Bicara Therapeutics Inc.

2024 Annual Report

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 001-42271

Bicara Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	**85-2903745**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
116 Huntington Ave Suite 703 Boston, Massachusetts	**02116**
(Address of Principal Executive Offices)	(Zip Code)

(617) 468-4219

Registrant's telephone number, including area code

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, par value $0.0001	BCAX	Nasdaq Global Market

Securities registered pursuant to section 12(g) of the Act: None.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.

Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).

Yes ☒ No ☐

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

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

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

☐

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

☐

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

☐

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

☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act).

Yes ☐ No ☒

As of June 30, 2024, the last business day of the registrant's most recently completed second quarter, there was no established public trading market for the registrant's equity securities as the registrant was not a public company and therefore cannot calculate the aggregate market value of its voting and non-voting equity held by non-affiliates as of such date. The registrant's common stock began trading on the Nasdaq Global Market on September 13, 2024.

As of March 24, 2025, the registrant had 54,523,326 shares of common stock, $0.0001 par value per share outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates by reference portions of the registrant's Definitive Proxy Statement for its 2025 Annual Meeting of Shareholders, which the registrant anticipates will be filed with the Securities and Exchange Commission no later than 120 days after the end of its 2024 fiscal year pursuant to Regulation 14A.

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SUMMARY OF THE MATERIAL RISKS ASSOCIATED WITH OUR BUSINESS

We are subject to numerous risks and uncertainties, including those further described below in the section entitled "Risk Factors" in this Annual Report on Form 10-K, that represent challenges that we face in connection with the successful implementation of our strategy and the growth of our business. In particular, the following considerations, among others, may offset our competitive strengths or have a negative effect on our business strategy, which could materially adversely affect our business, financial conditions, results of operations, future growth prospects, or cause a decline in the price of our common stock:

- We are a clinical-stage biopharmaceutical company with a limited operating history, which may make it difficult to evaluate our current business and predict our future success and viability. We have incurred significant financial losses since our inception and anticipate that we will continue to incur significant financial losses for the foreseeable future;

- We will require additional funding in order to finance operations beyond 2029. If we are unable to raise capital when needed, or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

- Our business is highly dependent on the success of ficerafusp alfa. If we are unable to successfully complete clinical development, obtain regulatory approval for or commercialize ficerafusp alfa, or if we experience delays in doing so, our business will be materially harmed.

- The regulatory approval processes of the U.S. Food and Drug Administration and comparable foreign authorities are lengthy, time-consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be materially harmed.

- Clinical development involves a lengthy and expensive process with uncertain outcomes. We may incur additional costs and experience delays in developing and commercializing or be unable to develop or commercialize ficerafusp alfa and any future product candidates.

- Ficerafusp alfa or any future product candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved products or investigational new drugs that could halt their clinical development, delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

- The commercial success of ficerafusp alfa or any future product candidates will depend upon the degree of market acceptance of such product candidates by physicians, patients, healthcare payors and others in the medical community.

- Our ability to develop product candidates, leverage our potential and our future growth depends on attracting, hiring and retaining our key personnel and recruiting additional qualified personnel. If we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. Additionally, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

- We rely, and expect to continue to rely, on third parties, including independent clinical investigators and contract research organizations to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

- We currently and in the future may depend on other third-party collaborators for the discovery, development and commercialization of ficerafusp alfa and any of our future product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

- We have not yet demonstrated an ability to generate revenue, obtain regulatory approval, manufacture any 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 product commercialization.

The summary risk factors described above should be read together with the text of the full risk factors in the section titled "Risk Factors" and the other information set forth in this Annual Report, including our audited consolidated financial statements and the related notes, as well as in other documents that we file with the SEC. The risks summarized above or described in full elsewhere in this Annual Report are not the only risks that we face. Additional risks and uncertainties not presently known to us, or that we currently deem to be immaterial may also materially adversely affect our business, financial condition, results of operations and future growth prospects.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this Form 10-K include, but are not limited to, statements about:

- the initiation timing, progress, results and cost of ficerafusp alfa, including the FORTIFI-HN01 pivotal Phase 2/3 ("FORTIFI-HN01 Phase 2/3 trial" or "FORTIFI-HN01"), a trial in head and neck squamous cell carcinoma, or HNSCC, and the potential expansion Phase 1/1b trial in additional HNSCC patient populations, as well as our research and development programs and our current and future preclinical and clinical studies;

- the ability and the potential to secure pembrolizumab for our clinical trials and successfully manufacture our drug substances and ficerafusp alfa for preclinical use, for clinical trials and on a larger scale for commercial use, if approved;

- the ability of clinical trials to demonstrate safety and efficacy of ficerafusp alfa, and other positive results;

- the beneficial characteristics, and the potential safety, efficacy and therapeutic effects of ficerafusp alfa;

- the timing, scope and likelihood of regulatory filings and approvals, for ficerafusp alfa and future product candidates, including the timing of Investigational New Drug applications, or INDs, and final U.S. Food and Drug Administration, or FDA approval of ficerafusp alfa or any future product candidate;

- the timing, scope or likelihood of foreign regulatory filings and approvals;

- our estimates of the number of patients that we will enroll and our ability to initiate, recruit and enroll patients in and conduct and successfully complete our clinical trials at the pace that we project;

- our ability to maintain and further develop the specific shipping, storage, handling and administration of ficerafusp alfa at the clinical sites;

- the ability and willingness of our third-party strategic collaborators to continue research and development activities relating to our development candidates and ficerafusp alfa;

- our ability to obtain funding for our operations necessary to complete further development and commercialization of ficerafusp alfa;

- our ability to obtain and maintain regulatory approval of ficerafusp alfa;
- our ability to commercialize ficerafusp alfa, if approved;
- the pricing and reimbursement of ficerafusp alfa, if approved;
- the implementation of our business model, and strategic plans for our business, ficerafusp alfa and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering ficerafusp alfa and other product candidate we may develop, including the extensions of existing patent terms where available, the validity of intellectual property rights held by third parties and our ability not to infringe, misappropriate or otherwise violate any third-party intellectual property rights;
- estimates of our future expenses, revenues and capital requirements and our needs for additional financing;
- future agreements with third parties in connection with the development and commercialization of ficerafusp alfa and any other approved product;
- the size and growth potential of the markets for ficerafusp alfa and our ability to serve those markets;
- our financial performance;
- the rate and degree of market acceptance of ficerafusp alfa;
- regulatory developments in the U.S., Canada, European Union and other foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- our ability to produce our products or ficerafusp alfa with advantages in turnaround times or manufacturing cost;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the impact of laws and regulations;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under the caption “Risk Factors.”

In some cases, forward-looking statements can be identified by terminology such as “may,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk Factors” and elsewhere in this Form 10-K. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this Form 10-K and the documents that we reference in this Form 10-K and have filed with the Securities and Exchange Commission, or SEC, as exhibits hereto completely and with the understanding

that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this Form 10-K represent our views as of the date of this Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Form 10-K.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to unduly rely upon these statements.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for our product candidates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market, and other data from our own internal estimates and research as well as from reports, research surveys, studies, and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. While we are not aware of any misstatements regarding any third-party information presented in this Annual Report on Form 10-K, their estimates, in particular as they relate to projections, involve numerous assumptions, are subject to risks and uncertainties and are subject to change based on various factors, including those discussed under the section titled "Risk Factors" and elsewhere in this Annual Report on Form 10-K.

NOTE REGARDING TRADEMARKS

Bicara Therapeutics, Inc. is the owner of the Bicara trademark, as well as certain other trademarks, including design versions of some of these trademarks. The symbols ™ and ® are not used in connection with the presentation of these trademarks in this report and their absence does not indicate a lack of trademark rights. Certain other trademarks used in this report are the property of third-party trademark owners and may be presented with or without trademark references.

All brand names or trademarks appearing in this report are the property of their respective owners. Unless the context requires otherwise, references in this report to "Bicara," the "Company," "we," "us" and "our" refer to Bicara Therapeutics, Inc. and its subsidiary.

Part I

Item 1. Business

Overview

We are a clinical-stage biopharmaceutical company committed to bringing transformative bifunctional therapies to patients with solid tumors. We have built a platform designed to facilitate the development of bifunctional therapies that precisely target the tumor and deliver a tumor-modulating payload to the tumor site. This dual-targeting approach both enhances drug exposure within the tumor microenvironment, or TME, and limits systemic toxicity. This approach was deployed in the development of our lead program ficerafusp alfa, formerly BCA101, where we believe the bifunctional design can potentially improve upon the therapeutic profile of immunotherapies and targeted therapies by addressing resistance mechanisms and limiting off-target toxicity, therefore, enhancing the treatment effect and tolerability for targeted patient populations with cancer.

Our lead program ficerafusp alfa is a bifunctional antibody that combines two clinically validated targets, an epidermal growth factor receptor, or EGFR, directed monoclonal antibody with a domain that binds to human transforming growth factor beta, or TGF-β. Through this dual-targeting mechanism, ficerafusp alfa has the potential to exert potent anti-tumor activity by simultaneously blocking both cancer cell-intrinsic EGFR survival and proliferation, as well as the immunosuppressive TGF-β signaling within the TME. Ficerafusp alfa directs the TGF-β inhibitor into the immediate TME through the binding of EGFR on tumor cells, which we believe will lead to durable responses and an increase in overall survival, or OS, while reducing the adverse effects typically associated with systemic TGF-β inhibition. Ficerafusp alfa is initially being developed in head and neck squamous cell carcinoma, or HNSCC, where there remains a significant unmet need. In June 2023, in an oral presentation at an American Society of Clinical Oncology meeting, we first presented data from our Phase 1/1b dose expansion cohort evaluating ficerafusp alfa in combination with pembrolizumab in first-line recurrent/metastatic, or R/M, HNSCC patients with a CPS greater than or equal to one which demonstrated meaningful response rates, progression-free survival, and was generally well-tolerated.

Based on the preliminary clinical data generated to date, we believe that ficerafusp alfa in combination with pembrolizumab has the potential to become a first-line standard of care therapy in R/M HNSCC. In February 2025, we enrolled the first patients in FORTIFI-HN01, a pivotal Phase 2/3 trial ("FORTIFI-HN01 Phase 2/3 trial" or "FORTIFI-HN01") of ficerafusp alfa in combination with pembrolizumab as a first-line therapy in R/M HNSCC excluding patients with oropharyngeal squamous cell carcinoma, or OPSCC, associated with human papillomavirus infection, or HPV-positive OPSCC patients.

We believe ficerafusp alfa also has the potential to provide meaningful clinical benefit in other solid tumors where there is a strong biologic rationale for the dual inhibition of both EGFR and TGF-β, such as colorectal cancer or CRC, and other squamous cell carcinomas which typically overexpress EGFR and TGF-β pathways such as cutaneous squamous cell carcinoma, or CSCC, and squamous cell carcinoma of the anal canal, or SCAC. We have demonstrated preliminary activity of ficerafusp alfa in combination with pembrolizumab or as a monotherapy in both CSCC and SCAC within our Phase 1/1b dose expansion cohorts conducted in the U.S. and Canada.

Ficerafusp alfa: a bifunctional EGFR-directed antibody x TGF-β trap

EGFR is the primary member of a larger family of cell-surface growth factor receptors harboring intrinsic tyrosine kinase function. EGFR is involved in many tumor-promoting pathways. Its overexpression has been linked to multiple squamous cell cancers, including HNSCC, where EGFR expression has been shown to be greater than 90%. EGFR has been a long-standing focus for cancer drug development due to the correlation between EGFR expression, poor prognosis and resistance to therapy. Cetuximab is an EGFR-directed monoclonal antibody approved for HNSCC and colorectal cancer that drives anti-tumor responses by inhibiting EGFR signaling and through antibody-dependent cell-mediated cytotoxicity, or ADCC. However, acquired resistance mechanisms to cetuximab can prevent durable responses. We believe that there is a significant market opportunity for EGFR targeted therapies with improved efficacy, durability and OS compared to cetuximab.

TGF-β is a cytokine that controls a range of biological functions and is widely understood to play a critical role in cancer. TGF-β perpetuates tumor survival by promoting tumor cell proliferation, migration, invasion and metastasis. TGF-β also serves as an immunosuppressant, inhibiting both natural killer, or NK, cells and cytotoxic T cells. The inhibition of TGF-β has been demonstrated to improve anti-tumor responses in vivo. However, these findings have not been translated into substantial improvements in clinical efficacy, which we believe may be due to the inability to sufficiently inhibit TGF-β directly within the TME. Increased TGF-β expression within the TME contributes to an immune-excluded environment that can hinder an effective immune response to tumor formation and growth.

Ficerafusp alfa is a bifunctional antibody that combines the well-established biologies of both the clinically validated anti-EGFR antibody cetuximab and a TGF-β binding domain to deliver a potent anti-tumor therapy, sequestering TGF-β directly to EGFR-expressing tumors with the goal of limiting off-target toxicity. We have shown both in vitro and in vivo that ficerafusp alfa performs as expected, by binding to both targets, localizing to the tumor, inhibiting tumor growth and suppressing TGF-β levels within tumors.

Our initial focus with ficerafusp alfa: R/M HNSCC

HNSCC is one of the most common cancers in the U.S. and globally with a rising incidence anticipated to reach one million new global cases annually by 2030. There are approximately 67,000 cases of HNSCC each year in the U.S with a 13% 5-year survival rate. Ten percent of HNSCC patients are diagnosed with metastatic disease and up to 30% develop a recurrence or metastases over time after initial treatment for advanced HNSCC. There are approximately 23,000 cases of R/M HNSCC each year in the U.S. Median OS for patients with R/M HNSCC is only 12 months. Most cases of HNSCC are believed to arise from mutations that accumulate due to carcinogenic exposure, such as tobacco smoke, or by HPV. Approximately 80% of patients with R/M HNSCC are not associated with HPV infection or HPV-negative, a status associated with a worse prognosis. Pembrolizumab with or without chemotherapy is the standard of care for R/M HNSCC patients who have evidence of PD-L1 expressing tumors is pembrolizumab monotherapy. The KEYNOTE-048 Phase 3 trial of pembrolizumab conducted by Merck & Co. Inc., or Merck & Co, demonstrated an ORR of 19% to pembrolizumab monotherapy with a median progression-free survival, or mPFS of 3.2 months in a population of HPV-negative and HPV-positive patients with CPS greater than or equal to one. For patients with a CPS less than one and no PD-L1 expression within their TME, the typical standard of care is a combination of cetuximab and chemotherapy, referred to as the EXTREME regimen, which has low response rates and survival, as well as a difficult tolerability profile.

We believe the poor prognoses in HPV-negative R/M HNSCC and the low ORR associated with available therapies may be attributed to the elevated levels of TGF-β observed in these patients. It has been shown in translational studies that EGFR inhibition leads to further increases in TGF-β levels which result in the development of resistance to EGFR-targeted therapeutics. We believe blocking TGF-β has the potential to prevent resistance and improve the anti-tumor activity of anti-EGFR therapies, leading to more durable responses and an increase in OS. Similarly, inhibiting TGF-β may reduce the fibrosis and immune-exclusion within the TME that could be responsible for the low efficacy seen with checkpoint inhibitors in these immunosuppressive, or “cold” tumors. We believe promoting immune activation via TGF-β blockade may translate to significant increases in anti-tumor efficacy, particularly in the depth and durability of responses in combination with anti-PD1 therapies.

We are working to bring ficerafusp alfa, a potentially transformative therapy, to patients as quickly as possible. In February, 2025 we enrolled the first patients in FORTIFI-HN01, a double-blind, placebo-controlled Phase 2/3 trial in R/M HNSCC patients, excluding patients with HPV-positive OPSCC, which we believe is sufficiently powered to achieve results that may lead to accelerated approval. This trial will enroll approximately 650 patients with a PD-L1 CPS greater than or equal to one, and who have not received systemic therapy in the R/M setting. We intend to conduct an interim analysis to determine if the ORR within 6 months of follow-up on durability is sufficient to seek accelerated approval and will continue the trial with the goal of demonstrating a statistically significant improvement in OS. We anticipate that the ORR interim analysis may occur in 2027.

We believe our competitive strengths will allow us to successfully develop, commercialize and maximize the impact of ficerafusp alfa:

- **Validated dual-targeting mechanism of action with potential to exert potent and durable anti-tumor activity.**

  Ficerafusp alfa is a bifunctional antibody designed to simultaneously block both cancer cell-intrinsic EGFR survival and proliferation, as well as the well-understood immunosuppressive TGF-β signaling within the TME. Ficerafusp alfa leverages the established biology of the clinically validated anti-EGFR antibody cetuximab. However, ficerafusp alfa is differentiated from existing therapies through the targeting of TGF-β, which localizes the ligand to EGFR expressing tumor cells, potentially increasing its activity at the tumor site and limiting systemic toxicity. Importantly, TGF-β inhibition synergizes with EGFR, which we believe will prevent resistance to treatment and lead to more durable responses.

- **Clinical data generated to date representing meaningful improvements over standard of care.**

  We have generated compelling interim clinical data for ficerafusp alfa in a Phase 1/1b trial of R/M HNSCC patients. In this trial, treatment with ficerafusp alfa in combination with pembrolizumab led to a 64% ORR (18/28) in HPV-negative patients. The combination also demonstrated an 18% (5/28) CR rate and mPFS of 9.8 months in the same patient population. As of April 2024, with at least 12 months of follow-up, median OS and mDOR had not yet been reached, and we expect to announce updated interim Phase 1/1b data at a future medical meeting in the first half of 2025. We believe that ficerafusp alfa in combination with pembrolizumab has the potential to become a first-line standard of care therapy in HPV-negative R/M HNSCC.

- **Potential to address significant unmet need in HPV-negative R/M HNSCC with clear development pathway.**

  HNSCC is one of the most common cancers, accounting for approximately 4% of all cancers in the U.S. An estimated 80% of R/M HNSCC cases are HPV-negative, a status associated with significantly worse outcomes compared to HPV-positive patients. We are prioritizing our initial development efforts in HPV-negative R/M HNSCC given the significant unmet need for durable therapies in this patient population. We also believe that ficerafusp alfa will be most effective in this patient subset given the (1) high expression of EGFR, (2) elevated levels of TGF-β and (3) current preclinical and clinical data, including from our own Phase 1/1b study, supporting increased activity within HPV-negative patients. We believe our deliberate patient selection strategy provides the best opportunity to demonstrate the potential of ficerafusp alfa as a first-line therapy.

- **Potential to expand the clinical development of ficerafusp alfa in additional patient populations within HNSCC and other solid tumors of squamous cell origin.**

  Beyond our initial development plans, we believe there are significant opportunities to expand the clinical development of ficerafusp alfa to other populations of HNSCC patients with greater than 60,000 cases each year in the U.S., including for the treatment of locally advanced HPV-negative HNSCC and in the neoadjuvant or adjuvant setting. We also believe ficerafusp alfa has the potential to provide meaningful clinical benefit in other EGFR-expressing solid tumors of squamous cell origin, such as colorectal cancer, SCAC, CSCC and other squamous cell carcinomas where there is a strong biologic rationale for the dual-inhibition of EGFR and TGF-β pathways. We plan to explore these additional development opportunities to maximize the potential of ficerafusp alfa for the treatment of cancer.

The Established Role of EGFR and TGF-β in Squamous Cell Carcinomas and other Solid Tumors

Targeting EGFR in squamous cell carcinomas and other solid tumors

EGFR is a cell-surface tyrosine kinase growth factor receptor that is involved in many tumor-promoting pathways. Activation of EGFR pathways leads to cell cycle progression, reduction in cell death, blood vessel formation and a metastatic phenotype. EGFR overexpression has been linked to several cancers of squamous cell origin, including HNSCC, CSCC, SCAC and colorectal cancer. Several of these cancer types show EGFR expression in tumors to be greater than 50%, with greater than 90% expression in HNSCC. EGFR overexpression in tumors has been shown to correlate with poor prognosis and resistance to therapy. For this reason, the development of therapies targeting EGFR has been a long-standing focus in cancer drug development.

EGFR-directed monoclonal antibodies, such as cetuximab, drive anti-tumor responses both through inhibiting EGFR signaling and through ADCC. ADCC-mediated cell killing occurs when NK cells recognize and bind to antibodies containing an IgG1 Fc domain, which are bound to their respective tumor cell surface antigens. Cetuximab is approved in HNSCC and colorectal cancer, two tumor types where EGFR overexpression is at its highest and has also shown the highest anti-tumor efficacy. The durability of EGFR-targeted therapies has been limited by acquired resistance mechanisms.

Due to its role as a well-validated tumor antigen, EGFR-directed monoclonal antibodies are utilized to deliver anti-tumor payloads directly to the tumor. Currently, there are several EGFR antibody-drug conjugates and bispecific antibodies in development that aim to mitigate the systemic toxicities of chemotherapy-derived drug conjugates by delivering these payloads directly to EGFR-expressing tumors.

The role of TGF-β in cancer progression

TGF-β is a cytokine molecule that functions as a master regulator of immunity and cellular signaling that controls a wide range of biological functions. TGF-β plays multiple essential roles in the body's early development and survival as well as in maintaining health in mature organisms.

In oncogenesis, or the process by which normal, healthy cells turn into cancerous cells, TGF-β both promotes tumor growth and shields tumors from immune surveillance and removal. TGF-β1 is the most commonly expressed isoform of TGF-β in various human tumor types and is predominantly expressed in cancers of squamous-cell origin, such as HNSCC. Third party studies have demonstrated that TGF-β1 expression and activation likely contribute to immune escape, which is linked to the primary resistance observed in human tumors against certain cancer therapies. As depicted in Figure 1 below, its immunosuppressive functions are accomplished through a variety of tumor survival mechanisms.

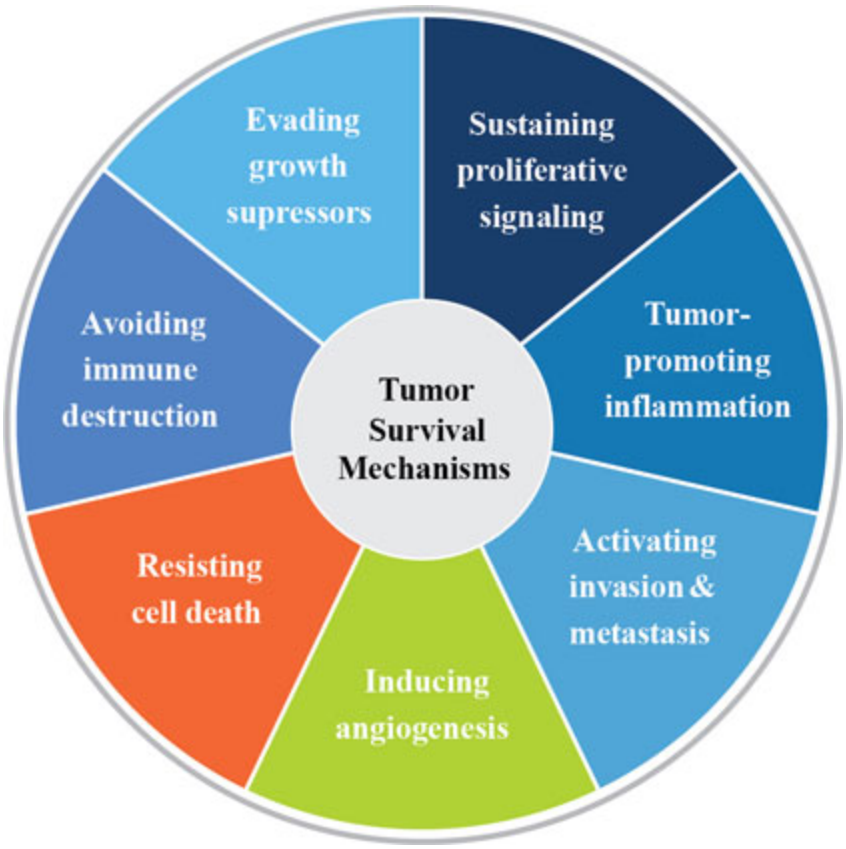


Figure 1. TGF-β promotes tumor survival through multiple mechanisms

TGF-β also serves as a tumor promoter by transforming cells from a more differentiated state to a less differentiated, more primitive state that is no longer dependent on EGFR signaling for proliferation and survival. This shift is known as the epithelial-mesenchymal transition, or EMT, which leads to tumor cell proliferation, migration, invasion and metastasis. Due to its role in cancer progression, we believe the inhibition of TGF-β has the potential to both limit the tumors' ability to escape EGFR inhibition by switching to an EGFR signaling independent phenotype, as well as restore the immune system's ability to repress tumor growth.

