1, "Nature of Business", Tourmaline Sub, Inc. was merged with and into Tourmaline Bio, Inc., with Tourmaline Bio, Inc. as the surviving entity, upon consummation of the Roll-Up Merger on June 30, 2024. All historical intercompany transactions and balances have been eliminated in consolidation.

Segment Information

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company's chief operating decision maker ("CODM"), the Company's Chief Executive Officer, views the Company's operations and manages its business as a single operating and reportable segment. The Company operates only in the United States. Refer to Note 17, "Segment Information", for additional disclosures regarding segment information.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, accrued expenses and stock-based compensation expense. The Company bases its estimates on historical experience and other market specific or other relevant assumptions it believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Fair Value of Financial Instruments

ASC Topic 820, *Fair Value Measurement*, ("ASC 820") establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.

- Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

- Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Cash Equivalents

Cash equivalents are highly-liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. These assets include investments in money market funds that invest in U.S. Treasury and government agency obligations. Cash equivalents are reflected at fair value based on quoted market prices, as further described in Note 5, "Fair Value Measurements".

Investments

Investments consist of securities with original maturities greater than three months when purchased. Short-term investments consist of investments that are available for use in current operations. Long-term investments consist of investments with maturities of greater than one year that are not available for use in current operations. The Company did not maintain any long-term investments as of December 31, 2023.

The Company classifies all of its investments as available-for-sale securities. Accordingly, these investments are recorded at fair value. Realized gains and losses and amortization and accretion of discounts and premiums are included in "Other income, net". Unrealized gains and losses on available-for-sale securities are included in "Accumulated other comprehensive income" as a component of stockholders' equity until realized.

For available-for-sale debt securities in unrealized loss positions, the Company is required to assess whether to record an allowance for credit losses using an expected loss model. A credit loss is limited to the amount by which the amortized cost of an investment exceeds its fair value. A previously-recognized credit loss may be decreased in subsequent periods if the Company's estimate of fair value for the investment increases. To determine whether to record a credit loss, the Company considers, among other factors, adverse conditions related to the security, industry, or geographic area, failure of the issuer to make scheduled payments, and changes in the issuer's credit rating.

Property and Equipment

Property and equipment are recorded at cost and consist of computer and office equipment and leasehold improvements. The Company capitalizes property and equipment that is acquired for research and development activities and that has

alternative future use. Expenditures for repairs and maintenance are recorded to expense as incurred, whereas major betterments are capitalized as additions to property and equipment. Leasehold improvements are depreciated over the lesser of their useful lives or the term of the lease. Depreciation is calculated over the estimated useful lives of the assets using the straight-line method.

Impairment of Long-Lived Assets

The Company reviews long-lived assets when events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. Recoverability is measured by comparing the carrying value of the asset to the future undiscounted cash flows from the use and eventual disposition of the asset. If an asset is considered to be impaired, the impairment loss to be recognized is measured as the amount by which the carrying value of the asset exceeds its fair value.

Leases

The Company accounts for leases pursuant to ASC Topic 842, *Leases* ("ASC 842"). Upon the adoption ASC 842, the Company elected to utilize certain practical expedients, which among other things, permit the Company to not separate lease and non-lease components. Additionally, the Company elected an accounting policy whereby it does not apply the recognition requirements of ASC 842 to short-term leases with a term of 12 months or less.

The Company determines if an arrangement is or contains a lease by evaluating whether the arrangement conveys the right to use an identified asset and whether the Company obtains substantially all of the economic benefits from and has the ability to direct the use of the asset. If a lease is determined to exist, at the lease commencement date, the Company recognizes a lease liability and a right-of-use ("ROU") asset representing its right to use the underlying asset over the lease term. The Company determines the lease term at the lease commencement date, with the lease term including periods covered by renewal options that are reasonably certain of being exercised and periods covered by termination options that are reasonably certain of not being exercised. The initial measurement of the lease liability is calculated on the basis of the present value of the remaining lease payments and the ROU asset is measured on the basis of this liability, adjusted by prepaid and accrued rent, lease incentives, and initial direct costs. The subsequent measurement of a lease is dependent on whether the lease is classified as an operating lease or a finance lease. Operating lease cost is recognized on a straight-line basis over the lease term, with the cost presented as a component of general and administrative expenses in the consolidated statements of operations and comprehensive loss. The Company has not recognized any financing leases to date.

The Company's lease requires other payments such as costs related to service components, real estate taxes, common area maintenance, and insurance. These costs are generally variable in nature and based on the actual costs incurred and required by the lease. As the Company has elected to not separate lease and non-lease components for all classes of underlying assets, all variable costs associated with the lease are expensed in the period incurred and presented and disclosed as variable lease costs.

ASC 842 requires that a lessee use the rate implicit in the lease when measuring the lease liability and ROU asset, unless that rate is not readily determinable. When the rate implicit in the lease is not readily determinable, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of future lease payments. The Company gives consideration to the Company's credit standing, the term of the lease, total lease payments and adjusts for the impacts of collateral, as necessary, when calculating its incremental borrowing rates.

Research and Development Expenses

Expenditures relating to research and development are expensed as incurred. Research and development expenses include external expenses incurred under arrangements with third parties; consulting costs; salaries and personnel-related costs, including non-cash stock-based compensation expense; license fees to acquire in-process research and development that does not have an alternative future use and other expenses. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made. Where contingent milestone payments are due to third parties under research and development or license agreements, the milestone payment obligations are expensed when the related milestone events are achieved.