TGF-β as a known EGFR-therapy resistance mechanism

When EGFR signaling is blocked by targeted therapy, tumors respond by increasing TGF-β expression within the TME. This results in an increase in tumor cell proliferation and a decrease in the tumor's dependence on EGFR activation, thus making the tumor less sensitive to EGFR inhibition.

In addition to inhibiting direct cell killing by EGFR inhibition, TGF-β protects cells from ADCC both by the activation of survival pathways in tumor cells and through the modulation of the NK cell response. Furthermore, TGF-β both blocks the differentiation of NK cells and reduces NK cell cytotoxicity.

Preclinical studies suggest that targeting TGF-β may lead to improvements in overall efficacy. As depicted in Figure 2 below, experiments published in Molecular Cancer Therapeutics in a squamous cell carcinoma cell line xenograft model demonstrate that simultaneous treatment with EGFR and TGF-β blocking antibodies led to complete tumor regression.

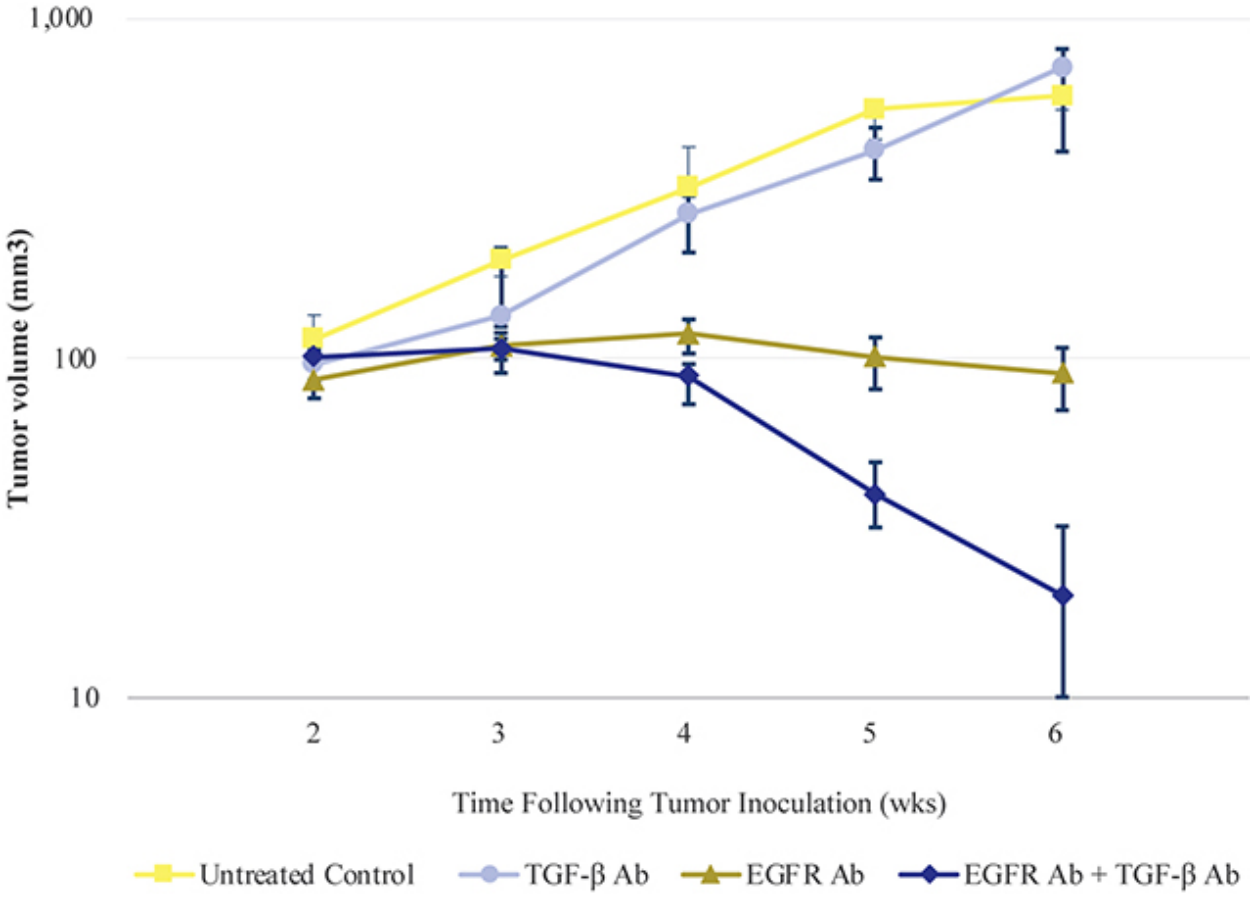


Figure 2. The combination of an anti-EGFR and an anti-TGF-β antibody led to complete regression of a squamous cell carcinoma cell line xenograft tumors

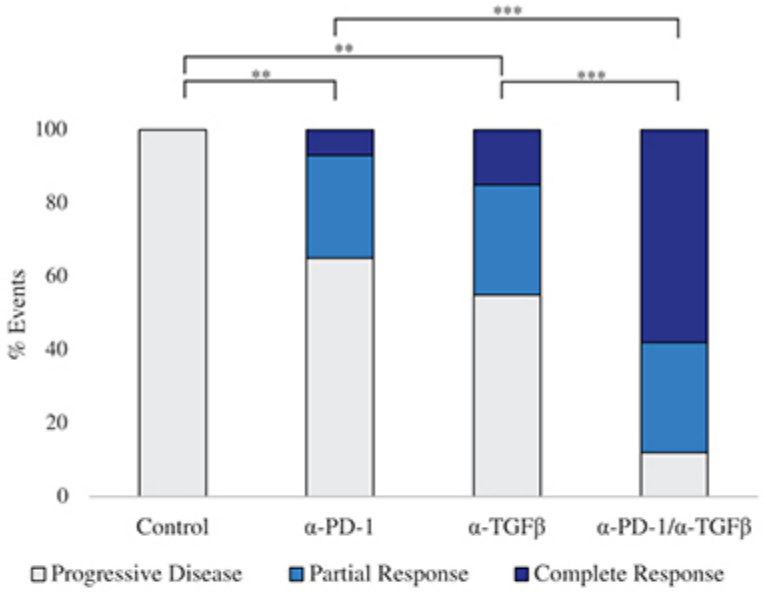
TGF-β as a known checkpoint inhibitor resistance mechanism

The activities of TGF-β extend to the inhibition of cancer immunotherapies known as checkpoint inhibitors. TGF-β inhibits the activation of T cells by PD-1 checkpoint inhibitors and can lead to resistance to anti-PD-1/PD-L1 therapy by promoting immunosuppression and immune exclusion within the TME.

TGF-β promotes immune tolerance of tumors by inducing differentiation of naïve CD4 T cells into regulatory T cells, or Treg cells. Treg cells are components of the immune system that contribute to the maintenance of immune tolerance. TGF-β can shift the differentiation of naïve CD4 T cells towards Treg cells, thereby leading to immunosuppression. In addition, TGF-β inhibits tumor cell killing by immune cell populations, including CD4 and CD8 T cells and NK cells.

Increased TGF-β expression within the TME contributes to an immune-excluded environment. Specifically, cancer-associated fibroblasts, or CAFs, expressing TGF-β contribute to fibrosis within the TME and result in T-cell exclusion, further limiting the activity of immunotherapy.

As depicted in Figure 3 below, in vivo academic studies in an HNSCC xenograft model demonstrated that the effectiveness of anti-PD-1 checkpoint inhibitors was greatly enhanced when administered in combination with anti-TGF-β therapy. Combining an anti-PD-1 antibody with an anti-TGF-β antibody led to significant increases in both CR (top figure) and OS (bottom figure) in this model.



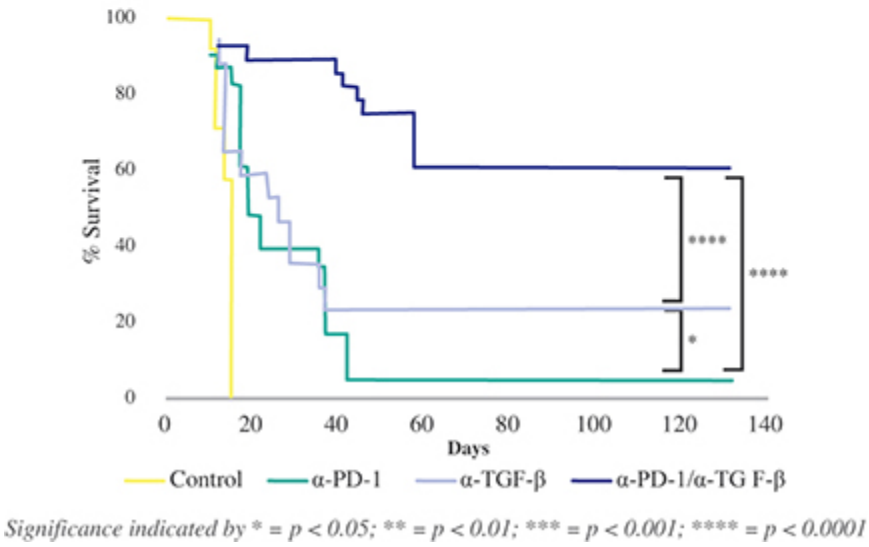


Figure 3. The combination of anti-PD-1 and anti-TGF-β led to improved CR and OS in a SCC xenograft model

Systemic inhibition of TGF-β has had significant limitations in the clinic

The multiple tumor-promoting roles associated with TGF-β have led to multiple attempts to develop systemic anti-TGF-β therapies for the treatment of cancer. These strategies include molecules that inhibit TGF-β activation, molecules that prevent the binding of TGF-β to its cognate receptors, and inhibitors that block intracellular signaling. Despite promising in vitro and in vivo activity, the outcomes from clinical trials have shown side effects and inadequate improvement in survival.

The first generation of anti-TGF-β therapies had dose-limiting side effects including cardiotoxicities, heart valve lesions, increased risk of bleeding and formation of benign tumors, that were associated with inhibiting all three isoforms of TGF-β. Adverse events associated with systemic inhibition of TGF-β led to dose reductions and treatment interruptions that may have contributed to limited efficacy in cancer clinical trials.

Similarly, given the role of TGF-β in checkpoint inhibitor resistance, prior attempts have been made to combine checkpoint inhibitors and anti-TGF-β therapies, although they have not been clinically successful. These approaches include bintrafusp alfa, a bifunctional fusion protein that combines a PD-L1 monoclonal antibody and a TGF-β trap. These agents failed to demonstrate sufficient efficacy in large clinical studies, which we believe may be due to insufficient anti-tumor activity within the TME, a result of PD-L1 predominately being expressed in immune tissue rather than within the TME. We believe a tumor-targeted TGF-β inhibitor may differentiate in its ability to deliver potent anti-tumor activity directly within the TME and minimize toxicity, where untargeted approaches may have struggled.

Our Solution: ficerafusp alfa, a Novel Bifunctional Antibody

Ficerafusp alfa is a bifunctional antibody that combines the well-established biologies of two targets—the anti-EGFR antibody, cetuximab, fused to the extracellular domain of TGF-β receptor 2, or TGF-βRII. As indicated in Figure 4 below, ficerafusp alfa was designed to use EGFR-binding to deliver potent anti-TGF-β therapy directly to EGFR-expressing tumors, potentially removing circulating TGF-β and neutralizing its signaling activity using a strategy known as a "ligand trap". We believe that localized TGF-β inhibition within the TME has the potential to increase its anti-tumor efficacy and durability, while limiting systemic toxicity. We also deliberately chose EGFR as the tumor-targeting antigen for a TGF-β ligand trap given academic literature supports potential synergistic mechanisms of TGF-β blockade and EGFR signaling inhibition.

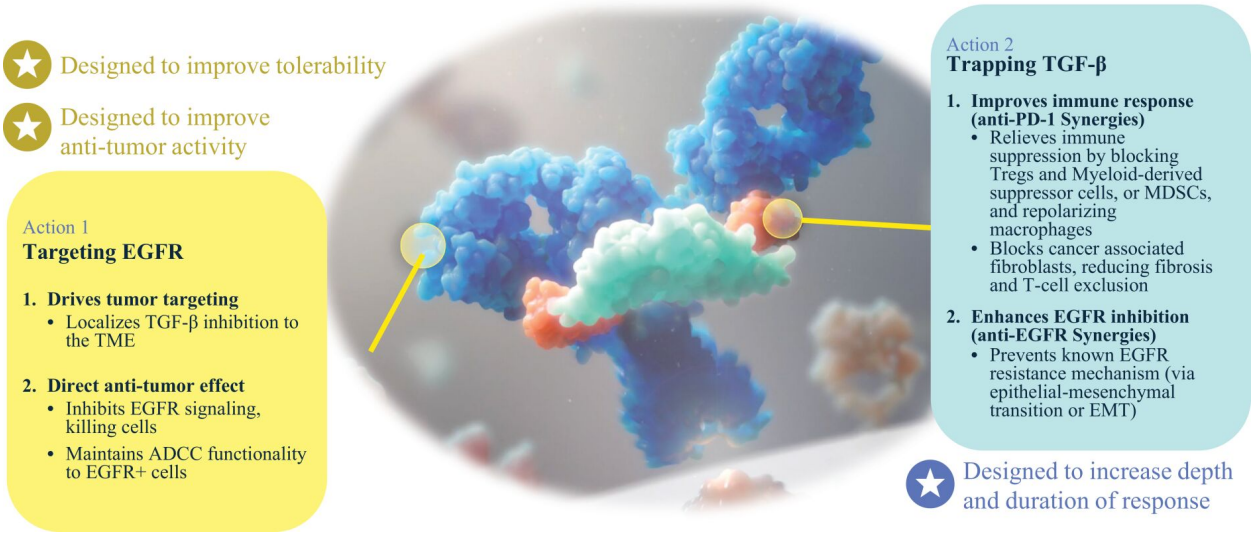


Figure 4. Schematic of intended mechanism of action of ficerafusp alfa within the TME to overcome anti-EGFR and anti-PD-1 drug resistance

Ficerafusp alfa was designed to overcome key shortcomings of prior approaches to targeting EGFR and TGF-β

Specifically, we believe that ficerafusp alfa is differentiated from previous and existing approaches given the following:

- **ficerafusp alfa localizes TGF-β inhibition directly to EGFR expressing tumor cells.** We believe this will lead to higher concentrations within the TME to increase the inhibition, reduce overall dose and enhance tolerability.

- **ficerafusp alfa may help prevent acquired resistance to EGFR-targeted therapies.** Dual targeting of TGF-β alongside EGFR may prevent key resistance mechanisms driven by upregulation of TGF-β and may drive durable tumor responses.

- **ficerafusp alfa synergizes with anti-PD-1 therapies.** Targeting TGF-β directly in the TME may relieve immune cell suppression and exclusion and enhance both the immune response as well as the activity of anti-PD-1 therapies.

Ficerafusp alfa simultaneously binds both EGFR and TGF-β1 with high specificity and drives improved anti-tumor activity

As depicted in Figure 5 below, ficerafusp alfa has a similar affinity for EGFR as cetuximab and the same selectivity for TGF-β1, the cancer-associated isoform of TGF-β, as TGF-βRII-Fc. As illustrated in the graphic on the right in Figure 5 below, in a head-to-head study it was demonstrated that ficerafusp alfa is differentiated in its ability to simultaneously bind to both EGFR and TGF-β1, while no such binding to TGF-β1 was observed when cetuximab was used in place of ficerafusp alfa.

Sample	Mean Binding Affinity K_D (nmol/L)	Standard Deviation
EGFR Binding		
ficerafusp alfa	2.58	0.63
cetuximab	1.16	0.19
TGF-β1 Binding		
ficerafusp alfa	61.3	13.29
TGF-βRII-Fc	64.3	7.35

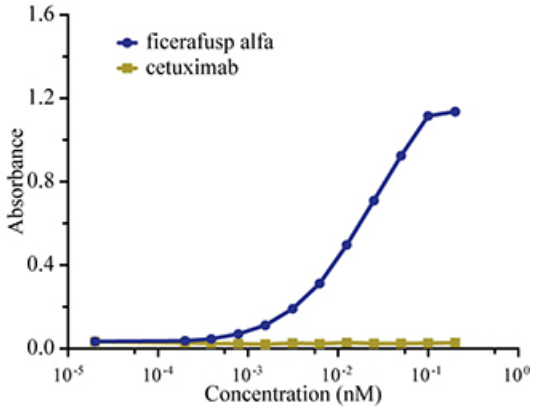


Figure 5. Ficerafusp alfa has potent binding affinities for both EGFR and TGF-β1

Furthermore, Figure 6 below illustrates that in a cutaneous cell carcinoma cell line xenograft model, treatment with ficerafusp alfa showed improved anti-tumor activity compared to both cetuximab monotherapy and to the combination of cetuximab with an equimolar TGF-βRII-Fc construct. This demonstrates the improved anti-tumor activity associated with the bifunctional nature of ficerafusp alfa driving the localization of anti-TGF-β activity to the TME through an EGFR-directed approach.

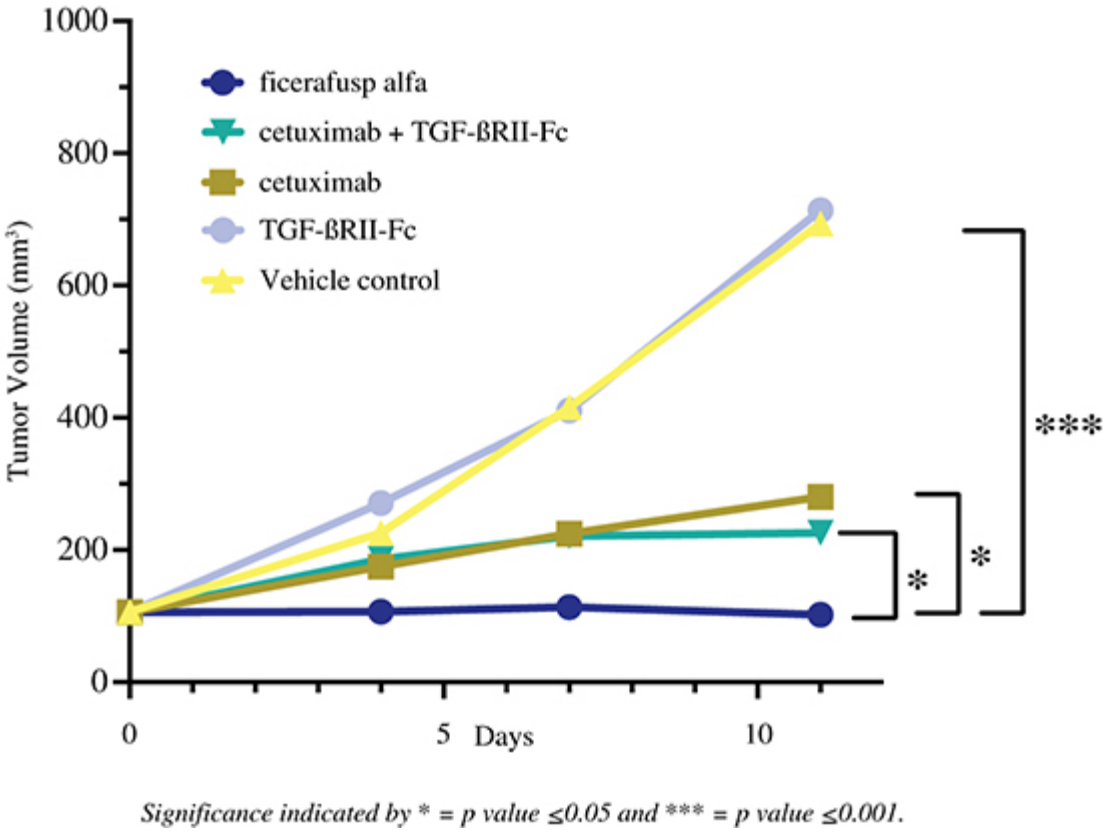


Figure 6. Ficerafusp alfa showed improved anti-tumor activity in a cutaneous cell carcinoma cell line xenograft model compared to cetuximab or the combination of cetuximab and TGF-βRII-Fc

Clinical biomarker data demonstrates ficerafusp alfa inhibits TGF-β in tumors

Biomarkers sampled from patients treated with ficerafusp alfa in our Phase 1/1b trials demonstrated direct TGF-β inhibition within the TME and support ficerafusp alfa's tumor targeted inhibition. As shown in Figure 7 below, treatment with ficerafusp alfa monotherapy at doses greater than 750mg led to statistically significant reductions in phospho-SMAD2, or pSMAD2, which is a direct downstream biomarker of the TGF-β pathway. Figure 7 below also depicts a representative immunohistochemistry, or IHC, slide derived from patient tumor biopsies both prior to and after one dose of 1000mg of ficerafusp alfa monotherapy. Importantly, to our knowledge, this biomarker data represents the first definite demonstration of pSMAD2 inhibition in patient tumors by a TGF-β inhibitor.

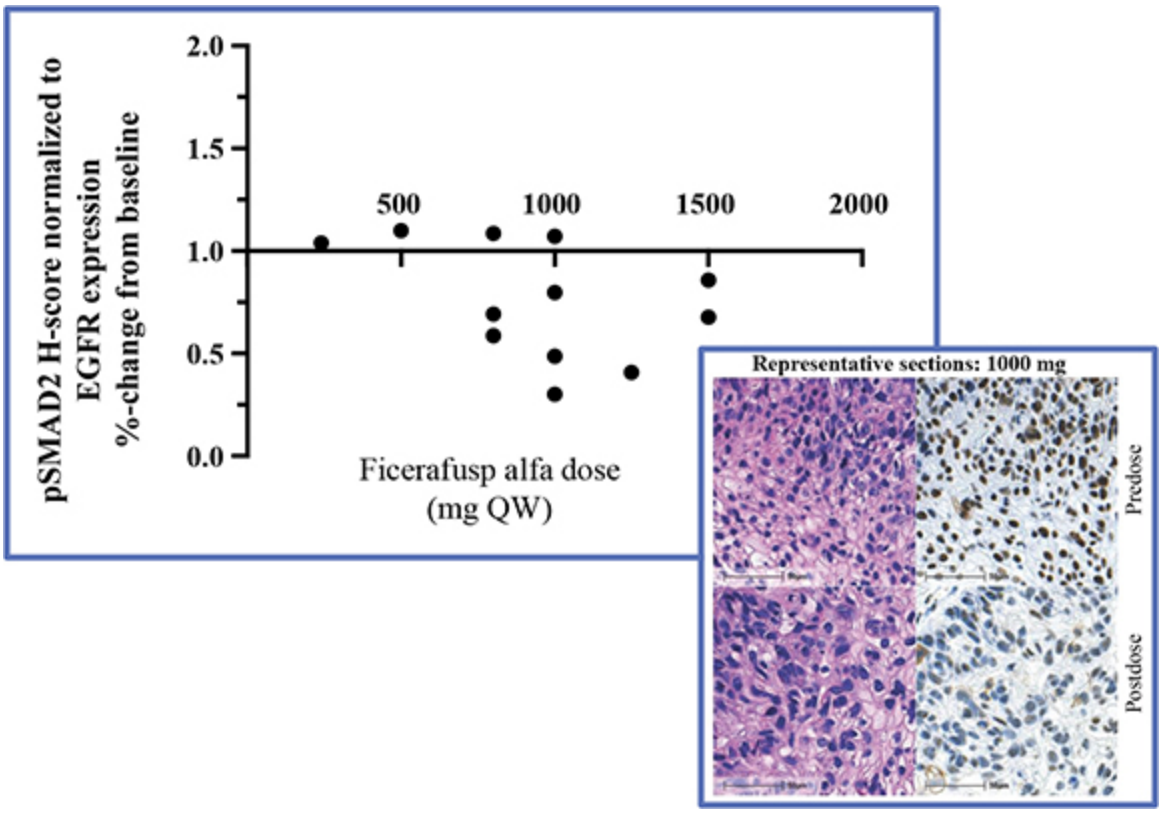


Figure 7. Percent Change from baseline in pSMAD2 from pre-dose to post-dose in patient tumors (left) and representative IHC slide showing statistically significant reduction in pSMAD2 from pre-dose to post-dose at 1000mg of ficerafusp alfa monotherapy in solid tumors (right)

Preclinical in vivo models demonstrate ficerafusp alfa may have an enhanced ability to prevent tumor relapse compared to cetuximab

Preclinical experiments in patient derived xenograft models of EGFR-expressing treatment-naïve HNSCC tumors demonstrate that ficerafusp alfa may have an enhanced ability to prevent tumor relapse compared to cetuximab. While both agents show significant reductions in tumor growth, treatment with ficerafusp alfa demonstrates sustained anti-tumor effects in a treatment-free, or relapse, phase post day 28. This is demonstrated in Figure 8 below in which 5 out of 10 mice receiving cetuximab had a tumor relapse post day 28 that was not observed for those receiving ficerafusp alfa. We believe the prevention of relapse may be attributable to the TGF-β arm of ficerafusp alfa, which is consistent with the mechanistic rationale behind ficerafusp alfa's design in which inhibiting TGF-β may prevent acquired resistance to anti-EGFR therapy and result in durable anti-tumor activity.