As part of the process of preparing the consolidated financial statements, the Company is required to estimate its accrued research and development expenses as of each balance sheet date. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. This process involves reviewing open contracts, communicating with internal personnel to identify services that have been performed on the Company's behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of the actual cost. The Company periodically confirms the accuracy of its estimates with its service providers and makes adjustments if necessary. The majority of the Company's service providers invoice monthly in arrears for services performed or when contractual milestones are met. The financial terms of agreements with these service providers are subject to negotiation, vary from contract-to-contract and may result in uneven payment flows. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense.

Intellectual Property Expenses

The Company expenses legal costs related to patent applications as they are incurred. Such costs are classified as general and administrative expenses within the consolidated statements of operations and comprehensive loss.

Stock-Based Compensation

The Company accounts for stock-based payments in accordance with ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). This guidance requires all stock-based payments, including grants of stock options and restricted common units, to be recognized as expense in the consolidated statements of operations and comprehensive loss based on their grant date fair values. For stock options granted to employees, non-employees and members of the Company's Board of Directors for their services on the Board of Directors, the Company estimates the grant date fair value of each stock option using the Black-Scholes option-pricing model. For stock-based payments subject to service-based vesting conditions, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock-based payment on a straight-line basis over the requisite service period.

Prior to the Company being publicly-traded, Legacy Tourmaline estimated the grant date fair value of its common stock using an appropriate valuation methodology, in accordance with the framework of the American Institute of Certified Public Accountants' Technical Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*. Each valuation methodology included estimates and assumptions that required the Company's judgment. These estimates and assumptions included a number of objective and subjective factors, including external market conditions, guideline public company information, the prices at which the Company sold convertible preferred stock to third parties in arms' length transactions, the rights and preferences of securities senior to the Company's common stock at the time and the likelihood of achieving a liquidity event such as an initial public offering or sale. Significant changes to the assumptions used in the valuations could result in different fair values at each valuation date.

In addition to the grant date fair value of the Company's common stock, the Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the calculation of expected term of the stock-based payment, (ii) the risk-free interest rate, (iii) the expected stock price volatility and (iv) the expected dividend yield. The Company uses the simplified method as prescribed by SEC Staff Accounting Bulletin No. 107 to calculate the expected term for stock options granted to employees as the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The Company determines the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. Because the Company has only been publicly-traded for a short period of time, there is a lack of Company-specific historical and implied volatility data. Accordingly, the Company bases its estimates of expected volatility on the historical volatility of a group of publicly-traded companies with similar characteristics to itself, including stage of product development and therapeutic focus within the life sciences industry. Historical volatility is calculated over a period of time commensurate with the expected term of the stock-based payment. The Company uses an assumed dividend yield of zero as the Company has never paid dividends on its common stock, nor does it expect to pay dividends on its common stock in the foreseeable future.

The Company accounts for forfeitures of all stock-based payments when such forfeitures occur.

Income Taxes

Income taxes are recorded in accordance with ASC Topic 740, *Income Taxes*, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax

consequences of events that have been included in the consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors, including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position.

Interest and penalty charges, if any, related to income taxes would be classified as a component of the "Provision for income taxes" in the consolidated statements of operations and comprehensive loss.

Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders is presented in conformity with the two-class method required for participating securities. The Company considers its Series A convertible preferred stock and common stock issued subject to repurchase (related to early exercised stock options) to be participating securities. Net loss is attributed to common stockholders and participating securities based on their participation rights. Net loss attributable to common stockholders is not allocated to the Series A convertible preferred stock or common stock issued subject to repurchase as these holders do not have a contractual obligation to share in any losses.

Under the two-class method, basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted-average number of shares of common stock outstanding during the period.

Diluted net loss per share attributable to common stockholders includes the effect, if any, from common stock issued subject to repurchase and the potential exercise or conversion of securities such as stock options and convertible preferred stock, which would result in the issuance of incremental shares of common stock. The Company has not adjusted its weighted average number of common shares outstanding in the calculation of diluted loss per share attributable to common stockholders as the Company reported a net loss for all periods presented and the effect of the aforementioned securities is anti-dilutive.

Concentration of Credit Risk

Financial instruments that potentially expose the Company to concentrations of credit risk primarily consist of cash, cash equivalents and investments. Cash balances are deposited with federally-insured financial institutions in the United States and may, at times, exceed federally-insured limits. The Company maintains its cash, cash equivalents and investments with high-quality financial institutions and, consequently, the Company believes that such funds are subject to minimal credit risk. The Company's cash equivalents are comprised of money market funds that are invested in U.S. Treasury and government agency obligations. The Company's investments are comprised of commercial paper, government securities, and corporate debt securities. Credit risk in these securities is reduced as a result of the Company's investment policy to limit the amount invested in any single issuer and to only invest in securities of a high credit quality.

The Company has no significant off-balance sheet risk such as foreign exchange contracts, option contracts or other foreign hedging arrangements.

Recently Adopted Accounting Pronouncements

In November 2023, the FASB issued Accounting Standards Update ("ASU") 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures*. This guidance is intended to improve reportable segment disclosure requirements through enhanced disclosures as well as clarify that entities with a single reportable segment are subject to new and existing segment reporting requirements. This guidance is effective for annual periods in fiscal years beginning after December 15, 2023, and interim periods within fiscal years beginning after December 15, 2024, with early adoption permitted. Entities must apply this guidance on a retrospective basis. Accordingly, the Company adopted this new standard for the fiscal year ended December 31, 2024. The adoption of ASU 2023-07 resulted in the inclusion of additional disclosures within Note 17, "Segment Information".