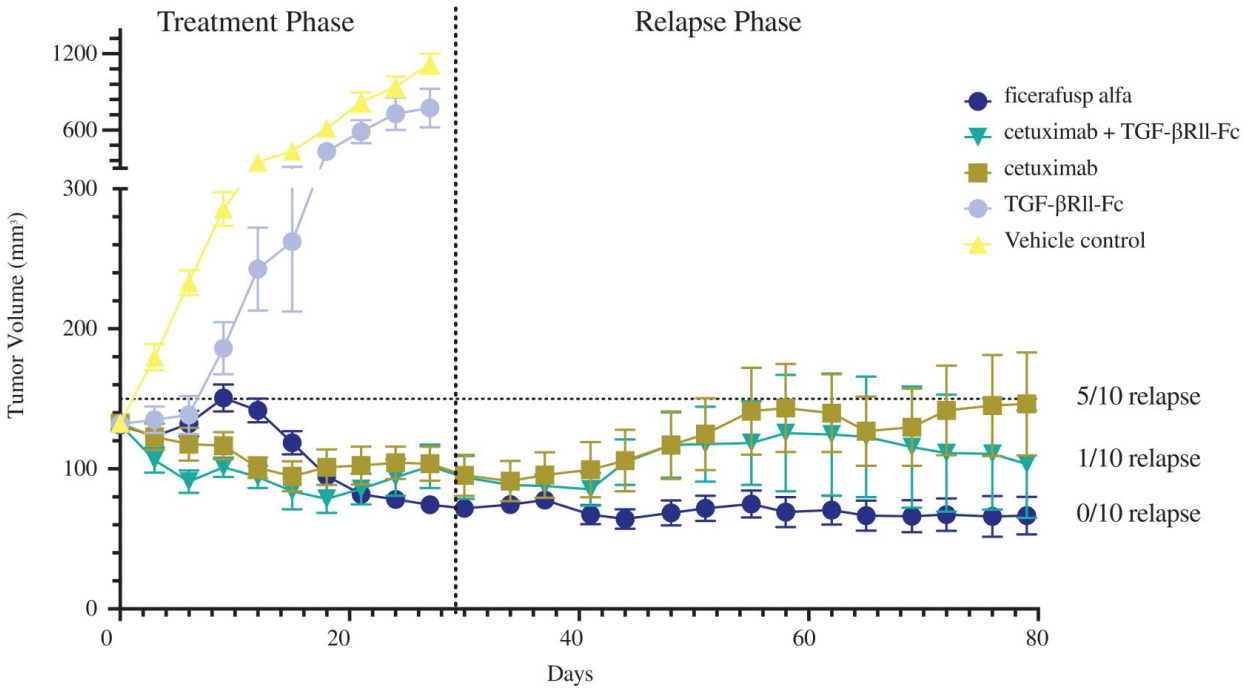


Figure 8. Ficerafusp alfa demonstrates sustained anti-tumor effects in a patient-derived HNSCC xenograft model compared to cetuximab

Ficerafusp alfa synergizes with anti-PD-1 therapies, with anti-tumor activity superior to anti-PD-1 therapy alone

To assess the synergy between ficerafusp alfa and anti-PD-1 therapies, we developed a cancer mouse model, in which mice were dosed with an anti-PD-1 antibody in combination with ficerafusp alfa. For this Hu-NOG EXL model published in Cancer Research, anti-PD-1 refractory prostate cancer PC3 cells were implanted into mice and once the tumor had grown to 130mm3, mice were randomized into control (n = 10) and test groups which were treated with ficerafusp alfa (n = 10), pembrolizumab (n = 10), or combination of ficerafusp alfa and pembrolizumab (n = 10). This model was powered for statistical significance. These results showed treatment with ficerafusp alfa in combination with pembrolizumab led to a statistically significant improvement in anti-tumor activity compared to pembrolizumab monotherapy, shown in Figure 9 below. We believe this data supports the ability of ficerafusp alfa to synergize with anti-PD-1 therapy in an anti-PD-1 refractory setting and potentially address TGF-β-driven immunosuppression.

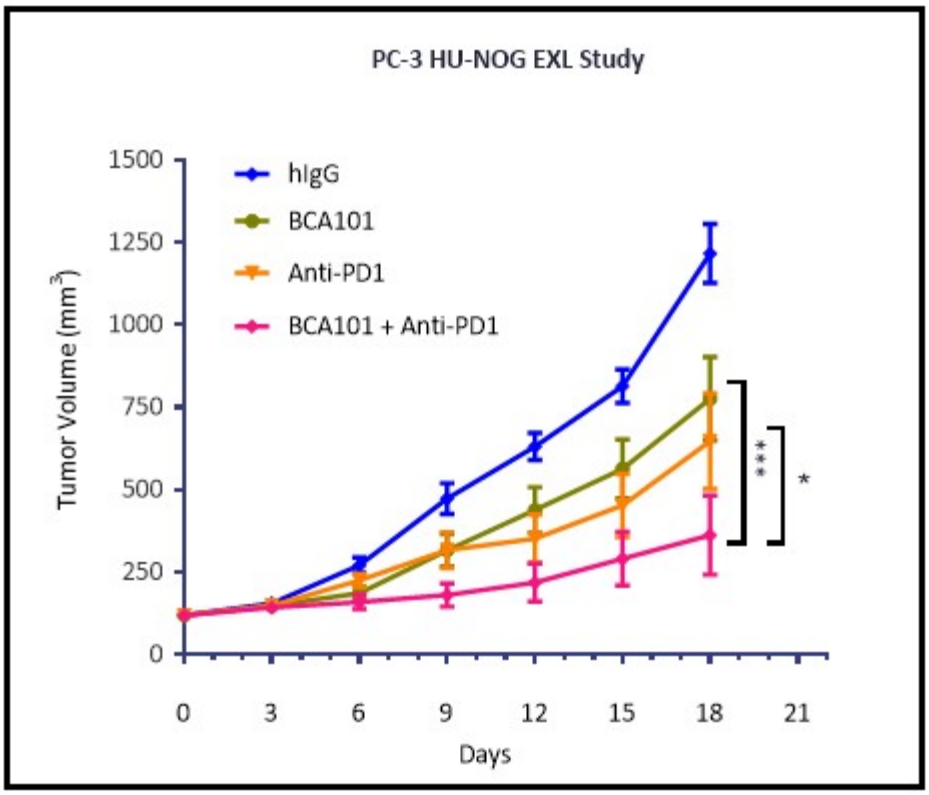


Figure 9. The combination of ficerafusp alfa and anti-PD-1 therapy demonstrates improved anti-tumor activity vs. anti-PD-1 therapy alone in a humanized xenograft model.

Ficerafusp Alfa Clinical Development Guided by Strong Biologic Rationale

We believe ficerafusp alfa has the potential to provide meaningful clinical benefit in solid tumors where there is a strong biologic rationale for the dual inhibition of both EGFR and TGF-β, such as head and neck cancers, colorectal cancer and other squamous cell carcinomas which typically overexpress EGFR and TGF-β pathways.

HNSCC background

Head and neck cancer accounts for approximately 4% of all cancers in the U.S. with over 90% of cases presenting with squamous cell origin. As depicted in Figure 10 below, HNSCC commonly originates in the mouth and throat, from the mucosa of the oral cavity, oropharynx, hypopharynx and larynx. It is estimated that by 2030 there will be approximately one million new cases of HNSCC worldwide annually. At the time of diagnosis, an estimated 10% of patients have metastatic disease, and up to 30% of additional patients develop a recurrence or metastases over time after initial treatment for advanced HNSCC. The median survival of patients with local-regional recurrences or distant metastases is approximately 12 months.

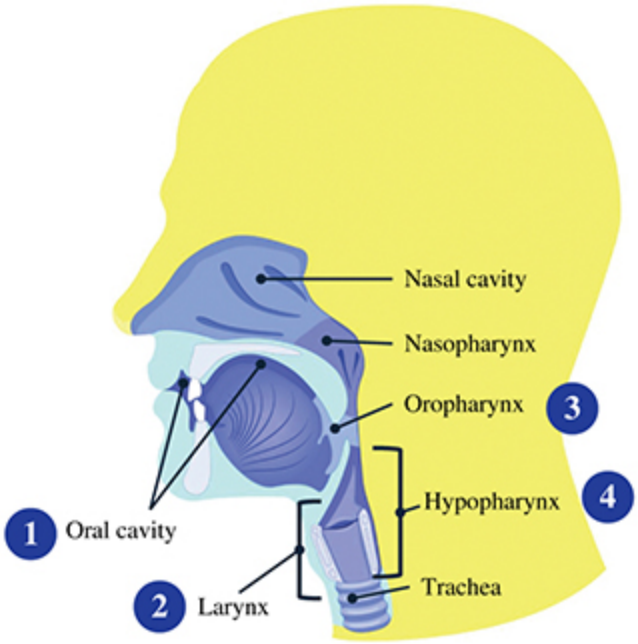


Figure 10. Subtypes of HNSCC by primary tumor origin. Numbered subtypes indicate where ficerafusp alfa is currently being tested.

Most cases of HNSCC are believed to arise from mutations that accumulate due to carcinogenic exposure, such as tobacco smoke or by HPV. An estimated 80% of cases of R/M HNSCC are HPV-negative, with testing for HPV status typically only being conducted in tumors originating from the oropharynx. HPV-negative patients have significantly worse outcomes compared with HPV-positive patients. HPV-negative HNSCC tumors typically recur locally and are associated with an increased risk of fatal tumor bleeding, excruciating pain and difficulty swallowing. Thus, there is a significant unmet need for therapies with a durable anti-tumor response in this population. HPV-negative HNSCC is also associated with a higher rate of genomic instability resulting in an increased resistance to therapy.

Treatment of R/M HNSCC

The standard of care first-line therapy for R/M HNSCC is determined by CPS which corresponds to the number of PD-L1 positive cells in relation to the total number of viable tumor cells. Patients with high CPS scores tend to respond better to PD-1 checkpoint inhibitors, as observed across multiple tumor types. In R/M HNSCC, pembrolizumab monotherapy is recommended for patients with a CPS greater than or equal to one. Pembrolizumab combined with platinum and 5-fluorouracil is recommended for patients with any PD-L1 status. The addition of chemotherapy to pembrolizumab increases the response rate; however, it also significantly reduces the duration of response while increasing toxicity and leads to roughly equivalent median OS with both treatments. For patients with a CPS less than one and no PD-L1 expression within their TME, the typical standard of care is the EXTREME regimen, a combination of cetuximab and chemotherapy, which has low response rates and survival, as well as a difficult tolerability profile.

The Phase 3 KEYNOTE-048 trial conducted by Merck & Co investigated pembrolizumab as a monotherapy or in combination with chemotherapy, compared to cetuximab with chemotherapy in first-line R/M HNSCC. The pembrolizumab monotherapy and pembrolizumab and chemotherapy combination response rates of 19% and 36%, respectively, were comparable to the 36% ORR for cetuximab and chemotherapy combination in patients with CPS greater than or equal to one. In these patients, pembrolizumab monotherapy and in combination with chemotherapy led to median OS of 12.3 and 13.6 months, respectively, compared to 10.4 months in the active control arm. While this represents a step forward, there remains significant unmet need in R/M HNSCC for more efficacious therapies that can extend survival, especially for chemotherapy-free alternatives with superior tolerability.

TGF-β expression may limit the effectiveness of HNSCC therapies

Immune checkpoint inhibitors, such as pembrolizumab, activate T cells to attack tumors and their efficacy is dependent on the number of mutations in the tumor. Tumors with more mutations are easier to recognize and are attacked by T cells, thus are the types of tumors that respond more favorably to immune checkpoint inhibitors. Despite the high mutation load in HPV-negative HNSCC, monotherapy with immune checkpoint inhibitors is associated with relatively low ORR compared to other indications such as NSCLC.

Similar observations of poor response rates have been reported for cetuximab in R/M HNSCC. EGFR is expressed in greater than 90% of HNSCC tumors and its overexpression is correlated with decreased survival, resistance to radiation, local treatment failure and increased distant metastasis. In R/M HNSCC, only 13% of patients respond to cetuximab monotherapy, suggesting that there is some form of intrinsic resistance. Third-party clinical studies have demonstrated a statistically significant positive correlation in EGFR-overexpression in HPV-negative HNSCC tumor biopsies.

As depicted in Figure 11 below, third-party clinical studies have shown plasma samples from patients with HPV-negative HNSCC to have significantly higher levels of TGF-β than non-HNSCC controls, whereas TGF-β levels in HPV-positive HNSCC patients are not significantly different than those of controls.

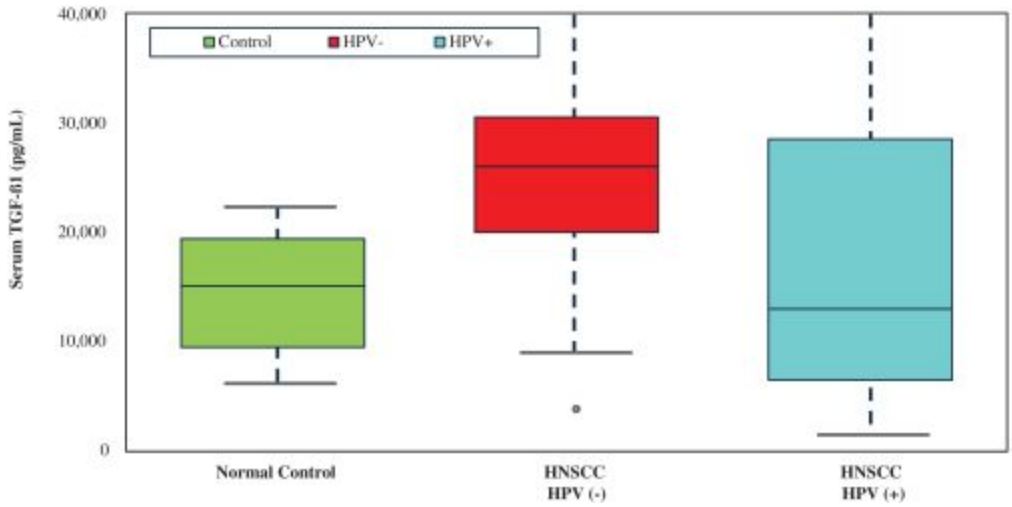


Figure 11. Serum levels of TGF-β are elevated in HPV-negative HNSCC

Therefore, due to the link between EGFR and TGF-β levels and their HPV status, we believe that the dual-inhibition of EGFR and TGF-β signaling in HPV-negative R/M HNSCC has the potential to improve clinical responses and delay or prevent emergence of resistance. Furthermore, third-party studies have shown that TGF-β is an emerging biomarker of resistance to anti-PD-L1 and anti-EGFR-based therapy in advanced HNSCC. Thus, we believe there is strong rationale to pursue the clinical development of ficerafusp alfa, an anti-EGFR and TGF-β-trap bifunctional antibody combined with anti-PD-L1 therapy, such as pembrolizumab, in HNSCC and other squamous cell carcinomas.

Ongoing Phase 1/1b Trial Evaluating Ficerafusp Alfa

We have conducted an open-label Phase 1/1b trial in patients with EGFR-driven solid tumors which remains open and ongoing. This trial has the goal of establishing safety and tolerability, as well as the recommended dose for expansion for both ficerafusp alfa monotherapy and ficerafusp alfa in combination with pembrolizumab across various tumor types. As illustrated in Figure 12, a total of 46 patients with EGFR-driven advanced solid tumors were given increasing doses of ficerafusp alfa in monotherapy. The first dose tested was 64mg weekly increasing to 1500mg weekly using a "3+3" dose escalation trial design. In combination with pembrolizumab, 15 patients with late-line R/M HNSCC and squamous cancer of the anal canal were dosed. The lowest dose tested in combination with pembrolizumab was 240mg of ficerafusp alfa weekly. Across both monotherapy and in combination, a maximum tolerated dose was not reached. However, an initial recommended dose of 1500mg weekly is being assessed across multiple dose expansion cohorts, including a cohort of patients with first-line R/M HNSCC in combination with pembrolizumab. We expect to enroll up to 200 additional patients across the multiple dose expansion cohorts. This dose was chosen based on safety, tolerability and preliminary efficacy as depicted in the bottom graph in Figure 12.

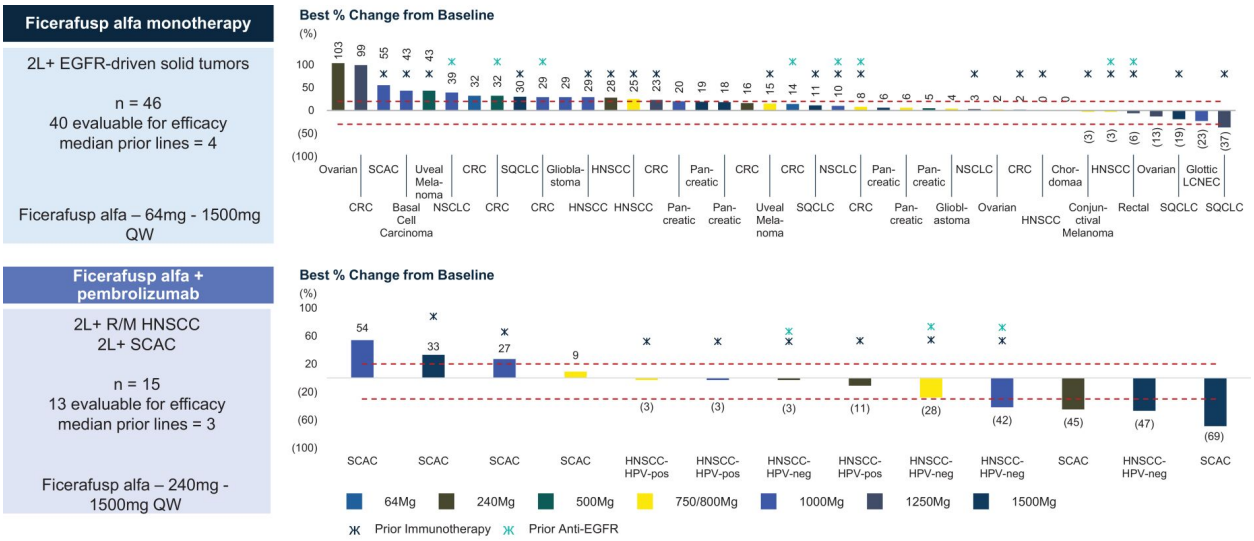


Figure 12. Schematic of study of safety and tolerability of ficerafusp alfa monotherapy and in combination therapy in patients with EGFR-driven advanced solid tumors across dose escalation cohorts. Preliminary efficacy from dose escalation cohorts with ficerafusp alfa in monotherapy and in combination with pembrolizumab

Ficerafusp alfa in 1L R/M HNSCC

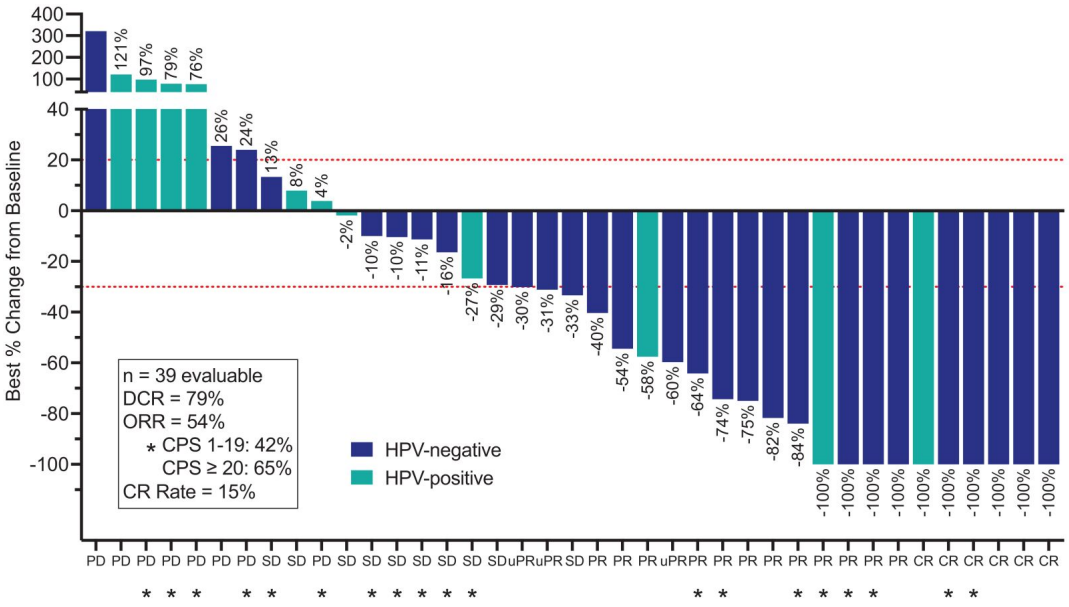
Our rationale for initial development in 1L R/M HNSCC in combination with pembrolizumab

Our decision to pursue the potential of combination therapy came from both our preclinical rationale and results showing synergy between ficerafusp alfa and pembrolizumab; and from two third-party investigator-sponsored trials, or ISTs, which showed that a combination of cetuximab and PD-1 checkpoint inhibitors in R/M HNSCC led to improved ORR compared to checkpoint inhibitor monotherapy. Importantly, though both of these ISTs are single-arm studies, they were the first demonstration that an approximate doubling in ORR could translate to an increased mPFS, and most notably, significant improvement in OS in first-line R/M HNSCC. The first IST, a 2021 publication in Lancet Oncology, reported an ORR of 48% in a clinical trial assessing cetuximab in combination with pembrolizumab in 33 patients. This was followed by a second IST published in 2022 in Clinical Cancer Research, which reported an ORR of 37% in a trial of cetuximab and nivolumab in 43 patients. These studies showed a 20-month and 18-month mOS in an HPV-negative and HPV-positive population, respectively, an improvement on the 12-month benchmark with pembrolizumab, and support the notion that the addition of anti-EGFR based therapy does not dampen durability of response or OS like a chemotherapy-containing regimen. Consistent with our hypothesis, we began to observe an encouraging objective response rate in late-line R/M HNSCC patients when treated with ficerafusp alfa and pembrolizumab. Based on these multiple data sets, we prioritized this combination treatment to allow for acceleration of its clinical development.

Our decision to rapidly move ficerafusp alfa into first-line therapy for R/M HNSCC in combination with pembrolizumab is aligned with the published goals of the Project FrontRunner initiative from the Oncology Center of Excellence at the FDA. The goals of this initiative include identifying candidate drugs that are appropriate to initially develop for the treatment of early metastatic disease, taking into account clinical, scientific, regulatory and operational considerations. We believe developing ficerafusp alfa as a first-line therapy may allow us to further address the significant unmet need in HNSCC while also potentially increasing durability and survival outcomes consistent with our biologic rationale.

Phase 1/1b expansion cohort of ficerafusp alfa in combination with pembrolizumab in 1L R/M HNSCC

Data from our Phase 1/1b dose expansion cohort evaluating 1500mg of ficerafusp alfa in combination with pembrolizumab in efficacy-evaluable first-line R/M HNSCC patients with a CPS greater than or equal to one was first presented in an oral presentation at an American Society of Clinical Oncology meeting in June 2023. As depicted in Figure 13 below, we demonstrated a meaningful 54% (21/39) ORR across both HPV-negative and HPV-positive R/M HNSCC. We also observed a markedly higher ORR of 64% (18/28) in the HPV-negative subset. This ORR result is consistent with the HPV-negative subset having elevated levels of EGFR and TGF-β where we believe ficerafusp alfa has potential to achieve differentiated clinical outcomes.

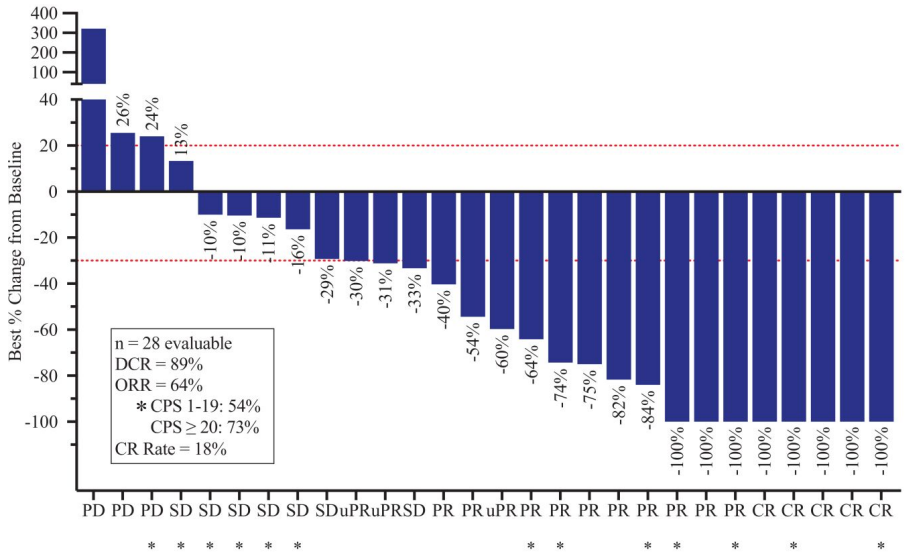


CPS=combined positive score, CR=complete response, DCR=Disease Control Rate, HPV=human papilloma virus, ORR=Overall response rate, PR=partial response, uPR =unconfirmed partial response, SD=stable disease, PD = progressive disease

Out of 42 patients, 3 patients were non-efficacy evaluable as they passed away prior to the first post-baseline efficacy assessments. Two of these subjects passed away due to adverse events that were not related to study treatment (incl. one case of respiratory failure and one case of aspiration).

Figure 13. Anti-tumor responses in HNSCC patients, treatment-naïve in the R/M setting, treated with ficerafusp alfa in combination with pembrolizumab

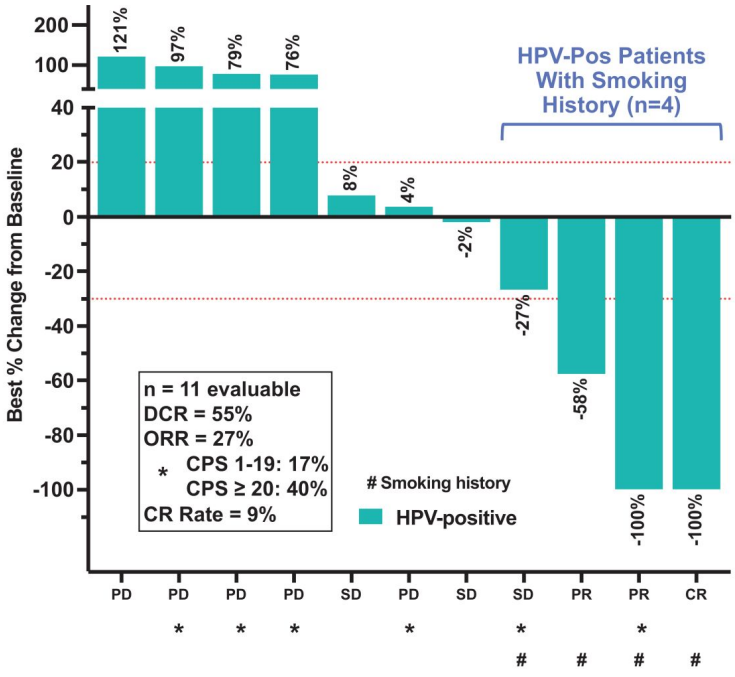
As depicted in Figure 14 below, in the HPV-negative subset, response rates of more than 50% were observed in both the CPS 1 through 19 and CPS greater than or equal to 20 subgroups, with a 70% (14/20) response rate in patients with locoregional disease involvement. This is notable as pembrolizumab is known to have a lower efficacy in the CPS1-19 subset. We also observed that 18% (5/28) of HPV-negative patients achieved a CR and several other patients achieved deep partial responses, including 5 other patients with responses greater than 80%. The CR rate of approximately 3-5% was previously reported in the ISTs of cetuximab in combination with pembrolizumab or nivolumab, as well as the KEYNOTE-048 study with pembrolizumab in patients with CPS greater than or equal to one. We believe these deep responses and high CR rate are driven by the TGF-β arm of ficerafusp alfa, which we believe, based on our hypothesized mechanism of action, is expected to synergize with pembrolizumab by remodeling the TME and activating the immune system (see Figure 4).



CPS=combined positive score, CR=complete response, DCR=Disease Control Rate, HPV=human papilloma virus, ORR=Overall response rate, PR=partial response, SD=stable disease, uPR= unconfirmed partial response, PD = progressive disease

Figure 14. Anti-tumor responses of HPV-negative HNSCC patients treated with ficerafusp alfa and pembrolizumab

In HPV-positive patients, we observed a 27% (3/11) ORR. To evaluate why certain patients seemed to be responding well while others were progressing, we conducted a post hoc analysis of the prior smoking history of the HPV-positive patients to understand its potential impact on responses observed. We hypothesized that patients with a history of smoking may resemble HPV-negative tumor biology as opposed to their disease being driven by the HPV-infection. Similarly, third party studies have demonstrated that a history of smoking has been associated with increased EGFR levels as well. Four of the eleven HPV-positive patients in our study had a heavy smoking history (defined as more than ten pack years in which one pack year is the equivalent of smoking one pack of cigarettes a day for one year) and demonstrated the best responses to ficerafusp alfa as shown below in Figure 15. In these four patients, ficerafusp showed a 75% (3/4) ORR and 100% (4/4) DCR, while it showed a 0% (0/7) ORR and 29% (2/7) DCR in the remaining HPV-positive patients who had no prior history of smoking. Given these results, we plan to initiate an additional expansion cohort of HPV-positive R/M HNSCC patients with a history of heavy smoking in the first half of 2025.



CPS=combined positive score, CR=complete response, DCR=Disease Control Rate, HPV=human papilloma virus, ORR=Overall response rate, PR=partial response, SD=stable disease

Figure 15. Prior smoking history may be a factor that impacts the activity seen of ficerafusp alfa + pembrolizumab in HPV-positive patients

In addition to the high ORR and deep partial responses, we observed that the responses in the combination trial were durable and suggestive of enhanced immunological memory. As depicted in Figure 16 below, the mPFS in HPV-negative subjects was 9.8 months, with 57% (16/28) of patients having a PFS greater than 6 months. The PFS benefit in published historical data for pembrolizumab monotherapy was 3.2 months in an HPV-negative and HPV-positive population, and the PFS benefit for cetuximab and anti-PD-1 combination ISTs was 6.2 to 6.5 months in an HPV-negative and HPV-positive population. Furthermore, the durability of response and time to response are demonstrated in Figure 17 below. Notably, several patients have responses lasting greater than 6 months (11/18) and 12 months (5/18), many of whom still remain on therapy. Amongst the responders, 56% (10/18) of responses occurred at the first post-baseline scan after 6 weeks, and 11/18 overall responses remain ongoing; the mDOR and median OS has not yet been reached. We expect to announce updated interim Phase 1/1b data at a future medical meeting in the first half of 2025. Interestingly, we observe patients responding to therapy after 4 months and several responses deepening over time, with 4 patients even converting to CRs after 6 months of follow-up. Median duration of response has not yet been reached. We believe these trends in the data are consistent with our mechanism of action related to the TGF-β inhibition within the TME. We aim to replicate this Phase 1/1b data in a pivotal randomized Phase 2/3 trial as we believe that ficerafusp alfa in combination with pembrolizumab has the potential to become a first-line standard of care therapy in HPV-negative R/M HNSCC.

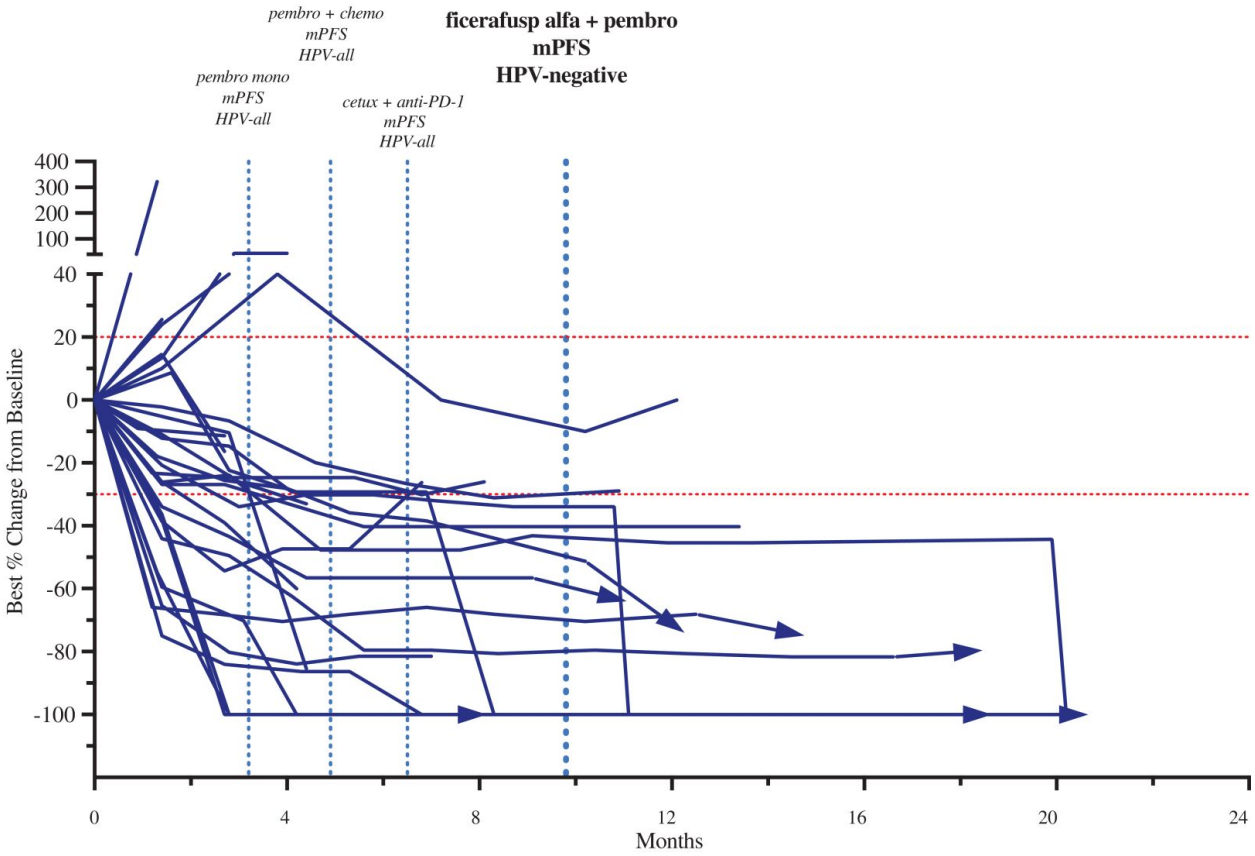


Figure 16. HPV-negative R/M HNSCC patients treated with ficerafusp alfa in combination with pembrolizumab had durable responses

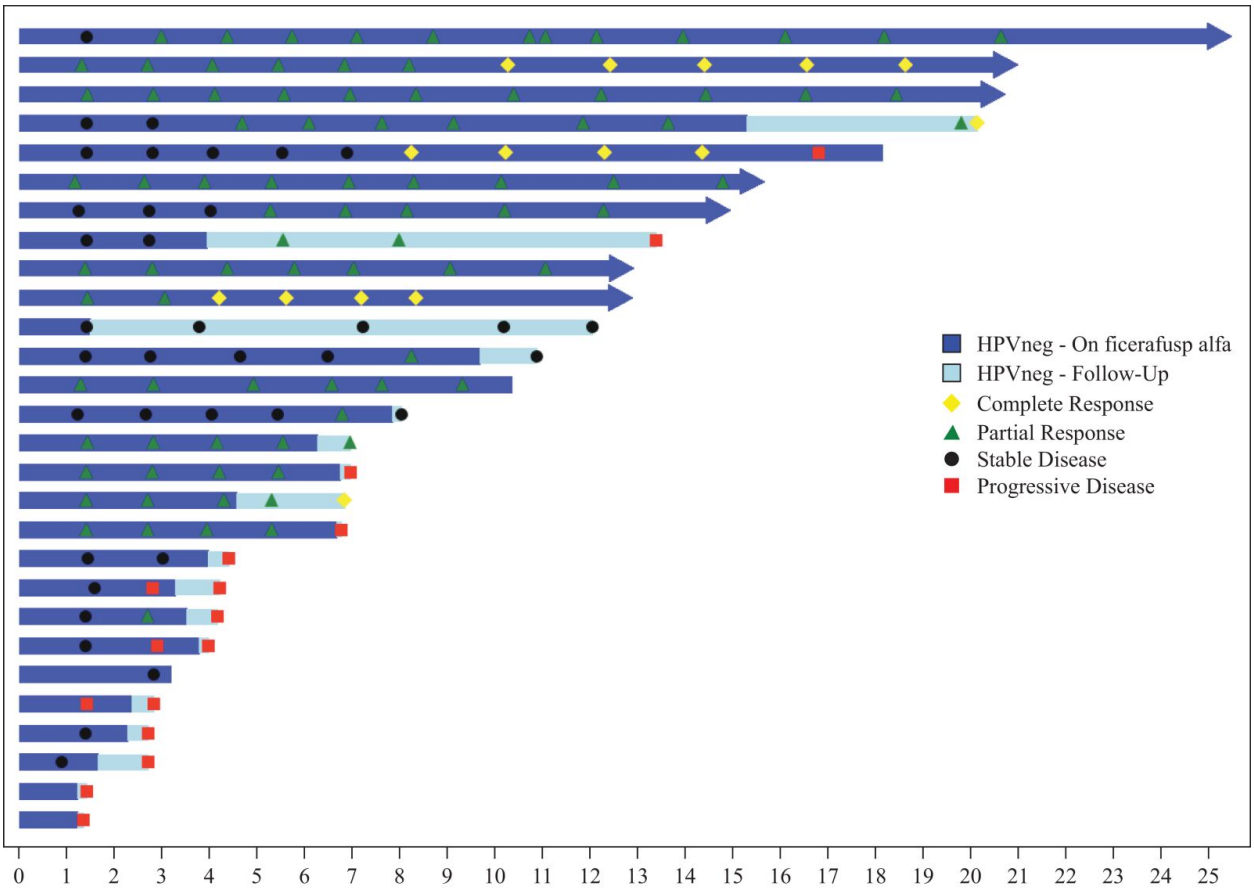


Figure 17. Ficerafusp alfa and pembrolizumab demonstrates an encouraging duration of response

We conducted an exploratory, post hoc biomarker analysis to evaluate ficerafusp alfa's impact on TGF-β levels in HPV-negative subjects from the Ph.1/1b dose expansion cohort for whom there were available tissue samples (n=7). Specifically, changes in pSMAD2, a direct downstream biomarker of the TGF-β pathway, were measured to characterize on target inhibition of TGF-β directly within the tumor microenvironment. As illustrated in Figure 18 below, treatment with ficerafusp alfa in combination with pembrolizumab demonstrated a marked reduction of pSMAD2 in tumor tissue. Within these seven HPV-negative patients, there were five objective responses (71% ORR). We believe these reductions in pSMAD2 occur in patients with deep responses to therapy, supporting the proposed mechanism of action of ficerafusp alfa.

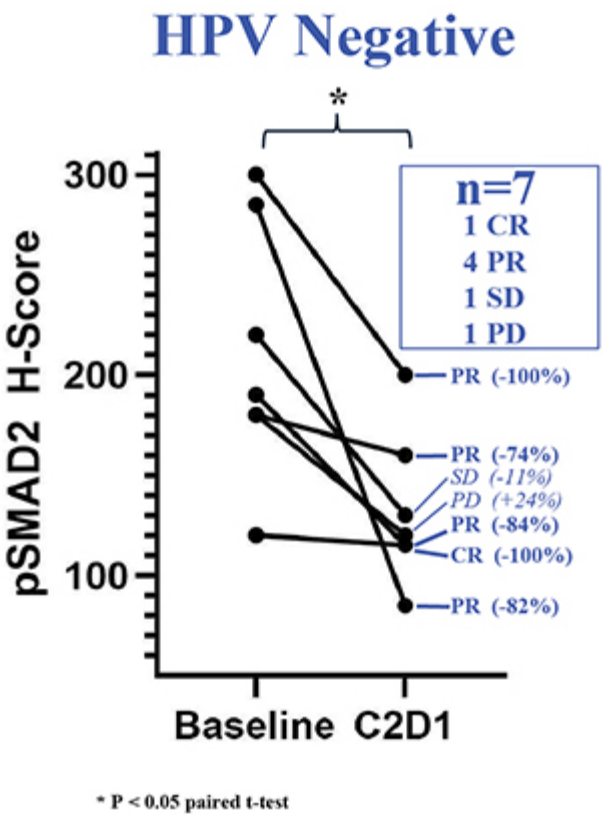


Figure 18. Biomarker analysis from HNSCC tumors supports inhibition of TGF-β within the tumor microenvironment

Ficerafusp alfa has been generally well-tolerated with a favorable tolerability profile

Ficerafusp alfa has demonstrated a favorable tolerability profile in this Phase 1/1b trial in combination with pembrolizumab. Across all cohorts to date, approximately 200 patients received at least one dose of ficerafusp alfa. As depicted in Figure 19 below, the most frequent adverse event suspected to be related to treatment with ficerafusp alfa was acneiform rash, which is an adverse event that is also observed in approximately 80% of HNSCC patients treated with cetuximab. It is mechanistically related to anti-EGFR activity and is typically well mitigated by treating physicians with the use of steroids and other topicals. Adverse events associated with TGF-β inhibition include mostly low-grade mucosal bleeding not requiring any medical intervention. Most importantly, there were no deaths determined to be related to ficerafusp alfa monotherapy or combination treatment. The 1500mg ficerafusp alfa weekly dose, which most R/M HNSCC patients received, resulted in approximately 150% greater molar concentration of cetuximab than the maximum approved dose of cetuximab. We believe that the anti-TGF-β activity of ficerafusp alfa may dampen the severity of acneiform rash through its impact on neutrophil trafficking, enabling patients to tolerate this higher dose, which may in turn help drive improved efficacy. Additionally, nearly all hypothesized TGF-β-related adverse events were transient grade 1-2 local mucosal bleeds or epistaxis.

The safety profile of ficerafusp alfa + pembrolizumab in our Phase 1/1b dose expansion cohort evaluating 1500mg of ficerafusp alfa in combination with pembrolizumab in efficacy-evaluable first-line R/M HNSCC patients with a CPS greater than or equal to one was generally well-tolerated. With a median safety follow-up of at least 11.7 months and a maximum follow up of 25 months, we observed treatment-related adverse events of dermatitis acneiform in 76% of patients, with 12% of these being Grade 3 or Grade 4 treatment-related adverse events, or TRAEs. Five subjects experienced treatment-related severe adverse events of dermatitis acneiform. Five subjects, or 12%, experienced TRAEs that led to discontinuation of ficerafusp alfa and/or pembrolizumab. Historical pembrolizumab combinations, including lenvatinib or chemotherapy, showed TRAEs leading to discontinuation rates of 28% and 33%, respectively.

	All 1L R/M HNSCC subjects received 1500mg QW and Pembrolizumab (n=42)		
Preferred term	**All Grades**	**Grade 3-4**	**Grade 5**
Any Related AE	**40 (95%)**	**17 (40%)**	**0 (0%)**
Dermatitis acneiform	32 (76%)	5 (12%)	0 (0%)
Fatigue	18 (43%)	2 (5%)	0 (0%)
Pruritus	17 (40%)	0 (0%)	0 (0%)
Anaemia	15 (36%)	6 (14%)	0 (0%)
Hypophosphataemia	16 (38%)	0 (0%)	0 (0%)
Hypomagnesaemia	15 (36%)	0 (0%)	0 (0%)
Dry skin	13 (31%)	0 (0%)	0 (0%)
Stomatitis	10 (24%)	1 (2%)	0 (0%)
Infusion related reaction	8 (19%)	1 (2%)	0 (0%)
Hypokalaemia	8 (19%)	0 (0%)	0 (0%)
Nausea	7 (17%)	0 (0%)	0 (0%)
Proteinuria	7 (17%)	0 (0%)	0 (0%)
Epistaxis	6 (14%)	0 (0%)	0 (0%)
Lipase increased	6 (14%)	0 (0%)	0 (0%)
Skin fissures	6 (14%)	0 (0%)	0 (0%)
Decreased appetite	6 (14%)	1 (2%)	0 (0%)
Headache	5 (12%)	1 (2%)	0 (0%)
Rash maculo-papular	5 (12%)	1 (2%)	0 (0%)
Diarrhoea	5 (12%)	0 (0%)	0 (0%)
Aspartate aminotransferase increased	5 (12%)	0 (0%)	0 (0%)
Gingival bleeding	5 (12%)	0 (0%)	0 (0%)

Figure 19. Most common (>10%) related adverse events summarized by preferred term and maximum grade

FORTIFI-HN01: Our Phase 2/3 trial in 1L R/M HNSCC

As a result of our discussions with the FDA, we believe that ficerafusp alfa has a path to accelerated approval using an ORR-based interim endpoint with confirmatory approval based on an OS endpoint. We have designed a double-blinded placebo-controlled pivotal FORTIFI-HN01 Phase 2/3 trial of ficerafusp alfa in combination with pembrolizumab as a first-line therapy in R/M HNSCC excluding patients with HPV-positive OPSCC. As seen in Figure 20 below, the registrational study begins with a dose optimization run-in that randomizes patients 1:1:1 to receive either ficerafusp alfa high dose (1500mg weekly) in combination with pembrolizumab, ficerafusp alfa low dose (750mg weekly) in combination with pembrolizumab, or placebo plus pembrolizumab. The total study will enroll approximately 650 patients, which we believe is sufficiently powered to achieve results that may lead to regulatory approval. We enrolled the first patients in our FORTIFI-HN01 Phase 2/3 trial in February 2025 and project that the ORR interim analysis conducted on approximately 415 patients may occur by 2027.