Recent Accounting Pronouncements - Yet to be Adopted

In December 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures*. The amendments in ASU 2023-09 address investor requests for enhanced income tax information primarily through changes to disclosure regarding rate reconciliation and income taxes paid both in the United States and in foreign jurisdictions. This guidance is effective for fiscal years beginning after December 15, 2024 on a prospective basis, with the option to apply the standard retrospectively, and early adoption is permitted. The Company is currently evaluating this guidance to determine the impact it may have on its consolidated financial statements.

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*. The amendments in ASU 2024-03 address investor requests for more detailed expense information and require additional disaggregated disclosures in the notes to financial statements for certain categories of expenses that are included on the face of the income statement. This guidance is effective for fiscal years beginning after December 15, 2026, and interim periods within fiscal years beginning after December 15, 2027, with early adoption permitted. The Company is currently evaluating this guidance to determine the impact it may have on its consolidated financial statements.

3. Reverse Merger

As described in Note 1, "Nature of Business", Merger Sub merged with and into Legacy Tourmaline, with Legacy Tourmaline surviving as a wholly owned subsidiary of the Company on October 19, 2023. The Reverse Merger was accounted for as a reverse recapitalization in accordance with U.S. GAAP with Legacy Tourmaline as the accounting acquirer of Talaris. Under reverse recapitalization accounting, the assets and liabilities of Talaris were recorded at their fair value in Tourmaline's financial statements at the effective time of the Reverse Merger. No goodwill or intangible assets were recognized. Consequently, the consolidated financial statements of the Company reflect the operations of Legacy Tourmaline for accounting purposes together with a deemed issuance of shares, equivalent to the shares held by the former stockholders of Talaris, the legal acquirer, and a recapitalization of the equity of Legacy Tourmaline, the accounting acquirer.

The Company acquired the following assets and liabilities as part of the Reverse Merger (in thousands):

	Amount
Cash and cash equivalents	$ 392
Short-term investments	65,515
Prepaid expenses and other current assets	4,254
Accounts payable	(726)
Accrued expenses	(543)
Net assets acquired	$ 68,892

The Company incurred $2.9 million in stock-based compensation expense as a result of the acceleration of vesting and settlement of Talaris share-based awards at the time of the Reverse Merger. In the consolidated statement of operations and comprehensive loss for the year ended December 31, 2023, $1.4 million and $1.5 million were recorded as research and development expense and general and administrative expense, respectively. Additionally, the Company incurred transaction costs of $6.1 million, which were recorded as a reduction to additional paid-in capital in the consolidated statement of convertible preferred stock and stockholders' equity for the year ended December 31, 2023.

4. Pfizer License Agreement

On May 3, 2022 (the "Effective Date"), the Company entered into a License Agreement (the "Pfizer License Agreement") with Pfizer Inc. ("Pfizer"), pursuant to which the Company obtained an exclusive, sublicensable, royalty-bearing, worldwide right to use and license under certain know-how for the development, commercialization and manufacture of PF-04236921 (the "Compound", now known as pacibekitug) and any pharmaceutical or biopharmaceutical product incorporating the Compound (the "Product"), for the treatment, diagnosis, or prevention of any and all diseases, disorders, illnesses and conditions in humans and animals. In consideration for the license and other rights the Company received under the Pfizer License Agreement, the Company paid Pfizer an upfront payment of $5.0 million and issued to Pfizer 7,125,000 Series A preferred units of Tourmaline Bio, LLC (the predecessor of Legacy Tourmaline), which subsequently converted to 7,125,000 shares of Series A convertible preferred stock of Legacy Tourmaline, representing a 15% interest in

the Company on a fully-diluted basis at the time of issuance. The units were issued for $1.00 per unit, representing a total value of $7.1 million. In accordance with ASC Topic 805, *Business Combinations*, the Pfizer License Agreement was accounted for as an asset acquisition as the licensed compound represented substantially all of the fair value of the gross assets acquired. On the Effective Date, the licensed compound had not yet received regulatory approval and did not have an alternative use. Accordingly, the total consideration transferred of $12.1 million was recorded as research and development expense in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2022.

As additional consideration for the license, the Company is obligated to pay Pfizer up to $128.0 million upon the achievement of specific development and regulatory milestones. The Company is also obligated to pay Pfizer up to $525.0 million upon the first achievement of specific sales milestones. The Company is also obligated to pay Pfizer a marginal royalty rate in the low double digits (less than 15%), subject to specified royalty reductions. The royalty term, on a Product-by-Product and country-by-country basis, begins on the first commercial sale of such Product and expires upon the later of twelve years following the date of the first commercial sale or the expiration of regulatory exclusivity protecting such Product. In the event the Company completes a Significant Transaction (as defined in the Pfizer License Agreement), the Company will be obligated to pay Pfizer a one-time payment in the low-eight digits (up to $20.0 million); the amount of such payment is based on the timing of the transaction.

As of December 31, 2024, the Company does not owe any milestone or royalties under the Pfizer License Agreement and no such milestones or royalties have been paid to date.

The Pfizer License Agreement originally contained an anti-dilution provision allowing Pfizer to maintain a 15% interest in the Company on a fully-diluted basis unless and until certain thresholds are met, whereupon the anti-dilution provision would no longer apply. As outlined further within Note 9, “Convertible Preferred Stock”, on May 2, 2023, the Company issued 8,823,529 additional shares of Series A convertible preferred stock to Pfizer pursuant this anti-dilution provision. The Company recognized research and development expense of $8.8 million in the consolidated statement of operations and comprehensive loss for the year ended December 31, 2023 related to this issuance of Series A convertible preferred stock. Subsequent to the issuance of these additional shares of Series A convertible preferred stock, the anti-dilution provision is no longer in force and effect.