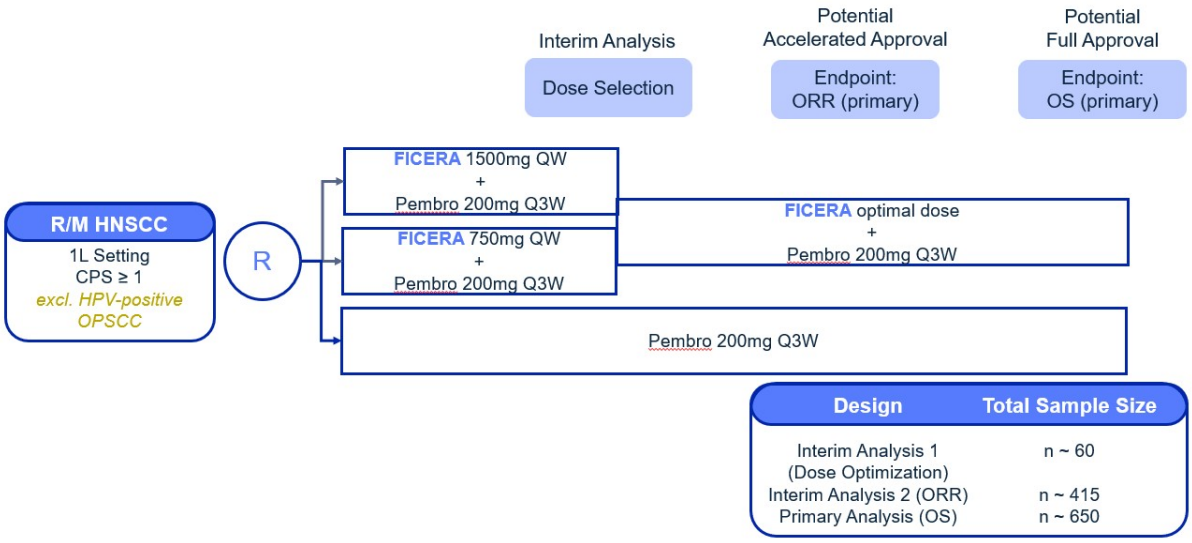


Figure 20. Schematic of ficerafusp alfa + pembrolizumab FORTIFI-HN01 Phase 2/3 trial design

FORTIFI-HN01 Phase 2/3 trial has a seamless design that potentially allows for efficient path-to-market

As seen in Figure 21 below, this registrational study is designed with a dose selection run-in of approximately 10-20 patients per arm, consistent with the objectives of the FDA's Project Optimus. Project Optimus is an initiative by the FDA's Oncology Center for Excellence which is an initiative to reform the dose optimization and dose selection paradigm in oncology drug development to emphasize selection of an optimal dose, which is a dose or doses that maximizes not only the efficacy of a drug but the safety and tolerability as well. In our FORTIFI-HN01 study, once 10-20 patients in each treatment arm have had at least 12 weeks of follow-up, the optimal dose will be assessed and then chosen. During this time period of dose selection, enrollment will not be stopped, so that by the time the optimal dose has been selected, we anticipate having enrolled between 60-80 patients in each treatment arm. Importantly, this FORTIFI-HN01 Phase 2/3 trial design enables the patients enrolled in the optimal dose treatment arm during dose selection to contribute to the primary analyses of the FORTIFI-HN01 Phase 2/3 trial, while those enrolled in the non-optimal treatment arm will not.

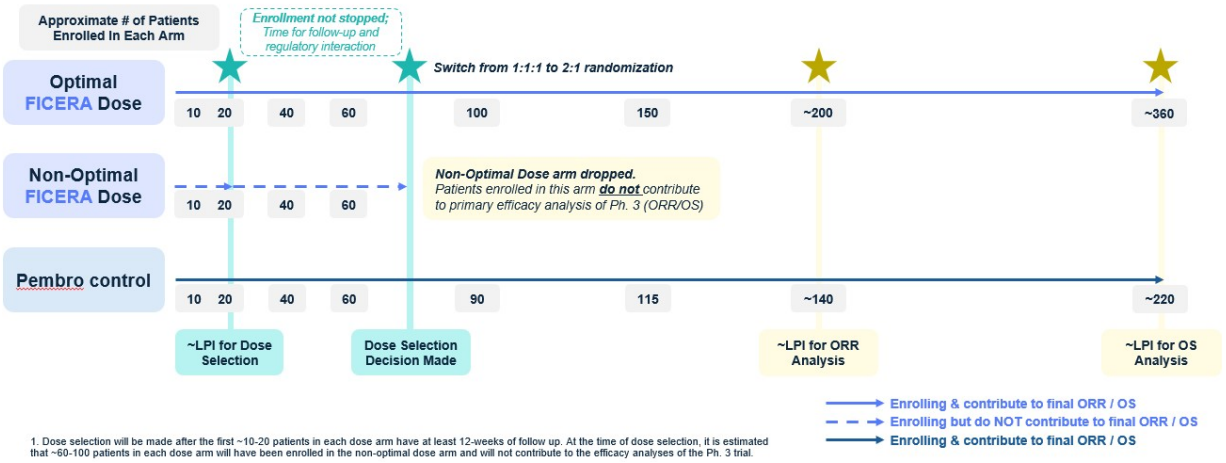


Figure 21. FORTIFI-HN01 Phase 2/3 trial is designed such that patients enrolled in dose selection at the optimal dose will contribute to the final efficacy analyses, while those at the non-optimal dose will not contribute to the final efficacy analyses.

FORTIFI-HN01 optimal biological dose (OBD) decision will be informed by the totality of both open-label and randomized data in the FORTIFI-HN01 Phase 2/3 trial

The dose determination in FORTIFI-HN01 Phase 2/3 trial will be informed by not only the 10-20 patients in each ficerafusp alfa containing treatment arm, but also open label data sets from our Phase 1/1b trial, as demonstrated in Figure 22 below. This includes data previously presented from our dose expansion cohort evaluating 1500mg QW of ficerafusp alfa in combination with pembrolizumab in HPV-negative R/M HNSCC. Additionally, we currently have an ongoing open-label expansion cohort of approximately 30 patients with HPV-negative R/M HNSCC to evaluate a 750mg weekly dose that will also help inform the dose selection. We believe this ongoing expansion cohort will be critical to assess the extended safety and durability of 750mg QW dose of ficerafusp alfa, given it will have at least 1 year of follow up in all patients by the time of dose selection.

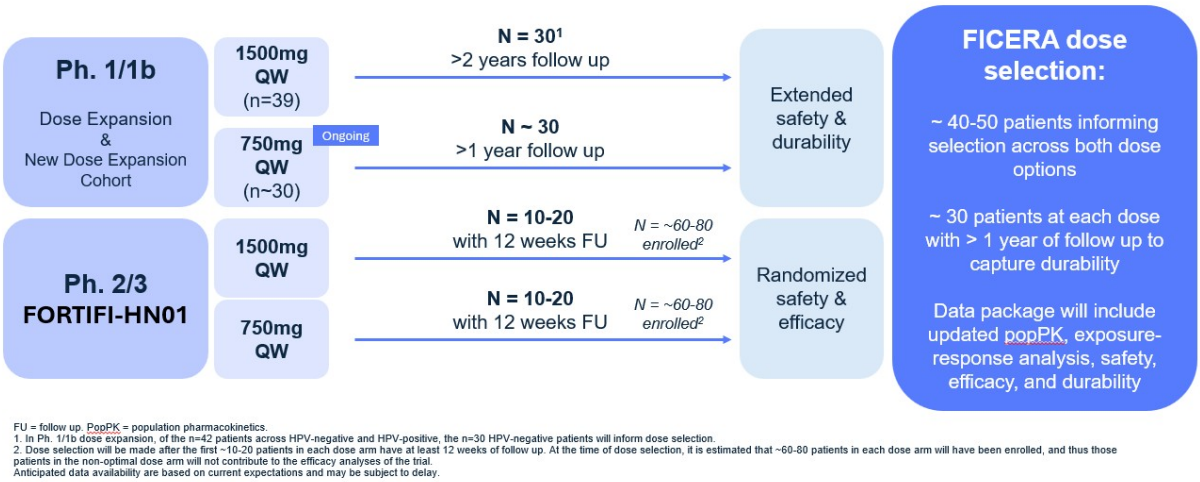


Figure 22: The totality of data in 1L HPV-negative R/M HNSCC will inform the dose selection in FORTIFI-HN01 Phase 2/3 trial

Separately, we are also evaluating alternative dosing schedules, such as a once every two weeks (Q2W) dose that will not impact the FORTIFI-HN01 Phase 2/3 trial dose selection or trial itself but may inform a bridging strategy to a Q2W dose in parallel to FORTIFI-HN01 Phase 2/3 trial and in advance of a potential approval.

Potential expansion opportunities for ficerafusp alfa

We believe that there is potential to expand the use of ficerafusp alfa to other populations of HNSCC patients. Preliminary data from our dose escalation cohort in combination with pembrolizumab have shown durable responses in R/M patients who are refractory to both cetuximab and pembrolizumab, and in patients with a CPS of zero. These early data potentially suggest an ability for ficerafusp alfa to synergize with pembrolizumab in checkpoint-refractory tumors, and we have initiated an expansion cohort in patients with HPV-negative R/M HNSCC with a CPS of zero and expect to present preliminary efficacy data at a future medical meeting in 2026. Should we see responses beyond what is typically expected with chemotherapy regimens, we believe there is an opportunity to expand the development of ficerafusp alfa in combination with pembrolizumab to the approximately 20% of the R/M HNSCC that do not express PD-L1 and provide a chemotherapy-free alternative. Additionally, in R/M HNSCC, given the results observed in our Phase 1/1b expansion cohort in HPV-positive patients with a history of heavy smoking, we plan to initiate an additional expansion cohort in these patients in the first half of 2025.

In addition, the encouraging anti-tumor activity of ficerafusp alfa, specifically its durability and its tolerability profile, suggests that there is potential to develop it for the treatment of HPV-negative LA-HNSCC. Treatment for LA-HNSCC often involves combinations of radiation therapy and chemotherapy or cetuximab, and potentially surgical resection for eligible candidates. Radiation therapy has been associated with increases in TGF-β and thus there is mechanistic rationale to explore ficerafusp in combination with radiation therapy in LA-HNSCC. Not only does this approach target potential resistance early in the course of disease, but it may also reduce potential effects of radiation therapy such as scarring and fibrosis to preserve organ function and improve quality of life in patients. We believe that our investigator-initiated studies will start in 2025 to signal-seek in several areas in LA-HNSCC, including in the neoadjuvant setting.

Ficerafusp alfa expansion into colorectal cancer (CRC)

Beyond HNSCC, we believe that there is also potential to develop ficerafusp alfa both in monotherapy and in combination for the treatment of other EGFR-expressing tumors, such as colorectal cancer where EGFR-targeted

therapies have already demonstrated clinical efficacy, and are key agents of current standard of care. Importantly in CRC, TGF-β inhibition has the potential to improve upon both the efficacy and durability of existing therapies. As highlighted previously, TGF-β impacts metastasis in CRC in several ways including EMT, in which tumor cells transition to become more invasive and spread to distant sites. Upon treatment with EGFR therapy, increases in TGF-β levels, EMT signature, and cancer associated fibroblasts have been observed in CRC, which supports the rationale to simultaneous inhibit TGF-β while targeting EGFR with ficerafusp alfa. Additionally, TGF-β facilitates metastasis in CRC by promoting angiogenesis, immunosuppression, and stemness.

We plan to initiate an initial Ph. 1/2 proof of concept study in unresectable, metastatic CRC patients in 2025. This study will evaluate ficerafusp alfa as a monotherapy and in combination with pembrolizumab in microsatellite stable (MSS) patients that do not have a RAS/BRAF mutation and who have received 2-3 prior lines of therapy. As highlighted in Figure 23 below, the initial cohorts will enroll ~20 patients in Stage 1 to evaluate safety, tolerability, and preliminary efficacy, with the opportunity to expand to ~50 patients in each arm pending a positive signal.

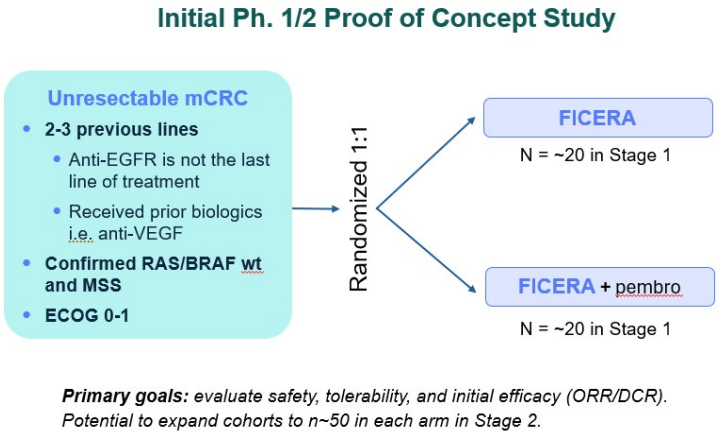


Figure 23: Overview of Ph.1/2 study evaluating ficerafusp alfa monotherapy or in combination with pembrolizumab in metastatic CRC

Ficerafusp alfa expansion into squamous cell carcinoma of the anal canal (SCAC)

The global incidence and mortality of anal cancer have increased in recent years, with more than 54,000 cases and 22,000 deaths reported in 2022; the most common form of anal cancer is squamous cell carcinoma of the anal canal (SCAC). Treatments for advanced SCAC often include combination chemotherapy with carboplatin and paclitaxel or other chemotherapy combinations, followed by PD-1 immune checkpoint blockade. Anti-PD1 monotherapy has limited efficacy in patients with treatment-refractory advanced SCAC. For example, results from the KEYNOTE-158 study of pembrolizumab alone in 2L SCAC showed an ORR = 11%, DCR = 26% and 12-month PFS rate of 15%.

Preliminary data from our Phase 1/1b dose expansion cohort evaluating 1500mg of ficerafusp alfa in combination with pembrolizumab in second-line or later SCAC patients was recently presented in a poster session at the 2025 American Society of Clinical Oncology Gastrointestinal (ASCO-GI) Cancers Symposium in January 2025. This cohort enrolled locally advanced / unresectable or metastatic SCAC patients who had received 1-2 prior lines of chemotherapy and had not previously received a checkpoint inhibitor. As depicted in Figure 24 below, the combination demonstrated a meaningful 29% (8/28) ORR, as well as a 64% (18/28) DCR. Median duration of response for patients who demonstrated a CR or PR was not reached as of data cutoff, but included four patients with responses maintained for at least 6 months. Median PFS was 2.9 months with a 12-month PFS rate of 40.7%.

Importantly, the combination demonstrated activity in patients with liver metastasis with a 31% (4/13) ORR. Given these encouraging results, we plan to evaluate future development paths in SCAC, including potential development in the first-line setting.

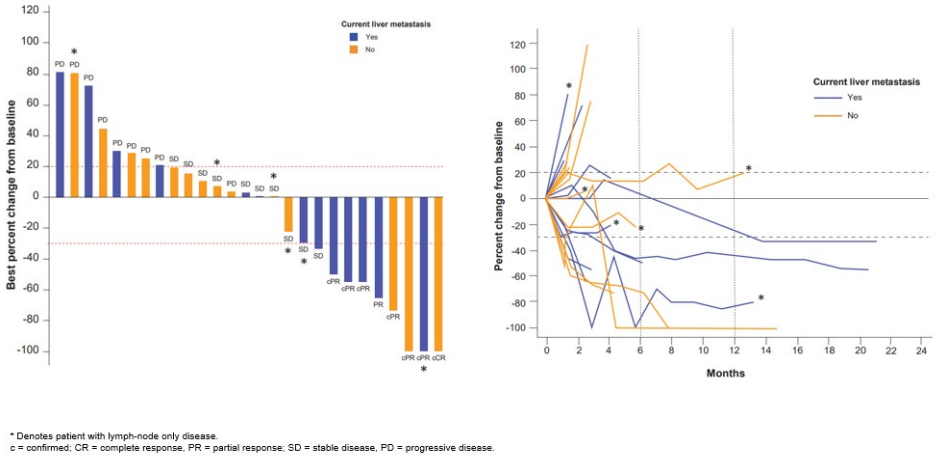


Figure 24: Anti-tumor activity of ficerafusp alfa in combination with pembrolizumab in locally advanced / unresectable or metastatic SCAC previously treated with 1-2 prior lines of chemotherapy

Ficerafusp alfa expansion into cutaneous squamous cell carcinoma (CSCC)

We believe ficerafusp alfa has the potential to provide meaningful clinical benefit in CSCC, a cancer type that results in up to 8,800 deaths annually in the U.S and in which there is a strong biologic rationale for the dual inhibition of both EGFR and TGF-β. We have demonstrated preliminary activity of ficerafusp alfa as a monotherapy in CSCC in our ongoing Phase 1/1b trial. As shown in Figure 25, ficerafusp alfa showed a preliminary 42% (5/12) ORR as a second-line therapy in patients with CSCC who were refractory to a PD-1 checkpoint inhibitor, a population in which historical response rates are approximately 5% with chemotherapy. This cohort continues to enroll patients and we expect to share updates to this preliminary data set at a future medical meeting in the first half of 2025.

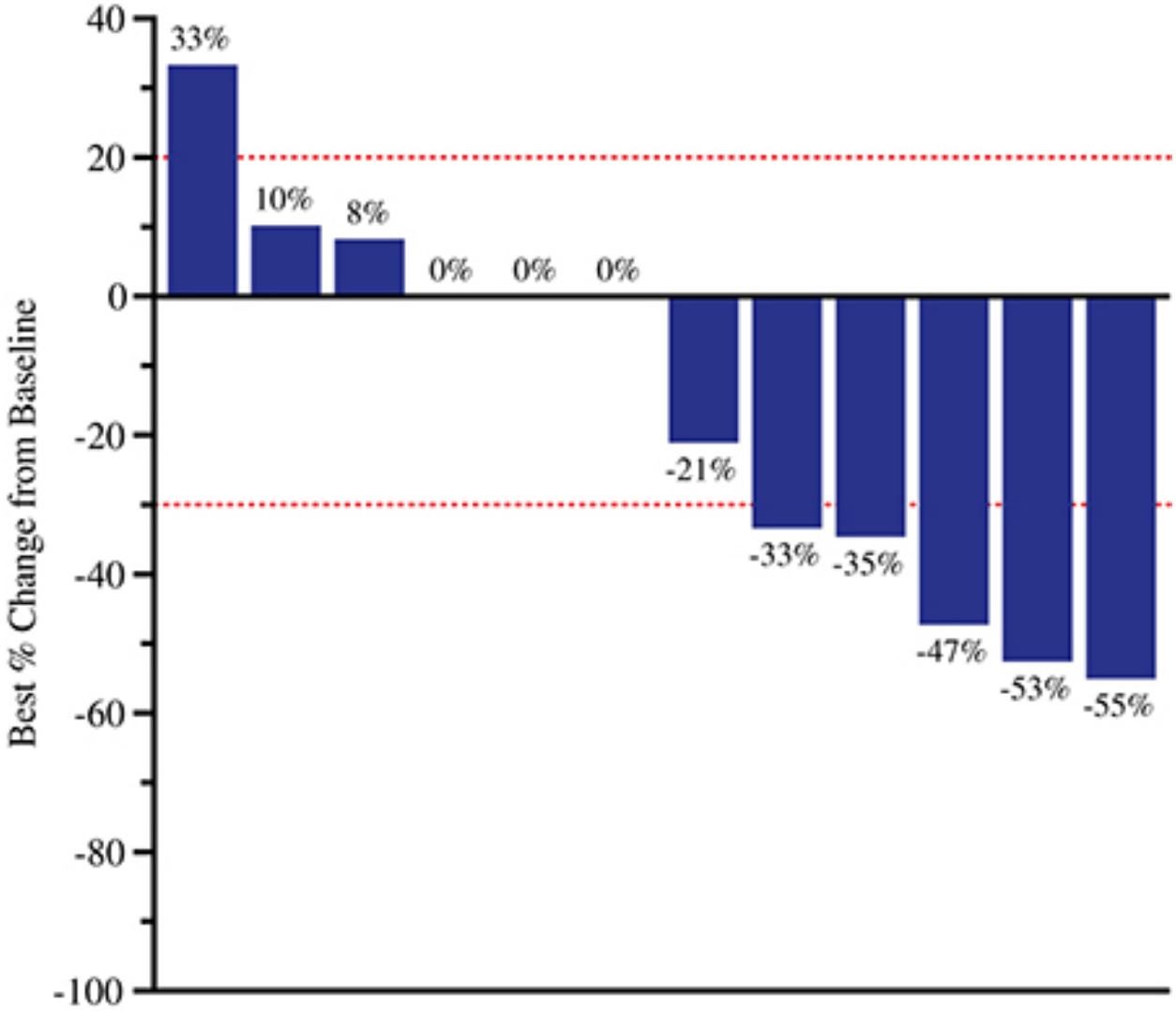


Figure 25. ficerafusp alfa monotherapy led to a preliminary 42% (5/12) ORR in 12 patients

Competition

The biotechnology and pharmaceutical industries are characterized by intense competition to develop new products and technologies. We compete directly with companies dedicating their resources to advance novel therapies for the treatment of cancer. We face substantial competition from multiple sources, including large pharmaceutical and biotechnology companies, academic research institutions, governmental agencies and public and private research institutions. We anticipate that we will continue to face increasing competition as new therapies, technologies and data emerge within the field of oncology and, more specifically, for the treatment of HNSCC.

We expect to compete with commercially available therapies for the treatment of HNSCC, including pembrolizumab (marketed as Keytruda by Merck & Co); the combination of pembrolizumab, platinum chemotherapy and 5-fluorouracil; and the combination of cetuximab (marketed as Erbitux by Eli Lilly in the U.S. and by Merck KGaA outside of the U.S.), platinum chemotherapy and 5-fluorouracil. In addition, there are numerous companies that are developing new treatments for HNSCC, including Merck & Co, Pfizer Inc., Johnson & Johnson, Exelixis, Inc., Incyte Corporation, Beigene, Ltd., Merus N.V., iTeos Therapeutics Inc., Immutep, Inc., Inhibrix Biosciences, Inc., Iovance Biotherapeutics, Inc., Kura Oncology, Inc. and ALX Oncology Holdings, Inc.

Some of our competitors have significantly greater financial resources and expertise in areas such as research and development, manufacturing, regulatory protocols and marketing. Mergers and acquisitions in the pharmaceutical, biopharmaceutical and biotechnology industries may result in a concentration of incremental resources amongst a fewer number of our competitors. Early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with larger and more well-established companies. These companies also compete with us in the recruitment and retainment of top qualified scientific and/or management personnel, establishment of clinical trial sites and patient registration for clinical trials and acquisition of technologies complementary to, or necessary for, our programs.

If our product candidates do not offer sustainable advantages over other available products, we may not be able to successfully compete against current and future competitors. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly, resulting in a stronger or dominant market position before we are able to enter the market. The key factors that will ultimately affect the success of our bifunctional therapies, if approved, are likely their safety, efficacy, convenience and cost.

Contract Transfer And License Agreement with Biocon

On October 1, 2019, we entered into a Contract Transfer and License Agreement, or the Biocon Agreement, with Biocon Limited, or Biocon. Pursuant to the Biocon Agreement, we and Biocon agreed that Biocon would grant us a license, with the right to grant and authorize sublicenses to make, use, sell, offer to sell, import, and otherwise exploit certain fusion protein products of which ficerafusp alfa was the most advanced program. Under the Biocon Agreement, Biocon also assigns to us the "Assumed Contracts," which include master services agreements, an authorization letter, an evaluation license agreement with Life Technologies Corporation, or the Life Technologies Agreement, consultancy agreements, a research agreement and a quality agreement.

Each Assumed Contract was fully transferred to us at the time we executed the Biocon Agreement. With exception of the Life Technologies Agreement, each Assumed Contract has been terminated. While the Life Technologies Agreement is still in effect, it imposes no material obligations on us and no costs have been incurred since 2019.

In connection with the Biocon Agreement, we paid INR 550 million as consideration for the license grant. Under the Biocon Agreement, Biocon is required on a calendar quarterly basis to deliver any additional materials or know-how relating to the product up until a mid-single digit anniversary from the effective date of the Biocon Agreement. In the event of an acquisition of all or substantially all of our assets and business by a third party, this obligation shall terminate. Additionally, we have assumed sole responsibility for complying with any post-approval developments and post-marketing activities such as routine and non-routine pharmacovigilance monitoring and post-marketing surveillance for the products – including any and all clinical trials.