5. Fair Value Measurements

The Company measures the fair value of money market funds based on quoted prices in active markets for identical securities. Investments also include commercial paper, government securities, and corporate debt securities which are valued either based on recent trades of securities in inactive markets or based on quoted market prices of similar instruments and other significant inputs derived from or corroborated by observable market data. The carrying amounts reflected in the consolidated balance sheets for cash, prepaid expenses and other current assets, accounts payable and accrued expenses and other current liabilities approximate their fair values, due to their short-term nature.

Assets measured at fair value on a recurring basis as of December 31, 2024 were as follows (in thousands):

	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents and short-term investments:				
Money market funds, included in cash equivalents	$ 23,324	$ 23,324	$ —	$ —
Commercial paper	46,773	—	46,773	—
Government securities	59,170	46,813	12,357	—
Corporate debt securities	121,854	—	121,854	—
Total cash equivalents and short-term investments	251,121	70,137	180,984	—
Long-term investments:				
Government securities	10,888	10,888	—	—
Corporate debt securities	25,745	—	25,745	—
Total long-term investments	36,633	10,888	25,745	—
Total cash equivalents and investments	$ 287,754	$ 81,025	$ 206,729	$ —

Assets measured at fair value on a recurring basis as of December 31, 2023 were as follows (in thousands):

	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents and short-term investments:				
Money market funds, included in cash equivalents	$ 4,604	$ 4,604	$ —	$ —
Commercial paper	32,555	—	32,555	—
Government securities	26,724	7,907	18,817	—
Corporate debt securities	2,947	—	2,947	—
Total cash equivalents and short-term investments	$ 66,830	$ 12,511	$ 54,319	$ —

There were no liabilities measured at fair value on a recurring basis as of December 31, 2024 or 2023. There were no changes in valuation techniques, nor were there any transfers among the fair value hierarchy levels during the year ended December 31, 2024.

6. Investments

Cash equivalents, short-term and long-term investments as of December 31, 2024 were comprised as follows (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents and short-term investments:				
Money market funds, included in cash equivalents	$ 23,324	$ —	$ —	$ 23,324
Commercial paper	46,738	50	(15)	46,773
Government securities	59,130	48	(8)	59,170
Corporate debt securities	121,713	162	(21)	121,854
Total cash equivalents and short-term investments	250,905	260	(44)	251,121
Long-term investments:				
Government securities	10,878	10	—	10,888
Corporate debt securities	25,675	84	(14)	25,745
Total long-term investments	36,553	94	(14)	36,633
Total cash equivalents and investments	$ 287,458	$ 354	$ (58)	$ 287,754

Cash equivalents and short-term investments as of December 31, 2023 were comprised as follows (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash equivalents and short-term investments:				
Money market funds, included in cash equivalents	$ 4,604	$ —	$ —	$ 4,604
Commercial paper	32,515	44	(4)	32,555
Government securities	26,703	25	(4)	26,724
Corporate debt securities	2,941	6	—	2,947
Total cash equivalents and short-term investments	$ 66,763	$ 75	$ (8)	$ 66,830

The aggregate fair value of securities that were in an unrealized loss position for less than twelve months was $30.6 million and $49.3 million at December 31, 2024 and December 31, 2023, respectively. The Company did not hold any securities that were in an unrealized loss position for greater than twelve months as of either December 31, 2024 or December 31, 2023. Based upon its assessment of securities in an unrealized loss position, the Company did not record any allowances for credit losses during the years ended December 31, 2024 or December 31, 2023.

7. Property and Equipment, Net

Property and equipment, net as of December 31, 2024 and 2023 was comprised as follows (in thousands):

	Estimated Useful Life (in Years)	December 31, 2024	December 31, 2023
Leasehold improvements	Shorter of useful life or remaining lease term	$ 74	$ 74
Computer and office equipment	3 years	58	49
Total property and equipment, gross		132	123
Less: accumulated depreciation		(77)	(38)
Total property and equipment, net		$ 55	$ 85

Depreciation expense was less than $0.1 million for each of the years ended December 31, 2024 and 2023.

8. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities as of December 31, 2024 and 2023 were comprised as follows (in thousands):

	December 31,	
	2024	2023
Accrued bonus	$ 3,830	$ 1,994
Accrued clinical and manufacturing costs	696	438
Accrued consulting fees	153	341
Accrued external audit and tax fees	73	351
Accrued legal fees	—	237
Other accrued expenses and other current liabilities	347	349
Total accrued expenses and other current liabilities	$ 5,099	$ 3,710

9. Convertible Preferred Stock

On April 18, 2022, the Company entered into a Securities Purchase Agreement (the "Initial Series A Securities Purchase Agreement") with various entities and individuals for the purchase of Series A convertible preferred units. As part of the Initial Series A Securities Purchase Agreement, the Company authorized the issuance and sale of up to 20,000,000 shares of its Series A convertible preferred units at a price of $1.00 per unit for total proceeds of $20.0 million. The Series A convertible preferred units were convertible into the Company's Common Units at a 1:1 ratio. The obligations of the parties to purchase and sell the Series A convertible preferred units were subject to the Company entering into the Pfizer License Agreement. As outlined further within Note 4, "Pfizer License Agreement", the Company also issued to Pfizer 7,125,000 Series A convertible preferred units in May 2022 conjunction with the Pfizer License Agreement.