The Biocon Agreement is governed by English law and does not contain any termination rights. Under English law, we and Biocon could mutually agree to terminate the Biocon Agreement. Additionally, there are no future milestone payments, royalty terms or any additional payments required.

Clinical Trial Collaboration And Supply Agreement with MSD

On May 19, 2022, we entered into a Clinical Trial Collaboration and Supply Agreement, or the MSD Agreement, with MSD International GmbH, or MSDIG, and MSD International Business GmbH, MSDIB, and collectively with MSDIG, MSD. Pursuant to the MSD Agreement, we provide ficerafusp alfa and MSD provides pembrolizumab to be used in combination in a clinical trial sponsored by us. The clinical trial is a First-in-Human, Phase 1/1b, Open-label, Multicenter Study intended to characterize the safety, tolerability and recommended dose of single agent ficerafusp alfa and combination ficerafusp alfa plus pembrolizumab. To facilitate such collaboration activities and information exchange and pursuant to the MSD Agreement, we and MSD created a joint development committee with an equal number of representatives from each party.

Pursuant to the MSD Agreement, all clinical data resulting from the portion of the clinical trial involving the combination of ficerafusp alfa and pembrolizumab is jointly owned by both us and MSD. We own all clinical data resulting from the part of the clinical trial involving ficerafusp alfa alone or in combination with other treatments that are not pembrolizumab, and MSD owns all clinical data resulting from the part of the clinical trial involving pembrolizumab alone or in combination with other treatments that are not ficerafusp alfa.

The MSD Agreement also sets forth our regulatory responsibilities as the sponsor of the clinical trial – such as obtaining all necessary regulatory approvals, maintaining reports and other related documentation in a scientific and legally compliant manner, and handling safety reporting. Prior to dosing any patient with MSD's compound, we are required to organize and invite MSD to attend a safety review meeting to discuss the most recent clinical safety data (and other data reasonably requested by MSD to evaluate the safety of the proposed study arms). We have also been responsible for preparing the patient informed-consent form for MSD's compound study (in consultation with MSD) and transmitting data on severe adverse events from the MSD compound study to MSD. Each party is responsible for its own internal costs and expenses to support the clinical trials.

The term of the MSD Agreement commenced on May 19, 2022 and will expire once we deliver the final documents, signifying the completion of the clinical trial, unless the MSD Agreement is earlier terminated in accordance with the terms of the MSD Agreement. Pursuant to the MSD Agreement, MSD may terminate the MSD Agreement early if it believes its products are being used unsafely. Either party may terminate the MSD Agreement early for breach, regulatory action, force majeure, or concerns about patient safety. Additionally, either party may terminate the MSD Agreement early if one is planning to discontinue development of its own compound for medical, scientific or legal reasons.

Intellectual Property

We seek to protect the intellectual property and proprietary technology that we consider important to our business, including by pursuing patent applications that cover our product candidates and methods of using the same, as well as any other relevant inventions and improvements that we believe to be commercially important to the development of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position. Our commercial success depends, in part, on our ability to obtain, maintain, enforce and protect our intellectual property and other proprietary rights for the technology, inventions and improvements we consider important to our business, and to defend any patents we may own or in-license in the future, prevent others from infringing any patents we may own or in-license in the future, preserve the confidentiality of our trade secrets, and operate without infringing, misappropriating or otherwise violating the valid and enforceable patents and proprietary rights of third parties.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties, may not result in the issuance of patents and any issued patents we may obtain do not guarantee us the right to practice our technology or commercialize our product candidates. We also cannot predict the breadth of claims that may be allowed or enforced in any patents we may own or in-license in the future. Any issued patents that we may own or in-license in the future may be challenged, invalidated, circumvented or have the scope of their claims narrowed. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide.

The term of individual patents depends upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a nonprovisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier expiring patent. The term of a patent claiming a new drug product may also be eligible for a limited patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. The restoration period cannot be longer than five years, and the restoration period may not extend the patent term beyond 14 years from the date of FDA approval. Only one patent applicable to an approved product is eligible for the extension, and only those claims covering the approved product, a method for using it, or a method for manufacturing it may be extended. Additionally, the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA. In the future, if our product candidates receive approval by the FDA, we expect to apply for patent term extensions on one issued patent covering each of those products, depending upon the length of the clinical studies for each product and other factors. There can be no assurance that patents will issue from our current or future pending patent applications, or that we will benefit from any patent term extension or favorable adjustments to the terms of any patents we may own or in-license in the future. In addition, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Patent term may be inadequate to protect our competitive position on our products for an adequate amount of time.

Our policy is to file patent applications to protect technology, inventions and improvements to inventions that may be commercially important to the development of our business. We seek patent protection in the U.S. and foreign countries for a variety of technologies, including our ficerafusp alfa product candidate and methods of treating cancer using the same.

Ficerafusp alfa

We have an exclusive license from Biocon Limited to one patent family directed to ficerafusp alfa and other fusion proteins. As of December 31, 2024, the patent contains one U.S. patent directed to ficerafusp alfa composition of matter; one U.S. patent directed to methods of using ficerafusp alfa; one European patent directed to ficerafusp alfa composition of matter and its use; and one issued patent in each of Australia, Canada, India, Japan, New Zealand, Russia, Malaysia, and the United Arab Emirates, each related to ficerafusp alfa. Each of the U.S. and foreign patents is expected to expire in 2033; in each instance provided that all appropriate maintenance fees are paid and not including any patent term adjustment, patent term extension, Supplementary Protection Certificate, or SPC, or the like. The patent family also contains a number of pending patent applications in the U.S., Europe, Canada, and China. Any patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in 2033, not including any patent term adjustment, patent term extension, SPC, or the like.

As of December 31, 2024, we also solely own a patent portfolio containing four patent families each containing pending patent applications that, if issued, may provide additional intellectual property protection for ficerafusp alfa. Each of the four patent families in this patent portfolio are listed below.

As of December 31, 2024, we solely own one patent family directed to formulations of ficerafusp alfa that contains pending patent applications in the U.S., Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, New Zealand, and the United Arab Emirates. Any patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in 2041, not including any patent term adjustment, patent term extension, SPC, or the like.

As of December 31, 2024, we solely own one patent family directed to methods of using ficerafusp alfa in combination with programmed cell death protein 1, or PD1, targeting agents that contains pending patent applications in the U.S., Australia, Brazil, Canada, China, Europe, Hong Kong, India, Japan, New Zealand, and the United Arab Emirates. Any patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in 2041, not including any patent term adjustment, patent term extension, SPC, or the like.

As of December 31, 2024, we solely own one patent family directed to methods of using ficerafusp alfa in combination with Kirsten ras oncogene homolog, or KRAS, targeting agents that contains a pending U.S. patent application, a pending PCT patent application, and a pending Taiwanese patent application. Any patents that issue based on these patent applications, if granted and all appropriate maintenance fees paid, are expected to expire in 2044, not including any patent term adjustment, patent term extension, SPC, or the like.

Manufacturing

We have leveraged multiple third-party manufacturers to support the manufacturing of ficerafusp alfa for clinical trials and, if we receive regulatory approval, we intend to rely on such third parties for commercial manufacture. We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We believe this strategy will enable us to maintain a nimble, efficient, and effective working model without making significant internal capital investments. We are focused on developing high-yield and scalable processes and analytical methods for the manufacture of ficerafusp alfa. We believe our manufacturing scale will support drug supply for our future clinical trials and commercial demand for ficerafusp alfa to treat R/M HNSCC squamous cell carcinoma, if approved. We currently obtain our supplies from third-party manufacturers on a purchase order basis and do not have any long-term supply agreements in place. Specifically, Biocon Biologics, Ltd., Syngene and WuXi Bio are our principal clinical drug suppliers, amongst others, and Thermo Fisher Scientific and affiliated entities are our drug product and packaging suppliers. We are currently considering options for commercial product suppliers and will finalize our decisions in due course. To de-risk our supply chain, and as we advance toward potential commercialization, we intend to enter into long-term supply agreements as well as evaluate additional product manufacturing sources.

Government Regulation

Government authorities in the U.S., including federal, state, and local authorities, and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, and export and import of biological products, such as those we are developing. In addition, some government authorities regulate the pricing of such products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

Review and Approval for Licensing Biologics in the U.S.

In the U.S., the FDA regulates biological products under the Federal Food, Drug, and Cosmetic Act, or the FDCA, the Public Health Service Act, or the PHSA, and their implementing regulations. FDA approval is required before any biological product can be marketed in the U.S. Biological products are also subject to other federal, state, and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the product development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions or other consequences, including the FDA's refusal to allow us to proceed with clinical testing, issuance of clinical holds for planned or ongoing studies, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, issuance of untitled or warning letters, product recalls, product seizures, import detentions or refusals, total or partial suspension of manufacturing or distribution, injunctions, fines, civil penalties or criminal prosecution. Any such action could have a material adverse effect on us.

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

- completion of extensive nonclinical laboratory tests and nonclinical animal studies in compliance with applicable good laboratory practices, or GLP, requirements;
- submission to the FDA of an investigational new drug, or IND, application, which must become effective before human clinical trials may begin in the U.S. and must be updated annually;
- approval by an independent institutional review board, IRB, or ethics committee representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCPs, to establish the safety and efficacy of the product candidate for each proposed indication;
- manufacture of the drug substance and drug product in accordance with the FDA's current good manufacturing practice, or cGMP, requirements, along with required analytical and stability testing;
- preparation of and submission to the FDA of a biologics license application, or BLA, requesting marketing approval for one or more proposed indications, that includes sufficient evidence of establishing the safety, purity and potency of the proposed biological product for its intended indication, including from results of nonclinical testing and clinical trials;
- review of the product application by an FDA Advisory Committee, where appropriate and if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;

- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the proposed product is produced to assess compliance with cGMPs and to assure that the facilities, methods, and controls are adequate to preserve the product's identity, quality, and strength;

- satisfactory completion of any FDA audits of the nonclinical studies and clinical trial sites to assure compliance with GLPs and GCPs, as applicable, and the integrity of data in support of the BLA;

- payment of user fees under the Prescription Drug User Fee Act, or the PDUFA, unless exempted; and

- the FDA's review and approval of the BLA.

The nonclinical and clinical testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

Nonclinical Studies and Investigational New Drug Application

Before testing any biological product in humans, a product candidate must undergo rigorous preclinical testing. Preclinical studies include laboratory evaluations of product chemistry, formulation, and stability, as well as in vitro and animal studies to assess safety and in some cases to establish the rationale for therapeutic use. The conduct of preclinical studies is subject to federal and state regulation and requirements, including GLP requirements for safety/ toxicology studies. The results of the preclinical studies, together with manufacturing information and analytical data, must be submitted to the FDA as part of an IND.

An IND is a request for authorization from the FDA to administer an investigational biological product to humans in clinical trials in the U.S. The central focus of an IND submission is on the general investigational plan, the protocol(s) for human trials and the safety of trial participants. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

At any time during the initial 30 day IND review period or while clinical trials are ongoing under the IND, the FDA may impose a partial or complete clinical hold. Clinical holds may be imposed by the FDA when there is concern for patient safety, and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing and controls or where there is non-compliance with regulatory requirements. A clinical hold would delay either a proposed clinical trial or cause suspension of an ongoing trial, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. A separate submission to an existing IND must also be made for each successive clinical trial to be conducted, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin.

Clinical Trials

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 trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

Additionally, approval must also be obtained from each clinical trial site's IRB, before the trials may be initiated and the IRB must monitor the trial until completed. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects and the possible liability of the institution. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries, including on clinicaltrials.gov.

The clinical investigation of a biological product is generally divided into three or four phases. Although the phases are usually conducted sequentially, they may overlap or be combined.

Phase 1. The investigational product is initially introduced into healthy human subjects or, in the case of some products designed to address severe or life-threatening diseases, patients with the target disease or condition. These trials are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions 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 to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy.

Phase 3. The investigational product is administered to an expanded patient population, generally at geographically dispersed clinical trial sites to generate enough data to statistically evaluate safety, purity and potency, to evaluate the overall benefit-risk profile of the investigational product, and to provide an adequate basis for physician labeling.

Phase 4. In some cases, the FDA may condition approval of a BLA for a product candidate on the sponsor's agreement to conduct additional clinical trials after approval or a sponsor may voluntarily conduct additional clinical trials after approval to gain more information about the biological product. Such post-approval trials are typically referred to as Phase 4 clinical trials.

Sponsors must also report to the FDA, within certain timeframes, serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product candidate. The FDA, the IRB, or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data and safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives or competitive climate.

A sponsor of an investigational biological product for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational biological product. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational biological product or, as applicable, 15 days after the biological product receives a designation as a breakthrough therapy or fast track product.

Concurrent with clinical trials, sponsors usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the drug product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality, and purity of the final drug product. 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.

During the development of a new biologic, sponsors are given opportunities to meet with the FDA at certain points. These points may be prior to submission of an IND, at the end of Phase 1, at the end of Phase 2, and before a BLA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development.

Submission of a BLA to the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational product information is submitted to the FDA in the form of a BLA requesting approval to market the product for one or more indications. Under federal law, the submission of most BLAs is subject to an application user fee, and the sponsor of an approved BLA is also subject to an annual program fee for each approved biological product on the market. Applications for orphan drug products are exempted from the BLA application fee and may be exempted from program fees, unless the application includes an indication for other than a rare disease or condition.

A BLA must include all relevant data available from pertinent nonclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including trials initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational product to the satisfaction of the FDA.

The FDA conducts a preliminary review of all BLAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an application for filing. Under the performance goals and policies implemented by the FDA under PDUFA, once a BLA has been submitted, the FDA's goal for novel biological products generally is to review the application within ten months after it accepts the application for filing, or, if the application is granted priority review, six months after the FDA accepts the application for filing. The FDA does not always meet its PDUFA goal dates, and the review process may be extended. For example, the review process and the PDUFA goal date may be extended by three months if the FDA requests or if the applicant otherwise provides additional data, analysis or information that FDA deems a major amendment.

Before approving a BLA, the FDA typically will 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 the sponsor and one or more clinical sites to assure compliance with GCPs. Material changes in manufacturing equipment, location, or process post-approval, may result in additional regulatory review and approval.

The FDA is required to refer an application for a novel biological product to an advisory committee or explain why such referral was not made. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on a BLA

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA inspections of nonclinical and clinical trial sites to assure compliance with GLPs or GCPs, the FDA may approve the BLA or issue a complete response letter. Under the PHSA, the FDA may approve a BLA if it determines the product is safe, pure, and potent, and that the facility in which the product will be manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, purity and potency. If the FDA determines the product meets those standards, it may issue an approval letter authorizing commercial marketing of the biological product with specific prescribing information for specific indications. If the application is not approved, FDA will issue a complete response letter, which indicates that the review cycle of the application is complete and the application is not ready for approval. A complete response letter will identify the deficiencies that prevent the FDA from approving the application and may require additional clinical data or an additional Phase 3 clinical trial(s), or other significant, expensive and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval and issue a denial.

The FDA could also approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, program to mitigate risks, which 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, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

Orphan Drug Designation

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

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Additionally, if a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor, or the sponsor is unable to provide sufficient quantities. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity. Orphan medicinal product status in the European Union has similar, but not identical, benefits.

The FDA has historically taken the position that the scope of orphan exclusivity aligns with the approved indication or use of a product, rather than the disease or condition for which the product received orphan designation. However, in Catalyst Pharms., Inc. v. Becerra, 14 F.4th 1299 (11th Cir. 2021), the court disagreed with this position, holding that orphan-drug exclusivity blocked the FDA's approval of the same drug for all uses or indications within the same orphan-designated disease. On January 24, 2023, the FDA published a notice in the Federal Register to clarify that the FDA intends to continue to apply its longstanding interpretation of the regulations to all matters outside of the scope of the Catalyst order and will continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved. It is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of orphan drug exclusivity.

Expedited Review Programs

The FDA offers a number of expedited development and review programs for qualifying product candidates.

New biological products are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast track designation applies to the combination of the 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. The sponsor of a fast track product has opportunities for more frequent interactions with the applicable FDA review team during product development and, once a BLA is submitted, the product candidate may be eligible for priority review. 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.

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

Any marketing application for a biologic submitted to the FDA for approval, including a product candidate with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite development and review, such as priority review. An application for a biological product will receive priority review designation if it is for a biological product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA will attempt to direct additional resources to the evaluation of an application for a new biological product designated for priority review in an effort to facilitate the review. For original BLAs, 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 (as compared to ten months under standard review).

Fast track designation, breakthrough therapy designation, and priority review do not change the standards for approval but may expedite the development or approval process. Even if a product candidate 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 or approval will not be shortened.

Accelerated Approval

Product candidates studied for their safety and effectiveness in treating serious 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. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, 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. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a biologic or indication approved under accelerated approval if, for example, the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the FDA, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to FDA for review during the pre-approval period. After 120 days following marketing approval, unless otherwise informed by the FDA, advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

Post-Approval Requirements

Biological products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new dosage forms, indications or other labeling claims, are subject to prior FDA review and approval.

Biological product manufacturers are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections for compliance with cGMPs. 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. Manufacturers and manufacturers' facilities are also required to comply with applicable product tracking and tracing requirements and notify the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the U.S. 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.

A biological product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official lot release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA. The FDA may perform certain confirmatory tests on lots of some products before releasing the lots for distribution.

We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates, and expect to rely in the future on third parties for the production of commercial quantities. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production, or distribution, or may require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing.

The FDA may suspend or revoke product license approvals 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 adverse events 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 trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. FDA has authority to require post-market studies, in certain circumstances, on reduced effectiveness of a biological product and FDA may require labeling changes related to new reduced effectiveness information. Other potential consequences of a failure to maintain regulatory compliance include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- issuance of safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- untitled letters or warning letters;
- imposition of clinical holds on ongoing clinical trials;
- refusal of the FDA to approve pending BLAs or supplements to approved BLAs, or suspension or revocation of approved BLAs;
- product seizure or detention, or refusal to permit the import or export of products;
- mandated modification of promotional materials and labeling, and the issuance of corrective information;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs; or
- fines, injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of prescription drug products, including biological products. These regulations include, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities and promotional activities involving the internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the BLA is approved. Once a BLA is approved, the sponsor can only make those claims relating to safety, efficacy, purity and potency that are consistent with the biological product's approved label. Additionally, promotional materials for prescription drug products must be submitted to the FDA in conjunction with their first use.

In the U.S., healthcare professionals are generally permitted to prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those approved by the FDA. The FDA does not regulate the practice of medicine or healthcare providers' choice of treatments; however, FDA restricts manufacturers' communications of off-label uses. If a company, including any agent of the company or anyone speaking on behalf of the company, is found to have promoted off-label uses, the company may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Pediatric Trials and Exclusivity

Under the Pediatric Research Equity Act of 2003, a BLA (or BLA supplement thereto) must contain data that are adequate to assess the safety and effectiveness of the product 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. A sponsor who is planning to submit a marketing application for a biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan, or PSP, within sixty days of an end of Phase 2 meeting or as may be agreed between the sponsor and FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. Generally, development program candidates designated as orphan drugs are exempt from the above requirements. FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from nonclinical studies, early phase clinical trials, and/or other clinical development programs.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. The FDA may send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent exclusivity in the U.S. and, if granted for a biologic, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity for all formulations, dosage forms, and indications of the biologic, including the five-year and three-year non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted.

Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA, plus the time between the submission date and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within 60 days of the product's approval. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, or the ACA, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or the BPCIA, which created an abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product. Biosimilarity, which requires that there be no clinically meaningful differences between the proposed biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product, can be expected to produce the same clinical results as the reference product and, for products administered multiple times, that the biologic and the reference biologic may be 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 first biologic submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product is eligible for a period of exclusivity against other biologics submitted under the abbreviated approval pathway during which time the FDA may not determine that another product is interchangeable with the same reference product for any condition of use. The FDA may approve multiple "first" interchangeable products so long as they are all approved on the same first day of marketing. This exclusivity period, which may be shared amongst multiple first interchangeable products, lasts for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologic's patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period. Products deemed "interchangeable" by the FDA may be readily substituted by pharmacies and such substitution is which are governed by state pharmacy law. The law also includes an extensive process for the innovator biologic and biosimilar manufacturer to litigate patent infringement, validity and enforceability prior to the approval of the biosimilar. Since the passage of the BPCIA, many states have passed laws or amendments to laws, including laws governing pharmacy practices to regulate the use of biosimilars.

Regulation of Companion Diagnostics

We believe that the success of certain of our product candidates may depend, in part, on the development and commercialization of a companion diagnostic. Companion diagnostics identify patients who are most likely to benefit from a particular therapeutic product; identify patients likely to be at increased risk for serious side effects as a result of treatment with a particular therapeutic product; or monitor response to treatment with a particular therapeutic product for the purpose of adjusting treatment to achieve improved safety or effectiveness. Companion diagnostics are regulated as medical devices by the FDA. In the U.S., the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption or FDA exercise of enforcement discretion applies, diagnostic tests generally require marketing clearance or approval from the FDA prior to commercialization. The primary types of FDA marketing authorization applicable to a medical device are clearance of a premarket notification, or 510(k), application, grant of a de novo request for classification, or de novo grant, and approval of a premarket approval, or PMA, application.

To obtain 510(k) clearance for a medical device, or for certain modifications to devices that have received 510(k) clearance, a manufacturer must submit a premarket notification demonstrating that the proposed device is substantially equivalent to a previously cleared 510(k) device or to a preamendment device that was in commercial distribution before May 28, 1976, or a predicate device, for which the FDA has not yet called for the submission of a PMA. In making a determination that the device is substantially equivalent to a predicate device, the FDA compares the proposed device to the predicate device or predicate devices and assesses whether the subject device is comparable to the predicate device or predicate devices with respect to intended use, technology, design and other features which could affect safety and effectiveness. If the FDA determines that the subject device is substantially equivalent to the predicate device or predicate devices, the subject device may be cleared for marketing. The 510(k) premarket notification pathway generally takes from three to twelve months from the date the application is completed, but can take significantly longer.

For novel medical devices that are low to moderate risk and are not substantially equivalent to a predicate device, a manufacturer may request a risk-based classification determination, called a "Request for Evaluation of Automatic Class III Designation," for the device in accordance with de novo classification process. This procedure allows a de novo requester whose novel device is automatically classified into Class III to request down-classification of its medical device into Class I or Class II on the basis that the device presents low or moderate risk, rather than requiring the submission and approval of a PMA. Under the FDCA, FDA must make a classification determination for the device that is the subject of a de novo request within 120 days of receipt of the request. However, as specified in FDA's Medical Device User Fee Amendments of 2022, or MDUFA V, commitment letter, the FDA's goal is to make a decision on most de novo requests within 150 FDA Days, although in practice the FDA's review may take significantly longer. During the pendency of FDA's review, the FDA may issue an additional information letter, which places the de novo request on hold and stops the review clock pending receipt of the additional information requested. In the event the de novo requestor does not provide the requested information within 180 calendar days, the FDA will consider the de novo request to be withdrawn.

The FDA may reject the de novo request if it identifies a legally marketed predicate device that would be appropriate for a 510(k) or determines that the device is not low to moderate risk or that General Controls would be inadequate to control the risks and Special Controls cannot be developed. In the event the FDA determines that the data and information submitted demonstrate that General Controls or General and Special Controls are adequate to provide reasonable assurance of safety and effectiveness, the FDA will grant the de novo request and a classification regulation will be established for the device type. When the FDA grants a de novo request for classification, the device is granted marketing authorization and can further serve as a predicate device for a future 510(k) by any person for future devices of that type.

PMA applications must be supported by valid scientific evidence, which typically requires extensive data, including technical, preclinical, clinical and manufacturing data, to demonstrate to the FDA's satisfaction the safety and effectiveness of the device. For diagnostic tests, a PMA application typically includes data regarding analytical and clinical validation studies. As part of its review of the PMA, the FDA will conduct a pre-approval inspection of the manufacturing facility or facilities to ensure compliance with the Quality System Regulation, or QSR, which requires manufacturers to follow design, testing, control, documentation and other quality assurance procedures. The FDA's review of an initial PMA application is required by statute to take between six to ten months, although the process typically takes longer, and may require several years to complete. If the FDA evaluations of both the PMA application and the manufacturing facilities are favorable, the FDA will either issue an approval letter or an approvable letter, which usually contains a number of conditions that must be met in order to secure the final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny the approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. Once granted, PMA approval may be withdrawn by the FDA if compliance with post-approval requirements, conditions of approval or other regulatory standards is not maintained or problems are identified following initial marketing.

On July 31, 2014, the FDA issued a final guidance document addressing the development and approval process for "In Vitro Companion Diagnostic Devices." According to the guidance document, for novel therapeutic products that depend on the use of a diagnostic test and where the diagnostic device could be essential for the safe and effective use of the corresponding therapeutic product, the premarket application for the companion diagnostic device should be developed and approved or cleared contemporaneously with the therapeutic, although the FDA recognizes that there may be cases when contemporaneous development may not be possible. However, in cases where a drug cannot be used safely or effectively without the companion diagnostic, the FDA's guidance indicates it will generally not approve the drug without the approval or clearance of the diagnostic device. The FDA also issued a draft guidance in July 2016 setting forth the principles for co-development of an in vitro companion diagnostic device with a therapeutic product. The draft guidance describes principles to guide the development and contemporaneous marketing authorization for the therapeutic product and its corresponding in vitro companion diagnostic.

Once cleared or approved, the companion diagnostic device must adhere to post-marketing requirements including the requirements of the FDA's quality system regulation, adverse event reporting, recalls and corrections along with product marketing requirements and limitations. Like biological product manufacturers, companion diagnostic manufacturers are subject to unannounced FDA inspections at any time during which the FDA will conduct an audit of the product(s) and the company's facilities for compliance with its authorities.

Other Regulatory Matters

Manufacturing, sales, promotion and other activities of product candidates following product approval, where applicable, or commercialization are also subject to regulation by numerous regulatory authorities in the U.S. in addition to the FDA, which may include the Centers for Medicare & Medicaid Services, or CMS, other divisions of the Department of Health and Human Services, or HHS, the Department of Justice, the Drug Enforcement Administration, the Consumer Product Safety Commission, the Federal Trade Commission, the Occupational Safety & Health Administration, the Environmental Protection Agency and state and local governments and governmental agencies.

European Union/Rest of World Government Regulation

In addition to regulations in the U.S., we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. The cost of establishing a regulatory compliance system for numerous varying jurisdictions can be very significant. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union and in other jurisdictions, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial authorization application must be submitted for each clinical trial protocol to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Under the EU Clinical Trials Regulation, this is now done through a single application submitted through the Clinical Trials Information System (CTIS), as described in more detail below.

The requirements and process governing the conduct of clinical trials vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP, the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of a medicinal product under European Union regulatory systems, we must submit a marketing authorization application. The content of the BLA filed in the U.S. is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product licensing, pricing, and reimbursement vary from country to country.

Countries that are part of the European Union, as well as countries outside of the European Union, have their own governing bodies, requirements, and processes with respect to the approval of biological products. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Clinical Trial Approval in the European Union

In April 2014, the European Union adopted the Clinical Trials Regulation (EU) No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022. The Clinical Trials Regulation is directly applicable in all European Union Member States meaning no national implementing legislation in each European Union Member State is required. The Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single-entry point, through the CTIS; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all European Union Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a reference Member State. Part II is assessed separately by each Member State concerned. Strict deadlines have also been established for the assessment of clinical trial applications.

Marketing Authorization Procedures in the European Union

Medicines can be authorized in the European Union by using either the centralized authorization procedure or national authorization procedures.

The European Commission implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the European Economic Area, or the EEA, which is comprised of the Member States of the European Union plus Norway, Iceland, and Liechtenstein. The centralized procedure is administered by the European Medicines Agency, or EMA, and is compulsory for human medicines that are: derived from certain biotechnology processes, such as genetic engineering; contain a new active substance indicated for the treatment of certain diseases, such as HIV, AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, advanced therapy medicines (gene therapy, somatic cell therapy or tissue-engineered medicines); and officially designated orphan medicines.

For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the medicine concerned contains a new active substance not yet authorized in the European Union, is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health in the European Union.

Under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use, or the CHMP, is responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Clock stops may extend the timeframe of evaluation of a marketing authorization application considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who makes the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. In this circumstance, the EMA ensures that the opinion of the CHMP is given within 150 days, excluding clock stops, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Prior to obtaining a marketing authorization in the European Union, applicants must demonstrate compliance with all measures included in an EMA-approved pediatric investigation plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The Pediatric Committee of the EMA, or the PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Data and Market Exclusivity in the European Union

In the European Union, innovative medicinal products approved on the basis of a complete and independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's pre-clinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar marketing authorization in the European Union, during a period of eight years from the date on which the reference product was first authorized in the European Union.

During an additional two-year period of market exclusivity, a generic or biosimilar marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be placed on the European Union market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. There is no guarantee that a product will be considered by the EMA to be an innovative medicinal product, and products may not qualify for data exclusivity. Even if a product is considered to be an innovative medicinal product so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained a marketing authorization based on a marketing authorization application with a complete and independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Reform of the Regulatory Framework in the European Union

The European Commission introduced legislative proposals in April 2023 that, if implemented, will replace the current regulatory framework in the European Union for all medicines (including those for rare diseases and for children). The European Commission has provided the legislative proposals to the European Parliament and the European Council for their review and approval and, in April 2024, the European Parliament proposed amendments to the legislative proposals. Once the European Commission's legislative proposals are approved (with or without amendment), they will be adopted into European Union law.

The aforementioned European Union rules are generally applicable in the EEA.

Brexit and the Regulatory Framework in the United Kingdom

The UK formally left the European Union on January 31, 2020. As a result of the Northern Ireland protocol, following Brexit, the EMA remained responsible for approving novel medicines for supply in Northern Ireland under the EU centralized procedure, and a separate authorization was required to supply the same medicine in Great Britain (i.e. England, Wales and Scotland).

On February 27, 2023, the UK government and the European Commission announced a political agreement in principle to replace the Northern Ireland Protocol with a new set of arrangements, known as the "Windsor Framework". The Windsor Framework was approved by the EU-UK Joint Committee on March 24, 2023, and the medicines aspects of the Windsor Framework have applied since January 1, 2025. This new framework fundamentally changes the previous system under the Northern Ireland Protocol, including with respect to the regulation of medicinal products in the UK. In particular, the MHRA is now responsible for approving all medicinal products destined for the UK market (i.e., Great Britain and Northern Ireland), and the EMA no longer has any role in approving medicinal products destined for Northern Ireland under the centralized procedure. A single UK-wide marketing authorization will be granted by the MHRA for all novel medicinal products to be sold in the UK, enabling products to be sold in a single pack and under a single authorization throughout the UK.

The MHRA has introduced changes to national licensing procedures, including procedures to prioritize access to new medicines that will benefit patients, an accelerated assessment procedure and new routes of evaluation for novel products and biotechnological products. On January 1, 2024, the MHRA put in place a new international recognition framework which means that the MHRA may have regard to decisions on the approval of marketing authorizations made by the EMA and certain other regulators when determining an application for a new UK marketing authorization.

Pharmaceutical Coverage, Pricing and Reimbursement

In the U.S. and foreign markets, sales of any products for which we may receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement for our products from third-party payors, such as government healthcare programs (e.g., Medicare, Medicaid), managed care organizations, private health insurers, health maintenance organizations, and other organizations. These third-party payors decide which medications they will pay for and will establish reimbursement levels. The availability of coverage and extent of reimbursement by governmental and other third-party payors is essential for patients depending on government or commercial insurance to pay for the costs of prescription medications and other medical products.

In the U.S., the principal decisions about reimbursement for new medicines are typically made by the CMS, an agency within the HHS. CMS decides whether and to what extent products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication.

Factors payors consider in determining reimbursement are based on whether the product 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.

Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors, including government healthcare programs (e.g., Medicare, Medicaid), managed care organizations, private health insurers, health maintenance organizations, and other organizations. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved.

In the U.S., no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party payors are increasingly challenging pharmaceutical prices and examining the medical necessity and cost- effectiveness of medical products and services, in addition to their safety and efficacy. In order to secure coverage and reimbursement for any product that might be approved for sale, 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 or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. A decision by a third-party payor not to cover a product could reduce utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition.

Further, the process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Even if we obtain coverage for a given product, the resulting reimbursement payment rates might not be adequate for us to achieve or sustain profitability or may require co-payments that patients find unacceptably high. There is significant uncertainty related to insurance coverage and reimbursement of newly approved products. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates.

Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and impacted 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.

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

Other U.S. Healthcare Laws

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of drug products for which we obtain marketing approval. Arrangements with third-party payors, healthcare providers and physicians, as well as patients and other third parties, in connection with the clinical research, sales, marketing and promotion of products, once approved, and related activities, may expose a pharmaceutical manufacturer to broadly applicable fraud and abuse and other healthcare laws and regulations. In the U.S., these laws include, without limitation, state and federal anti-kickback, false claims, transparency, consumer protection, and patient data privacy and security laws and regulations, including but not limited to those described below:

- The Anti-Kickback Statute, or AKS, makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully solicit, receive, offer or pay any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, that is intended to induce or reward, referrals including the purchase, recommendation, order or prescription of a particular drug for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value. The AKS has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, patients, and formulary managers on the other. 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. Further, courts have found that if "one purpose" of remuneration is to induce referrals, the AKS is violated. In addition, the government may assert that a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the federal False Claims Act, or FCA.

- The federal civil and criminal false claims laws, including the FCA, impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, claims for payment or approval from Medicare, Medicaid, or other federal or state health care programs that are false or fraudulent; knowingly making or causing a false statement material to a false or fraudulent claim or an obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing such an obligation. 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. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims. Pharmaceutical and other healthcare companies have been, and continue to be, prosecuted under these laws, among other things, for allegedly providing kickbacks to providers or patients or causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses. Similar to the AKS, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation.

- The Civil Monetary Penalties Law, which covers a variety of conduct, often violations under other laws, and includes penalties for violating the AKS, causing the submission of false claims, and offering or transfer of remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner, or supplier of services reimbursable by Medicare or a state healthcare program.

- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, imposes criminal and civil liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program (e.g., public or private) or making any false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Like the AKS, the Patient Protection and Affordable Care Act, or 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.

- HIPAA, also imposes requirements related to the privacy, security and transmission of individually identifiable health information that may apply to many healthcare providers, physicians, and third-party payors with whom we interact.

- The federal Physician Payments Sunshine Act and its implementing regulations, which 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 specific exceptions, to report annually to CMS, under the Open Payments Program, information related to payments or other transfers of value made to physicians (which has the same meaning as under Section 1861(r) of the Social Security Act, which generally includes doctors of medicine, osteopathy, dentists, optometrists, podiatrists and chiropractors who are legally authorized to practice by a state), to certain non-physician providers such as physician assistants and nurse practitioners, and to teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members.

- Federal government price reporting laws, which require manufacturers to calculate and report certain calculated product prices to the government or provide certain discounts or rebates to government authorities or private entities, often as a condition of reimbursement under governmental healthcare programs.

- Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers.

- Analogous state laws and regulations, such as state anti-kickback, false claims, consumer protection and unfair competition laws which may apply to pharmaceutical business practices, including but not limited to, research, distribution, sales and marketing arrangements as well as submitting claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; 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 that otherwise restricts payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to file reports with states regarding pricing and marketing information, such as the tracking and reporting of gifts, compensation and other remuneration and items of value provided to healthcare professionals and entities; state and local laws requiring the registration of pharmaceutical sales representatives; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. In addition, commercialization of any drug product outside the U.S. will also likely be subject to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws in the future. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to, on a corporate or individual basis, penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and even imprisonment, any of which could materially adversely affect our ability to operate our business and our financial results. In addition, the cost of implementing sufficient systems, controls, and processes to ensure compliance with all of the aforementioned laws could be significant. Any action for violation of these laws, even if successfully defended, could cause us to incur significant legal expenses and divert management's attention from the operation of the company's business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found noncompliant with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent inappropriate conduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights those actions, our business may be impaired.

In the ordinary course of our business, we and the third parties upon which we rely collect, receive, store, or otherwise process personal data, including information we may collect about participants in our clinical trials. Our data processing activities subject us to numerous, evolving privacy and data security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to privacy and data security.

The legislative and regulatory framework for the processing of personal data worldwide is rapidly evolving in a manner that is increasingly stringent and, globally, this legal and regulatory framework is likely to remain uncertain for the foreseeable future. In the U.S., numerous federal, state and local laws and regulations, including federal health information privacy laws, state information security and data breach notification laws, federal consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), state consumer protection and privacy laws, and other similar laws (e.g., wiretapping and communications interception laws) govern the processing of health-related and other personal data.

At the state level, numerous U.S. states have enacted comprehensive privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording individuals certain rights concerning their personal data. Similar laws are being considered in several other states, as well as at the federal and local levels, and we expect more states to pass similar laws in the future. While existing state comprehensive privacy laws exempt some data processed in the context of clinical trials, these developments may further complicate compliance efforts, and increase legal risk and compliance costs for us and the third parties upon whom we rely.

Additionally, a smaller number of states have passed or are considering laws governing the privacy of consumer health data. For example, Washington's My Health My Data Act broadly defines consumer health data, creates a private right of action to allow individuals to sue for violations of the law, imposes stringent consent requirements, and grants consumers certain rights with respect to their health data, including to request deletion of their information. Connecticut and Nevada have also passed similar laws regulating consumer health data. These various privacy and data security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products.

Additionally, to the extent we collect personal information from individuals outside of the United States, through clinical trials or otherwise, we are, or may become, subject to foreign data privacy and security laws, such as the European Union's General Data Protection Regulation 2016/679 (or EU GDPR) and other national data protection legislation in force in relevant EEA Member States, and the EU GDPR as it forms part UK law by virtue of section 3 of the European Union (Withdrawal) Act 2018 (or UK GDPR). Foreign privacy and data security laws impose significant and complex compliance obligations on entities that are subject to those laws, as more fully discussed in the section titled "Risk Factors".

Current and Future U.S. Healthcare Reform Legislation

Payors, whether domestic or foreign, or governmental or private, are developing increasingly sophisticated methods of controlling healthcare costs and those methods are not always specifically adapted for new and innovative technologies, such as pharmaceutical products like ficerafusp alfa. In both the U.S. and certain foreign jurisdictions, there have been a number of legislative and regulatory changes to the health care system that could impact our ability to sell products profitably.

By way of example, the U.S. and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the ACA, was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created the Medicare Part D coverage gap discount program, in which manufacturers agree to provide 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research. Current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price for any approved products.

Since its enactment, there have been, and continue to be, numerous judicial, administrative, executive, and legislative challenges to certain aspects of the ACA, and there could be additional amendments to the ACA in the future. It is unclear whether the ACA will be overturned, repealed, replaced, or further amended. We cannot predict what effect further changes to the ACA would have on our business.

Additionally, there have been several U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient support programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The IRA includes several provisions that may impact pharmaceutical companies to varying degrees, including provisions that create a $2,000 out-of-pocket cap for Medicare Part D beneficiaries; impose new manufacturer financial liability on all drugs in Medicare Part D; allow the U.S. government to negotiate Medicare Part B and Part D pricing caps for certain high-cost drugs and biologics without generic or biosimilar competition; require companies to pay rebates to Medicare for drug prices that increase faster than inflation; and delay the rebate rule that would require pass through of pharmacy benefit manager rebates to beneficiaries. The implementation of the IRA is currently subject to ongoing litigation that challenges the constitutionality of the IRA's Medicare drug price negotiation program. The full impact of the IRA on our business and the pharmaceutical and healthcare industry in general is not yet known.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical 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.

Employees and Human Capital Resources

As of March 24, 2025, we had 55 full-time employees. Within our workforce, 36 employees are engaged in research and development and 19 are engaged in business development, finance, legal, and general management and administration. Our human capital resources objectives include identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good. We believe the success of our mission largely depends on our ability to attract and retain highly skilled employees. We believe programs that foster company engagement, diversity, equity and inclusion, growth and development while providing competitive compensation and benefits will attract a diverse population of employees who will bring innovative ideas and creative solutions that will enable the achievement of our goals. Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Corporate Information

We were incorporated under the laws of the State of Delaware on December 12, 2018 under the name "Bicara Therapeutics Inc." Our principal corporate office is located at 116 Huntington Avenue, Suite 703, Boston, MA 02116, and our telephone number is 617-468-4219. We have one subsidiary, Bicara Securities Corporation, formed in October 2023 under the laws of the Commonwealth of Massachusetts. Our website address is www.bicara.com. We do not incorporate the information on or accessible through our website into this Annual Report on Form 10-K, and you should not consider any information on, or that can be accessed through, our website as part of this Annual Report on Form 10-K.

Available Information

Our website address is www.bicara.com. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, proxy and information statements and amendments to those reports filed or furnished pursuant to Sections 13(a), 14, and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, are available through the "Investors" portion of our website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information on our website is not part of this Annual Report on Form 10-K or any of our other securities filings unless specifically incorporated herein by reference. In addition, our filings with the SEC may be accessed through the SEC's Interactive Data Electronic Applications system at www.sec.gov. All statements made in any of our securities filings, including all forward-looking statements or information, are made as of the date of the document in which the statement is included, and we do not assume or undertake any obligation to update any of those statements or documents unless we are required to do so by law.

Our code of business conduct and ethics, corporate governance guidelines and the charters of our Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are available through the "Investors" portion of our website. We will also post to our website any amendments to our code of business conduct and ethics and any waivers that are required to be disclosed by SEC or Nasdaq Rules. Additionally, we routinely post information that may be important to inventors to the "Investors" section of our website. We encourage investors and potential investors to consult our website regularly for important information about our Company.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should consider and read carefully all of the risks and uncertainties described below, as well as the other information in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" before deciding whether to invest in our common stock. The risks described below are not the only ones facing us. The following risks or additional risks and uncertainties not presently known to us or that we currently believe to be immaterial could materially and adversely affect our business, financial condition, results of operations and growth prospects. In such an event, the trading price of our common stock could decline, and you may lose all or part of your investment.

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

Risks Related to Our Limited Operating History, Financial Condition and Need for Additional Capital

We are a clinical-stage biopharmaceutical company with a limited operating history, which may make it difficult to evaluate our current business and predict our future success and viability. We have incurred significant financial losses since our inception and anticipate that we will continue to incur significant financial losses for the foreseeable future.

We are a clinical-stage biopharmaceutical company with a limited operating history. We were formed in December 2018, and our operations to date have been limited to pre-commercial activities. We have not yet demonstrated an ability to generate revenue, obtain regulatory approval, manufacture any 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 product commercialization. Our limited operating history as a company makes any assessment of our future success and viability subject to significant uncertainty. We will encounter risks and difficulties frequently experienced by early-stage biopharmaceutical companies in rapidly evolving fields, and we have not yet demonstrated an ability to successfully overcome such risks and difficulties. If we do not address these risks and difficulties successfully, our business will suffer.

We have no products approved for commercial sale and have not generated any revenue from product sales to date. We will continue to incur significant research and development and other expenses related to our preclinical and clinical development and ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. Our net losses totaled $68.0 million and $52.0 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we have not yet generated revenues. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, ficerafusp alfa.

We anticipate that our expenses will increase substantially if, and as, we:

- advance ficerafusp alfa through clinical development;
- seek regulatory approvals for ficerafusp alfa and any future our product candidates that successfully complete clinical trials;
- hire additional clinical, quality control, medical, scientific and other technical personnel to support the clinical development of ficerafusp alfa and any future product candidate;
- experience an increase in headcount as we expand our research and development organization and market development and pre-commercial planning activities;
- undertake any pre-commercial or commercial activities to establish sales, marketing and distribution capabilities;
- advancing any future product candidates into clinical development; seek to identify, acquire and develop additional product candidates, including through business development efforts to invest in or in-license other technologies or product candidates;
- maintain, expand and protect our intellectual property portfolio;
- make any payments due under our license agreements and any potential milestones, royalties or other payments due under any future in-license or collaboration agreements; and
- make milestone, royalty, interest or other payments due under any future financing or other arrangements with third parties.

Biopharmaceutical product development entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate efficacy or an acceptable safety profile, gain regulatory approval, secure market access and reimbursement and become commercially viable, and therefore any investment in us is highly speculative. Accordingly, before making an investment in us, you should consider our prospects, factoring in the costs, uncertainties, delays and difficulties frequently encountered by companies in clinical development, especially clinical-stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they would otherwise be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives.

Additionally, our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration, or the FDA, Health Canada, the European Medicines Agency, or the EMA, or other comparable regulatory authorities to perform clinical trials in addition to those that we currently expect, or if there are any delays in establishing appropriate manufacturing arrangements for or in completing our clinical trials or the development of any of our product candidate.

We will require additional funding in order to finance operations. If we are unable to raise capital when needed, or on acceptable terms, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

Developing biopharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to continue to increase in connection with our ongoing activities, particularly as we conduct clinical trials of, and seek regulatory and marketing approval for, ficerafusp alfa. Even if ficerafusp alfa or any future product candidates are approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. To date, we have funded our operations principally through our IPO and private financings. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical and preclinical development of ficerafusp alfa, continue to develop and deploy our bifunctional approach, commence additional preclinical studies and clinical trials, and continue to identify and develop additional product candidates either through internal development or through acquisitions or in-licensing product candidates.

As of December 31, 2024, we had $489.7 million of cash and cash equivalents. Based upon our current operating plan, we believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements through at least the next 12 months. In addition, based upon our current operating plan, we believe that our existing cash and cash equivalents will enable us to fund our operating expenses and capital expenditure requirements into the first half of 2029. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we expect. We may also raise additional financing on an opportunistic basis in the future. For example, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop ficerafusp alfa. Our future capital requirements will depend on many factors, including but not limited to:

- the scope, timing, progress, costs and results of discovery, preclinical development and clinical trials for ficerafusp alfa or any future product candidates;
- the number of clinical trials required for regulatory approval of ficerafusp alfa or future product candidates;
- the costs, timing and outcome of regulatory review of ficerafusp alfa or any future product candidates;
- the costs associated with acquiring or licensing additional product candidates, technologies or assets, including the timing and amount of any milestones, royalties or other payments due in connection with our acquisitions and licenses;
- the cost of manufacturing clinical and commercial supplies of ficerafusp alfa or any future product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims, including any claims by third parties that we are infringing upon their intellectual property rights;
- the effectiveness of our approach at identifying target patient populations and utilizing our approach to enrich our patient population in our clinical trials;
- our ability to maintain existing, and establish new, strategic collaborations or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- expenses to attract, hire and retain skilled personnel;
- the costs of operating as a public company;
- our ability to establish a commercially viable pricing structure and obtain approval for coverage and adequate reimbursement from third-party and government payors;
- the effect of macroeconomic trends including inflation and rising interest rates;
- addressing any potential supply chain interruptions or delays;
- the effect of competing technological and market developments; and
- the extent to which we acquire or invest in business, products and technologies.

Because of the numerous risks and uncertainties associated with research and development of product candidates, we are unable to predict the timing or amount of our working capital requirements. In addition, if we obtain regulatory approval for ficerafusp alfa, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution which make it difficult to predict when or if we will be able to achieve or maintain profitability. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in order to support our continuing operations. Our ability to raise additional funds will depend on financial, economic, political and market conditions and other factors, over which we may have no or limited control. Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If we fail to obtain necessary capital when needed on acceptable terms, or at all, it could force us to delay, limit, reduce or terminate our product development programs, future commercialization efforts or other operations.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to ficerafusp alfa.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations with our existing cash and cash equivalents, the net proceeds from our initial public offering, short-term investments, or any future equity or debt financings and upfront and milestone and royalties payments, if any, received under any future licenses or collaborations. In the future, if we raise additional capital through the sale of equity or convertible debt securities or issue any equity or convertible debt securities in connection with a collaboration agreement or other contractual arrangement, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a holder of our common stock. In addition, the possibility of such issuance may cause the market price of our common stock to decline. Debt financing, if available, may result in increased fixed payment obligations and involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, declaring dividends or acquiring, selling or licensing intellectual property rights or assets, which could adversely impact our ability to conduct our business.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties in the future, we may have to relinquish valuable rights to our intellectual property, technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. We could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable. Any of these occurrences may have a material adverse effect on our business, operating results and prospects.