On September 2, 2022, Legacy Tourmaline converted from Tourmaline Bio, LLC, a Delaware limited liability company, to Tourmaline Bio, Inc., a Delaware corporation (the "Conversion"). As part of the Conversion, Series A convertible preferred units were converted at a 1:1 ratio to shares of Series A convertible preferred stock. Upon the Conversion, the Company was authorized to issue up to 27,125,000 shares of Series A convertible preferred stock with a par value of $0.0001.

The Company subsequently entered into a Series A Preferred Stock Purchase Agreement on May 2, 2023 (the "Closing Date") with various entities and individuals for the purchase of additional shares of Series A convertible preferred stock (the "Series A Extension"). On the Closing Date, the Company authorized the issuance and sale of 92,200,000 shares of Series A convertible preferred stock at a price of $1.00 per share for total gross proceeds of $92.2 million. In addition, pursuant to the anti-dilution provision of the Pfizer License Agreement, the Company issued 8,823,529 additional shares of Series A convertible preferred stock to Pfizer in connection with the Series A Extension and recognized corresponding research and development expense of $8.8 million during the second quarter of 2023. The additional shares of Series A convertible preferred stock had the same terms, conditions, rights and preferences as the Series A convertible preferred stock issued during the year ended December 31, 2022. Upon consummation of the Series A Extension, the anti-dilution provision of the Pfizer License Agreement was no longer in force and effect.

Prior to the completion of the Reverse Merger, the Company classified its Series A convertible preferred stock outside of permanent equity as the shares had redemption features that were not entirely within the control of the Company.

Upon the consummation of the Reverse Merger, all outstanding shares of Series A convertible preferred stock were converted into 10,222,414 shares of common stock. No shares of preferred stock were outstanding as of either December 31, 2024 or December 31, 2023.

Subsequent to consummation of the Reverse Merger, the Company is authorized to issue 10,000,000 shares of undesignated preferred stock, however no such shares were issued or outstanding as of December 31, 2024.

10. Common Stock

On January 25, 2024, the Company entered into an underwriting agreement with Jefferies LLC, Piper Sandler & Co., Guggenheim Securities, LLC and Truist Securities, Inc. (collectively, the "Underwriters") in connection with the offering, issuance and sale by the Company of 4,615,384 shares of the Company's common stock at a public offering price of $32.50 per share, less underwriting discounts and commissions, pursuant to an effective shelf registration statement on Form S-3 (the "January 2024 Offering"). Under the January 2024 Offering, the Company also granted the Underwriters a 30-day option to purchase up to 692,307 shares of common stock at the public offering price, less the underwriting discounts and commissions, which was exercised by the Underwriters in full on January 25, 2024. The January 2024 Offering closed on January 29, 2024.

Total gross proceeds from the January 2024 Offering were approximately $172.5 million, including the full exercise by the Underwriters of their option to purchase additional shares. Net proceeds were approximately $161.4 million after deducting underwriting discounts and commissions and offering expenses payable by the Company.

As of December 31, 2024, the Company was authorized to issue 140,000,000 shares of voting common stock and 10,000,000 shares of non-voting common stock. Holders of voting common stock are entitled to one vote per share. In addition, holders of voting common stock are entitled to receive dividends, if and when declared by the Company's Board of Directors. As of December 31, 2024, no dividends had been declared.

As of December 31, 2024 and 2023, the Company had reserved for future issuance the following number of shares of common stock:

	December 31,	
	2024	2023
Exercises of outstanding stock options under 2022 Equity Incentive Plan	1,244,691	1,403,409
Exercises of outstanding stock options under 2023 Equity Incentive Plan	1,479,091	1,042,291
Vesting of restricted stock units under 2023 Equity Incentive Plan	14,127	19,113
Common stock subject to repurchase related to early exercised stock options	170,210	388,943
Future issuances under 2023 Equity Incentive Plan	1,551,522	971,444
Future issuances under 2023 Employee Stock Purchase Plan	406,742	203,367
Total shares reserved for future issuance	4,866,383	4,028,567

11. Stock-Based Compensation

2022 Equity Incentive Plan

On September 2, 2022, the Board of Directors and the stockholders of the Company adopted the 2022 Equity Incentive Plan (the "2022 Plan"), which provided for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards and other stock awards to employees, consultants, and non-employee directors of the Company.

2023 Equity Incentive Plan

On October 17, 2023, the Company adopted the 2023 Equity Incentive Plan (the "2023 Plan") which became effective upon completion of the Reverse Merger. The 2023 Plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance awards and other forms of awards to employees, consultants, and non-employee directors of the Company. The terms of stock award agreements, including vesting requirements, are determined by the Company's Board of Directors and are subject to the provisions of the 2023 Plan. The term of each stock option shall be no more than ten years from the date of grant. Following the effectiveness of the 2023 Plan, no further grants will be made under the 2022 Plan; however, any outstanding equity awards granted under the 2022 Plan will continue to be governed by the terms of the 2022 Plan.

The 2023 Plan initially provided for the issuance of up to 2,033,677 shares of common stock (the "Initial EIP Share Reserve"). Subject to any other adjustments as defined in the 2023 Plan, such aggregate number of shares of common stock will automatically increase on January 1st of each year for a period of ten years commencing on January 1, 2024 and

ending on (and including) January 1, 2033, in an amount equal to 5% of the total number of shares of common stock issued and outstanding determined as of the day prior to such increase (such increase, the "2023 Plan Evergreen Refresh"); provided, however that the board of directors may act prior to January 1st of a given year to provide that the increase for such year will be a lesser number of shares of common stock. The aggregate maximum number of shares of common stock that may be issued pursuant to the exercise of incentive stock options is three multiplied by the Initial EIP Share Reserve.

Under the aforementioned 2023 Plan Evergreen Refresh, 1,016,878 shares were added to the Initial EIP Share Reserve effective January 1, 2024. As of December 31, 2024, there were 1,551,522 shares available for issuance under the 2023 Plan.

2023 Employee Stock Purchase Plan

On October 17, 2023, the Company adopted the 2023 Employee Stock Purchase Plan (the "2023 ESPP"), which became effective upon completion of the Reverse Merger. The maximum number of shares of common stock that may be issued under the 2023 ESPP will not exceed 203,367 shares (the "Initial ESPP Share Reserve"), plus the number of shares of common stock that are automatically added on January 1st of each year for a period of up to ten years commencing on January 1, 2024 and ending on (and including) January 1, 2033, in an amount equal to the lesser of (x) 1% of the total number of shares of common stock issued and outstanding determined as of the day prior to such increase and (y) a number of shares equal to three times the Initial ESPP Share Reserve (such increase, the "ESPP Evergreen Refresh"). Notwithstanding the foregoing, the board of directors may act prior to the first day of any calendar year to provide that there will be no January 1st increase in the share reserve for such calendar year or that the increase in the share reserve for such calendar year will be a lesser number of shares of common stock than would otherwise occur pursuant to the preceding sentence.

Under the aforementioned ESPP Evergreen Refresh, 203,375 shares were added to the Initial ESPP Share Reserve effective January 1, 2024 such that 406,742 shares of common stock may be issued under the 2023 ESPP as of December 31, 2024.

No offering periods under the 2023 ESPP had been initiated as of December 31, 2024.

Total stock-based compensation expense recognized in the consolidated statements of operations and comprehensive loss for the years ended December 31, 2024 and 2023 was as follows (in thousands):

	Year Ended December 31,	
	2024	**2023**
Research and development	$ 2,609	$ 2,322
General and administrative	3,984	3,447
Total stock-based compensation expense	$ 6,593	$ 5,769

Stock Option Activity

The estimated grant-date fair value of the Company's stock options was calculated using the Black-Scholes option pricing model, based on the following assumptions:

	Year Ended December 31,	
	2024	**2023**
Risk-free interest rate	3.5% – 4.7%	3.4% – 4.8%
Dividend yield	—%	—%
Volatility	81.1% – 85.7%	82.2% – 86.1%
Expected term (in years)	5.5 – 6.1	5.5 – 6.1

The weighted-average fair value of the Company's common stock utilized in the valuation of stock options granted during the years ended December 31, 2024 and 2023 was $18.00 and $8.33 per share, respectively. Using the Black-Scholes

option pricing model, the weighted-average grant date fair value of stock options granted during the year ended December 31, 2024 and 2023 was $13.16 and $6.60 per share, respectively.

The following table summarizes changes in stock option activity during the year ended December 31, 2024:

	Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2023	2,445,700	$ 9.29	9.6	$ 41,320
Granted	551,650	$ 18.00		
Exercised	—	$ —		
Cancelled	(273,568)	$ 8.98		
Outstanding as of December 31, 2024	2,723,782	$ 11.08	8.6	$ 25,998
Exercisable as of December 31, 2024	851,920	$ 9.17	7.9	$ 9,467

No stock options were exercised during the year ended December 31, 2024. The aggregate intrinsic value of stock options exercised during the year ended December 31, 2023 was $1.8 million.

As of December 31, 2024, the total unrecognized stock-based compensation expense related to unvested stock options was $15.7 million, which the Company expects to recognize over a weighted-average period of approximately 2.6 years.

Early Exercise of Stock Options

The 2022 Plan and certain stock options issued under the 2022 Plan were amended in February 2023 to permit the stock option holder to early exercise at any time between the grant date and the vesting date. The amendment did not result in any incremental stock-based compensation expense. During the year ended December 31, 2023, certain employees, advisors and non-employee directors early exercised 647,386 stock options. In the event of the termination of an employee, advisor or non-employee director's Continued Service (as defined in the 2022 Plan), the Company can repurchase common stock issued pursuant to early exercised and unvested stock options for a period of six months following the later of (i) the termination date of the employee or non-employee director or (ii) the exercise date. The Company received $0.1 million in cash proceeds related to the early exercise of stock options during the year ended December 31, 2023.

As a result of this repurchase right, the Company initially recorded the proceeds received from the early exercise of stock options as a liability in the consolidated balance sheets. Amounts are reclassified to additional paid-in capital when the underlying stock options vest and the Company's right of repurchase lapses. The aggregate liability associated with the early exercise of stock options was $0.1 million as of December 31, 2024. As of December 31, 2024, 170,210 shares of common stock issued pursuant to early exercised stock options remain unvested. The shares of common stock subject to the Company's repurchase right related to early exercised stock options are legally outstanding, as each holder is deemed to be a common stockholder that has dividend and voting rights during the vesting term.

During the year ended December 31, 2024, the Company repurchased an aggregate of 32,443 shares of common stock from former employees, originally issued upon early exercise of stock options pursuant to the aforementioned repurchase right. These shares were repurchased at the original exercise price.

Restricted Stock Unit Activity

The following table summarizes changes in restricted stock unit activity during the year ended December 31, 2024:

	Shares	Weighted-Average Grant Date Fair Value per Share
Unvested as of December 31, 2023	19,113	$ 11.89
Granted	—	—
Vested	(4,986)	11.89
Cancelled	—	—
Unvested as of December 31, 2024	14,127	$ 11.89

The total grant date fair value of restricted stock units vested for the year ended December 31, 2024 was less than $0.1 million. As of December 31, 2024, the total unrecognized stock-based compensation expense related to unvested restricted stock units was $0.2 million, which the Company expects to recognize over a weighted-average period of approximately 2.7 years.

12. Income Taxes

The Company recorded no income tax benefit for the net loss incurred for the years ended December 31, 2024 and 2023 due to its uncertainty of realizing a benefit from such losses. All of the Company's operating losses since inception have been generated in the United States.

A reconciliation of the federal statutory income tax rate to the Company's effective tax rate is as follows:

	Year Ended December 31,	
	2024	2023
U.S. federal statutory income tax rate	21.0%	21.0%
State income taxes, net of federal benefit	(9.6%)	5.1%
Change in valuation allowance	(16.8%)	(27.5%)
Tax credit carryforwards	6.5%	1.6%
Permanent items, including stock-based compensation	(1.1%)	(0.2%)
Effective tax rate	—%	—%

The principal components of the Company's deferred tax assets and liabilities as of December 31, 2024 and 2023 were comprised as follows (in thousands):

	December 31,	
	2024	2023
Deferred tax assets:		
Capitalized research and development expenses	$ 30,630	$ 28,753
Net operating loss carryforwards	11,233	5,483
Tax credit carryforwards	5,453	693
Stock-based compensation expense	1,220	781
Operating lease liability	53	114
Accrued expenses	830	—
Other	50	61
Total deferred tax assets	49,469	35,885
Less: valuation allowance	(46,370)	(34,040)
Net deferred tax assets	3,099	1,845
Deferred tax liabilities:		
Operating lease right-of-use asset	(46)	(100)
Accretion	(3,053)	(1,745)
Total deferred tax liabilities	(3,099)	(1,845)
Net deferred taxes	$ —	$ —

As of December 31, 2024, the Company had federal and state net operating loss ("NOL") carryforwards of $50.6 million and $9.9 million respectively. Federal NOLs may be carried forward indefinitely. State NOLs expire at various dates from 2038 through 2044. As of December 31, 2024, the Company had federal research and development tax credit carryforwards of $5.5 million which begin to expire in 2043.

The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are composed primarily of capitalized research and development expenses and net operating loss carryforwards. Management has considered the Company's history of net losses incurred since inception and the probability of future losses to conclude it is more likely than not that the Company will not recognize the benefits of deferred tax assets. As a result, the Company has established a valuation allowance for the full amount of its net deferred tax assets as of December 31, 2024. The increase in the valuation allowance of $12.3 million during the year ended December 31, 2024 was primarily due to the additional operating loss generated by the Company.

NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50% as defined under Sections 382 and 383 in the Internal Revenue Code ("IRC"). This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the Company's value immediately prior to the ownership change. As a result of ownership changes in the Company from its inception through December 31, 2024, the Company's NOL and tax credit carryforwards allocable to the periods preceding each such ownership change could be subject to limitations under IRC Section 382, however the Company has not yet completed an IRC Section 382 study.

The Company had no unrecognized tax benefits as of either December 31, 2024 or 2023. The Company has not conducted a study of its research and development credit carryforwards generated during any year. This study, once completed, may result in an adjustment to the Company's research and development credit carryforwards. However, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credit carryforwards, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the consolidated statements of operations and comprehensive loss if an adjustment were required.

The Company files income tax returns in the United States federal tax jurisdiction and various state jurisdictions. Since the Company is in a loss carryforward position, it is generally subject to examination by federal and state tax authorities for all tax years in which a loss carryforward is available.

As of December 31, 2024, the Company has not incurred any material interest or penalty charges.

13. Commitments and Contingencies

Litigation

From time to time, the Company may become subject to legal proceedings, claims and litigation arising in the ordinary course of business. From time to time, the Company may be involved in legal proceedings arising in the ordinary course of its business.

Between July 25 and October 3, 2023, Talaris received eleven demand letters (the "Demands") regarding the Proxy Statement (as defined below). In addition, three lawsuits were filed (captioned Wieder v. Talaris Therapeutics, Inc., et al., No. 1:23-cv-08355 (S.D.N.Y. filed Sept. 21, 2023), Carlisle v. Talaris Therapeutics, Inc., et al., No. 1:23-cv-08520 (S.D.N.Y. filed Sept. 27, 2023), and Roberts v. Talaris Therapeutics, Inc., et al., No. 1:23-cv-01063 (D. Del. filed Sept. 27, 2023)) (the "Lawsuits," and together with the Demands, the "Actions"), in each case, by purported stockholders of Talaris challenging the proposed Reverse Merger and the disclosures in the definitive proxy statement filed by Talaris with the SEC on July 20, 2023, and as amended on August 25, 2023 and September 11, 2023 (the "Proxy Statement"). The Actions generally alleged that certain disclosures in the Proxy Statement were false or misleading and asserted claims against Talaris and its Board of Directors for violations of Sections 14(a) and 20(a) of the Exchange Act of 1934. The purported stockholders sought unspecified monetary damages and an award of costs and expenses, including reasonable attorney's fees. On October 10, 2023, Talaris filed a Form 8-K to update and supplement the Proxy Statement, which contained certain additional disclosures relating to the Reverse Merger (the "Supplemental Disclosures"). Thereafter, plaintiffs in the Lawsuits voluntarily dismissed their complaints, and opposing counsel (for the stockholders in the Actions) requested a mootness fee in connection with the Supplemental Disclosures. The Reverse Merger subsequently closed on October 19, 2023.

Thereafter, the parties engaged in a negotiation over payment of a potential mootness fee(s) to resolve all the fee demands. On February 13, 2024, the parties entered into an agreement, under which the Company agreed to pay a total of approximately $0.2 million to resolve all the fee demands and the stockholders released all claims in connection with the Reverse Merger. This amount was recognized as general and administrative expense by the Company during the year ended December 31, 2023 and has been included within "Accrued expenses and other current liabilities" on the consolidated balance sheet as of December 31, 2023.

New York Office Lease

During the year ended December 31, 2022, the Company entered into a non-cancelable operating lease for its corporate offices in New York, New York (the "New York Office Lease"). The lease expires on February 28, 2026. The Company provided the landlord of the New York Office Lease with a security deposit in the form of a $0.2 million letter of credit, which is recorded as restricted cash on the consolidated balance sheets as of December 31, 2024 and 2023.

The Company recorded an ROU asset and corresponding lease liability related to the New York Office Lease on the consolidated balance sheets as of December 31, 2024 and 2023. As there was no rate implicit in the New York Office Lease, the Company estimated its incremental borrowing rate. Based on this analysis, the Company calculated a discount rate of 15.6% for the New York Office Lease.

As of December 31, 2024, the future minimum lease payments due under the New York Office Lease are as follows (in thousands):

Year Ending December 31,	Amount
2025	$ 227
2026	38
2027	—
Total lease payments	265
Less: effect of discounting	(21)
Total operating lease liability	$ 244

The Company recorded operating lease expense of $0.2 million for the years ended December 31, 2024 and 2023. Cash paid for operating lease liabilities for the year ended December 31, 2024 was $0.2 million. The Company did not incur any short-term or variable lease costs during the years ended December 31, 2024 or 2023. As of December 31, 2024, the remaining lease term of the New York Office Lease is 1.2 years.

14. 401(k) Savings Plan

The Company implemented a defined-contribution savings plan under Section 401(k) of the IRC (the "401(k) Plan") during the year ended December 31, 2023. The 401(k) Plan covers all employees who meet defined minimum age and service requirements and allows participants to defer a portion of their annual compensation, subject to statutory limitations. The Company did not make any matching contributions to the 401(k) Plan during the years ended December 31, 2024 or 2023.

15. Related Party Transactions

In May 2023, an advisor affiliated with Fourth Avenue FF Opportunities LP – Series Z, previously a beneficial owner the Company's outstanding capital stock, exercised stock options to purchase 75,782 shares of the Company's common stock for $0.13 per share. The Company subsequently repurchased the shares from the advisor at $2.76 per share, equivalent to fair value as of the repurchase date, for an aggregate purchase price of $0.2 million. Fourth Avenue FF Opportunities LP – Series Z then purchased the shares from the Company at the same amount $2.76 per share for an aggregate purchase price of $0.2 million .

As of December 31, 2024 and 2023, there were no amounts due to or from any related party.

16. Net Loss per Share

The following common stock equivalents have been excluded from the calculation of diluted net loss per share because their effect would be anti-dilutive:

	December 31,	
	2024	2023
Outstanding stock options under 2022 Equity Incentive Plan	1,244,691	1,403,409
Outstanding stock options under 2023 Equity Incentive Plan	1,479,091	1,042,291
Unvested restricted stock units under 2023 Equity Incentive Plan	13,711	18,697
Common stock subject to repurchase related to early exercised stock options	170,210	388,943
Total	2,907,703	2,853,340

17. Segment Information

In accordance with ASC Topic 280, *Segment Reporting*, the Company has determined that it operates as a single operating and reportable segment, the pacibekitug segment, which is engaged in the business of drug discovery and development.

The Company's CODM assesses performance and allocates resources on a consolidated basis. The CODM, assesses the performance of the pacibekitug segment and decides how to allocate resources based on net loss, which is also reported on

the consolidated statements of operations and comprehensive loss as net loss**.** Segment asset information is not used by the CODM to assess performance or allocate resources. The accounting policies of the pacibekitug segment are the same as those described in Note 2, "Basis of Presentation and Summary of Significant Accounting Policies".

As the Company is pre-commercial and does not yet generate revenue, net loss is used by the CODM to evaluate the performance of the pacibekitug segment based on costs incurred and determine where changes in expenditures are needed to achieve the pacibekitug program's goals. The CODM also uses the components of net loss to monitor budget versus actual results.

Significant segment expenses, as provided to the CODM, are presented below (in thousands):

	Year Ended December 31,	
	2024	2023
Research and development payroll-related costs	$ 16,582	$ 5,969
General and administrative payroll-related costs	7,117	3,369
Clinical trial expenses	19,910	1,843
Chemistry, manufacturing, and controls costs	19,034	11,332
License and milestones costs	—	8,824
Medical affairs expenses	2,461	—
Research and development consulting expenses	4,055	1,946
General and administrative consulting expenses	4,992	2,608
Other segment items[1]	(941)	6,233
Segment and consolidated net loss	$ 73,210	$ 42,124

[1]Other segment items include legal expenses, accounting expenses, IT and facilities expenses, insurance expenses, other operating expenses, interest income, investment income, stock-based compensation expense, depreciation expense, and other income, net.

Interest income was $5.7 million and $0.2 million for the years ended December 31, 2024 and 2023, respectively. There was no interest expense for the years ended December 31, 2024 or 2023.

All of the Company's long-lived assets are located in the United States. Depreciation expense related to long-lived assets was less than $0.1 million for each of the years ended December 31, 2024 and 2023.