We maintain the majority of our cash and cash equivalents in accounts with major U.S. and multi-national financial institutions, and our deposits at certain of these institutions exceed insured limits. Market conditions and changes in financial regulations and policies can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position. In addition, changes in regulations governing financial institutions are beyond our control and difficult to predict; consequently, the impact of such changes on our business and results of operations is difficult to predict and may have an adverse effect on us.

Risks Related to Our Business Operations and Industry

Our business is highly dependent on the success of ficerafusp alfa. If we are unable to successfully complete clinical development, obtain regulatory approval for or commercialize ficerafusp alfa, or if we experience delays in doing so, our business will be materially harmed.

To date, as an organization, we have not completed the development of any product candidates and ficerafusp alfa remains in clinical or preclinical development. Our future success and ability to generate revenue from ficerafusp alfa is dependent on our ability to successfully develop and commercialize ficerafusp alfa or any of our future product candidates. If any of our product candidates encounters safety or efficacy problems, development delays or regulatory issues or other problems, our development plans and business would be materially harmed.

We may not have the financial resources to continue development of ficerafusp alfa if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, ficerafusp alfa, including:

- our inability to demonstrate to the satisfaction of the FDA, Health Canada, EMA or other comparable regulatory authorities that ficerafusp alfa is safe and effective;
- delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial or a suspension, termination, or hold, of a clinical trial once commenced;
- conditions imposed by the FDA, Health Canada, the EMA or other comparable regulatory authorities regarding the scope or design of our clinical trials;
- delays or failures in reaching agreement on acceptable terms with clinical trial sites or contract research organizations, or CROs;
- poor effectiveness of ficerafusp alfa during clinical trials;
- better than expected performance of control arms, such as placebo groups, which could lead to negative or inconclusive results from our clinical trials;
- higher than anticipated clinical trial or manufacturing costs;
- unfavorable FDA, Health Canada, EMA or other comparable regulatory authority inspection and review of our clinical trial sites;
- failure of our CROs, clinical trial sites, or investigators to comply with regulatory requirements or the clinical trial protocol or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policies and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our therapies in particular; or
- varying interpretations of data by the FDA, Health Canada, EMA and other comparable regulatory authorities.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biotechnology industry is intensely competitive and subject to rapid and significant technological change. ficerafusp alfa or any future product candidates may face competition from major pharmaceutical companies, specialty pharmaceutical companies, universities and other research institutions and from products and therapies that currently exist or are being developed, some of which products and therapies we may not currently know about. Many of our competitors have significantly greater financial, manufacturing, marketing, product development, technical and human resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining marketing approvals, recruiting patients and manufacturing pharmaceutical products, and they may also have products that have been approved or are in late stages of development, and collaborative arrangements in our target markets with leading companies and research institutions. Established pharmaceutical companies may also invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make the product candidates that we develop obsolete. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. As a result of all of these factors, our competitors may succeed in obtaining patent protection and/or FDA, Health Canada, the EMA or other regulatory approval or discovering, developing and commercializing products in our field before we do, which could result in our competitors establishing a strong market position before we are able to enter the market.

Our competitors may obtain FDA, Health Canada, the EMA or other regulatory approval of their product candidates more rapidly than we may or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize ficerafusp alfa. Our competitors may also develop drugs or discovery platforms that are more effective, more convenient, more widely used or less costly than ficerafusp alfa or, in the case of drugs, have a better safety profile than ficerafusp alfa. These competitors may also be more successful than us in manufacturing and marketing their products and have significantly greater financial resources and expertise in research and development.

There are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. In addition, numerous compounds are in clinical development for cancer treatment. Many of these companies are well-capitalized and have significant clinical experience. More specifically, we expect to compete with commercially available therapies for the treatment of head and neck squamous cell carcinoma, or HNSCC, including pembrolizumab (marketed as Keytruda by Merck & Co); the combination of pembrolizumab, platinum chemotherapy and 5-fluorouracil; and the combination of cetuximab (marketed as Erbitux by Eli Lilly in the US and by Merck KGaA outside of the US), platinum chemotherapy and 5-fluorouracil. In addition, there are numerous companies that are developing new treatments for HNSCC, including Merck & Co, Pfizer Inc., Genmab A/S, Exelixis, Inc., Merus N.V., Iovance Biotherapeutics, Inc., Kura Oncology, Inc. and ALX Oncology Holdings, Inc.

Smaller and other early-stage companies may also prove to be significant competitors. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, ficerafusp alfa and any future product candidates. In addition, the biopharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or products developed by our competitors may render ficerafusp alfa obsolete, less competitive or uneconomical.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient, have a broader label, are marketed more effectively, are reimbursed or are less expensive than any products that we may develop. Our competitors may also obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize ficerafusp alfa. Even if ficerafusp alfa achieves marketing approval, it may be priced at a significant premium over competitive products if any have been approved by then, resulting in reduced competitiveness. If we do not compete successfully, we may not generate or derive sufficient revenue from any product candidate for which we obtain marketing approval and may not become or remain profitable.

Due to the significant resources required for the development of our pipeline, and depending on our ability to access capital, we must prioritize the development of certain product candidates over others. Moreover, we may fail to expend our limited resources on product candidates or indications that may have been more profitable or for which there is a greater likelihood of success.

Our lead program, ficerafusp alfa, is initially being developed in HNSCC. We initiated a pivotal FORTIFI-HN01 Phase 2/3 trial of ficerafusp alfa in combination with pembrolizumab as a first-line therapy in recurrent/metastatic HNSCC excluding patients with HPV-positive oropharyngeal squamous cell carcinoma, or OPSCC, and, more generally, we seek to bring transformative bifunctional therapies to patients with solid tumors.

Due to the significant resources required for the development of our product candidates, we must decide which product candidates and indications to pursue and advance and the amount of resources to allocate to each. Our decisions concerning the allocation of research, development, collaboration, management and financial resources toward particular product candidates, therapeutic areas or indications may not lead to the development of viable commercial products and may divert resources away from better opportunities. If we make incorrect determinations regarding the viability or market potential of any of our product candidates or misread trends in the pharmaceutical industry, in particular for disorders of the brain and nervous system, our business, financial condition and results of operations could be materially and adversely affected. As a result, we may fail to capitalize on viable commercial products or profitable market opportunities, be required to forego or delay pursuit of opportunities with other product candidates or other diseases and disease pathways that may later prove to have greater commercial potential than those we choose to pursue, or relinquish valuable rights to such product candidates through collaboration, licensing or royalty arrangements in cases in which it would have been advantageous for us to invest additional resources to retain sole development and commercialization rights.

We may seek to grow our business through acquisitions or investments in new or complementary businesses, products or technologies, through the licensing of products or technologies from third parties or other strategic alliances. The failure to manage acquisitions, investments, licenses or other strategic alliances, or the failure to integrate them with our existing business, could have a material adverse effect on our operating results, dilute our stockholders' ownership, increase our debt or cause us to incur significant expense.

Our success depends on our ability to continually enhance and broaden our product offerings in response to changing clinician and patients' needs, competitive technologies and market pressures. Accordingly, from time to time we may consider opportunities to acquire, make investments in or license other technologies, products and businesses that may enhance our capabilities, complement our existing products and technologies or expand the breadth of our markets or customer base. Potential and completed acquisitions, strategic investments, licenses and other alliances involve numerous risks, including:

- difficulty assimilating or integrating acquired or licensed technologies, products, employees or business operations;
- issues maintaining uniform standards, procedures, controls and policies;
- unanticipated costs associated with acquisitions or strategic alliances, including the assumption of unknown or contingent liabilities and the incurrence of debt or future write-offs of intangible assets or goodwill;
- diversion of management's attention from our core business and disruption of ongoing operations;
- adverse effects on existing business relationships with suppliers, sales agents, health care facilities, surgeons and other health care providers;
- risks associated with entering new markets in which we have limited or no experience;
- potential losses related to investments in other companies;
- potential loss of key employees of acquired businesses; and
- increased legal and accounting compliance costs.

We do not know if we will be able to identify acquisitions or strategic relationships we deem suitable, whether we will be able to successfully complete any such transactions on favorable terms, if at all, or whether we will be able to successfully integrate any acquired business, product or technology into our business or retain any key personnel, suppliers, sales agent, health care facilities, physicians or other health care providers. Our ability to successfully grow through strategic transactions depends upon our ability to identify, negotiate, complete and integrate suitable target businesses, technologies or products and to obtain any necessary financing. These efforts could be expensive and time-consuming and may disrupt our ongoing business and prevent management from focusing on our operations.

To finance any acquisitions, investments or strategic alliances, we may choose to issue shares of our common stock as consideration, which could dilute the ownership of our stockholders. If the price of our common stock is low or volatile, we may be unable to consummate any acquisitions, investments or strategic alliances using our common stock as consideration. Additional funds may not be available on terms that are favorable to us, or at all.

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

We are exposed to the risk of employee fraud or other illegal activity by our current and any future employees, independent contractors, consultants, contract manufacturing organizations, or CMOs, and vendors. Misconduct by these parties could include intentional, reckless, and/or negligent conduct that fails to comply with FDA, Health Canada, the EMA or other regulations, provide true, complete and accurate information to the FDA, Health Canada, EMA and other comparable regulatory authorities, comply with manufacturing standards we may establish, comply with healthcare fraud and abuse laws and regulations, report financial information or data accurately, or disclose unauthorized activities to us. If we obtain FDA approval of any of our product candidates and begin commercializing those products in the U.S., our potential exposure under these laws will increase significantly, and our costs associated with compliance with these laws are likely to increase. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

We, our collaborators and our service providers are subject to a variety of privacy and data security laws, regulations and contractual obligations, which may require us to incur substantial compliance costs, and any failure or perceived failure by us to comply with them could expose us to significant fines and other penalties and otherwise harm our business and operations.

The legislative and regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of personal information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, several jurisdictions, including those in which we operate or collect personal information, have established their own data security and privacy frameworks with which we must comply. In the U.S., numerous federal and state laws and regulations, including federal health information privacy laws, state information security and data breach notification laws, state health information privacy laws, and federal and state consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act), that govern the collection, use, disclosure and protection of health-related and other personal information, could apply to our operations or the operations of our collaborators and service providers. In particular, regulations promulgated pursuant to HIPAA establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and impose requirements regarding the privacy and security of individually identifiable health information, including mandatory contractual terms, for covered entities, or certain healthcare providers, health plans and healthcare clearinghouses, and their business associates that provide services to the covered entity that involve individually identifiable health information and their subcontractors that use, disclose or otherwise process individually identifiable health information. While pharmaceutical and biotechnology companies are typically not directly regulated by HIPAA, our business may be indirectly impacted by HIPAA in our interactions with providers, payors, and others that have HIPAA compliance obligations. If we are unable to properly protect the privacy and security of protected health information, we could be found to have violated these privacy and security laws and/or breached certain contracts. Further, if we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face significant civil and criminal penalties. U.S. Department of Health & Human Services, or HHS, enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources.

At the state level, numerous states have or are in the process of enacting or considering comprehensive data privacy and security laws, rules and regulations while other states have focused on more narrow aspects of privacy. Such proposed legislation, if enacted, may add additional complexity, variation in requirements, restrictions and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country would make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance. In the state of Washington, for example, the My Health My Data Act, which has a private right of action that further increases the relevant compliance risk, requires regulated entities to obtain consent to collect health-related information and grants consumers certain rights, including to request deletion of their information. Connecticut and Nevada have also passed similar laws regulating consumer health data. In addition, other states have proposed and/or passed legislation that regulates the privacy and/or security of certain specific types of information. For example, a small number of states have passed laws that regulate biometric data specifically. Although many of the existing state privacy laws exempt clinical trial information and health information governed by HIPAA, future privacy and data protection laws may be broader in scope. These various privacy and security laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of our products. State laws are changing rapidly and there is discussion in the U.S. Congress of a new comprehensive federal data privacy law to which we may likely become subject, if enacted.

If we conduct clinical trials in the European Economic Area, or the EEA, and/or the United Kingdom, or the U.K., we will be subject to additional, more stringent privacy laws in other jurisdictions, such as the General Data Protection Regulation, or the EU GDPR, as well as other national data protection legislation in force in relevant European Union, or EU, member states. The EU GDPR imposes strict regulations and establishes a series of requirements regarding the collection, transfer, storage and processing of personal data. Following the U.K.'s withdrawal from the EU on January 31, 2020 and the end of the transitional arrangements agreed between the U.K. and EU as of January 1, 2021, the EU GDPR has been incorporated into U.K. domestic law by virtue of section 3 of the European Union (Withdrawal) Act 2018 and amended by the Data Protection, Privacy and Electronic Communications (Amendments etc.) (EU Exit) Regulations 2019, or the U.K. GDPR, and, together with the EU GDPR, the GDPR. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including strict requirements relating to processing of sensitive data (such as health data), ensuring there is a legal basis or condition to justify the processing of personal data, where required strict requirements relating to obtaining consent of individuals, disclosures about how personal information is to be used, limitations on retention of information, implementing safeguards to protect the security and confidentiality of personal data, where required providing notification of data breaches, maintaining records of processing activities, documenting data protection impact assessments where there is high risk processing and taking certain measures when engaging third-party processors.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA or the U.K., including the United States (see below), and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million (£17.5 million GBP) or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Non-compliance could also result in the imposition of orders to stop data processing activities, which could have a material adverse effect on our business, financial position and results of operations.

When subject to GDPR, we will be required to put in place mechanisms to ensure compliance, including as implemented by national laws of EU Member States which may partially deviate from the EU GDPR and impose different and more restrictive obligations from country to country. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European and U.K. activities.

The U.K. GDPR and the U.K. Data Protection Act 2018 set out the U.K.'s data protection regime, which is independent from but, currently, aligned to the EU's data protection regime. The European Commission, or the EC, has adopted an adequacy decision in respect of transfers of personal data to the U.K. for a four-year period (until June 27, 2025). Similarly, the U.K. has determined that it considers all of the EEA to be adequate for the purposes of data protection. This ensures that data flows between the U.K. and the EEA remain unaffected. The U.K. Government has also introduced a Data Use and Access Bill (or the UK Bill) into the UK legislative process with the intention for this bill to reform the U.K.'s data protection regime which will likely have the effect of further altering the similarities between the U.K. and EU data protection regime.

In addition, we will be required to implement adequate safeguards to enable the transfer of personal data outside of the EEA or the U.K., in particular to the U.S., in compliance with the GDPR. In some cases, we may rely upon the EC's approved standard contractual clauses to legitimize transfers of personal data out of the EEA from controllers or processors established outside the EEA (and not subject to the GDPR). The U.K. is not subject to the EC's standard contractual clauses but has published its own transfer mechanism, the International Data Transfer Addendum/Agreement, which enables transfers from the U.K. Changes with respect to any of these matters may lead to additional costs and increase our overall risk exposure. The EU and U.S. have adopted its adequacy decision for the EU U.S. Data Privacy Framework, or the Framework, which entered into force on July 11, 2023. This Framework provides that the protection of personal data transferred between the EU and certified companies in the U.S. is comparable to that offered in the EU. Moreover, the U.K. Government adopted the Data Protection (Adequacy) Regulations 2023, also referred to as the "UK-U.S. Data Bridge", which, since 12 October 2023 allows companies to transfer personal data from the U.K. to the U.S. on the basis of the Framework. This provides a further avenue to ensuring transfers to the U.S. are carried out in line with GDPR. However, the long-term validity of the Framework remains uncertain and it has already been challenged before European courts.

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

Additionally, the NIS 2 Directive, or NIS 2 is replacing the cybersecurity legal framework under the current NIS framework in the EU, aiming to ensure a high level of cybersecurity in the region. NIS 2 brings new medium and large organisations providing services in the EU within scope of the legal framework. It extends to additional sectors and expands the list of in-scope healthcare organisations, including to certain providers engaged in research and development of medicinal products. The new regime imposes direct obligations on management in respect of an in-scope organization's compliance with NIS 2, requires covered organisations to put in place certain cyber risk management measures, strengthens incident reporting requirements and provides supervisory authorities with a greater oversight. The majority of obligations will come into force when national legislation implementing NIS 2 becomes effective in the relevant EU Member State. EU Member States had until 17 October 2024 to transpose NIS 2 into national legislation, although many countries have still not completed the transposition. As such, the cybersecurity regulatory landscape in the EU is currently fragmented and uncertain. To the extent we are subject to NIS 2, we will require additional investment of our resources in compliance programs. Under NIS 2 companies may be subject to administrative fines of up to the higher amount of €10 million or 2% of worldwide turnover.

If we are unable to protect the confidentiality of our proprietary information, the value of ficerafusp alfa could be adversely affected.

In addition to patent protection, we also rely on other proprietary rights, including protection of trade secrets and/or confidential know-how, unpatented know-how and/or other proprietary information. We may rely on other proprietary rights, including protection of trade secrets, confidential know-how, unpatented know-how and/or other proprietary information to protect ficerafusp alfa, especially where patent protection is believed to be of limited value. However, trade secrets and/or confidential know-how are difficult to maintain as confidential. To maintain the confidentiality of this type of information, it is our policy to enter into confidentiality agreements with our employees, consultants, advisors, collaborators, contractors (including CROs), and others upon the commencement of their relationships with us. These agreements require that all confidential information developed by the individual(s) or made known to the individual by us during the course of the individual's relationship or work with us be kept confidential and not disclosed to third parties. Our agreements with employees and our personnel policies also provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms, intentionally or unintentionally. Thus, despite such agreement, such inventions may become assigned to third parties. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets or other confidential information. To the extent that our employees, consultants, contractors or others use technology or know-how owned by third parties in their work for us, disputes may arise between us and those third parties as to the rights in related inventions. To the extent that an individual who is not obligated to assign rights in intellectual property to us or a current or future licensor is rightfully an inventor of intellectual property, we may need to obtain an assignment or a license to that intellectual property from that individual, or a third party or from that individual's assignee. Such assignment or license may not be available on commercially reasonable terms or at all. The disclosure of our trade secrets could impair our competitive position and may materially harm our business, financial condition and results of operations.

Enforcing a claim that a third party obtained illegally and is using trade secrets and/or confidential know-how is expensive, time consuming and unpredictable. The enforceability of confidentiality agreements and theft of trade secret claims may vary from jurisdiction to jurisdiction. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. As such, adequate remedies may not exist in the event of unauthorized use or disclosure of our proprietary information.

In addition, others may independently discover or develop our trade secrets and proprietary information, and the existence of our own trade secrets affords no protection against such independent discovery. Such persons may even apply for patent protection in respect of the same. If successful in obtaining such patent protection, such persons could limit our use of our trade secrets and/or confidential know-how. Under certain circumstances and to guarantee our freedom to operate, we may also decide to publish some know-how to prevent others from obtaining patent rights covering such know-how.

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

We may integrate AI into our operations, and this innovation presents risks and challenges that could affect its adoption, and therefore our business. The use of certain artificial intelligence technology can give rise to intellectual property risks, including compromises to proprietary intellectual property and intellectual property infringement. Additionally, we expect to see increasing government and supranational regulation related to artificial intelligence use and ethics, which may also significantly increase the burden and cost of research, development and compliance in this area. For example, the EU's Artificial Intelligence Act, or the AI Act—the world's first comprehensive AI law entered into force in 2024 and, with some exceptions, become effective 24 months thereafter. This legislation imposes significant obligations on providers and deployers of high risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems. If we deploy AI systems that are governed by the AI Act, we may be required to adopt higher standards of data quality, transparency, and human oversight, and adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements. Likewise, in the U.S., several states, including Colorado and California, passed laws that will take effect in 2026, to regulate various uses of artificial intelligence, including to make consequential decisions. In addition, various federal regulators have issued guidance and focused enforcement efforts on the use of AI in regulated sectors. The U.S. Food and Drug Administration, for example, issued guidance on the use of artificial intelligence in medical devices, requiring detailed risk management and review processes to obtain approvals. The rapid evolution of AI will require the application of significant resources to design, develop, test and maintain our products and services to help ensure that AI is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. Our vendors may in turn incorporate AI tools into their own offerings, and the providers of these AI tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of AI, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

Risks Related to the Discovery and Development of ficerafusp alfa or Future Product Candidates

Our business is dependent on our ability to advance ficerafusp alfa and future product candidates through clinical trials, obtain marketing approval and ultimately commercialize them.

We are early in our development efforts as ficerafusp alfa remains in clinical development. Our ability to generate product revenues, which we do not expect will occur for several years, if ever, will depend heavily on the successful development and eventual regulatory approval and commercialization of our current products or future product candidates we develop, which may never occur. Our current product candidate, ficerafusp alfa, and any future product candidates we develop will require additional preclinical or clinical development, management of clinical, preclinical and manufacturing activities, marketing approval in the U.S., Canada and other jurisdictions, demonstration of effectiveness to pricing and reimbursement authorities, sufficient manufacturing supply for both preclinical and clinical development and commercial production, building of a commercial organization and substantial investment and significant marketing efforts before we generate any revenues from product sales.

The clinical and commercial success of ficerafusp alfa and any future product candidates will depend on several factors, including the following:

- timely and successful completion of our clinical trials;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- our plans to successfully submit new Investigational New Drug, or IND, applications with the FDA for ficerafusp alfa and any future product candidates;
- our ability to complete preclinical studies for ficerafusp alfa or any future product candidates;
- successful enrollment in, and completion of clinical trials;
- successful data from our clinical program that supports an acceptable risk-benefit profile of our product candidates in the intended patient populations;
- our ability to establish agreements with third-party manufacturers on a timely and cost-efficient manner;
- whether we are required by the FDA, Health Canada, the EMA or comparable foreign regulatory authorities to conduct additional clinical trials or other studies beyond those planned or anticipated to support approval of our product candidates;
- acceptance of our proposed indications and the primary endpoint assessments evaluated in the clinical trials of our product candidates by the FDA and comparable foreign regulatory authorities;
- receipt and maintenance of timely marketing approvals from applicable regulatory authorities;
- successfully launching commercial sales of our product candidates, if approved;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates, if approved;
- entry into collaborations to further the development of our product candidates;
- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates;
- acceptance of the benefits and uses of our product candidates, if approved, by patients, the medical community and third-party payors;
- maintaining a continued acceptable safety, tolerability and efficacy profile of any product candidates following approval;
- our compliance with any post-approval requirements imposed on our products, such as post-marketing studies, a Risk Evaluation and Mitigation Strategy, or REMS, or additional requirements that might limit the promotion, advertising, distribution or sales of our products or make the products cost prohibitive;
- competing effectively with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement from third-party payors; and
- enforcing and defending intellectual property rights and claims.

These factors, many of which are beyond our control, could cause us to fall behind our competitors, experience significant delays or an inability to obtain regulatory approvals or commercialize ficerafusp alfa or future product candidates, and could otherwise materially harm our business. Successful completion of preclinical studies and clinical trials does not mean that ficerafusp alfa or any future product candidates we develop will receive regulatory approval. Even if regulatory approvals are obtained, we could experience significant delays or an inability to successfully commercialize our current and any future product candidates we develop, which would materially harm our business. If we are not able to generate sufficient revenue through the sale of ficerafusp alfa or any future product candidate, we may not be able to continue our business operations or achieve profitability.

Clinical development involves a lengthy and expensive process with uncertain outcomes. We may incur additional costs and experience delays in developing and commercializing or be unable to develop or commercialize ficerafusp alfa and any future product candidates.

To obtain the requisite regulatory approvals to commercialize any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe, pure and potent in humans and have a favorable risk-benefit profile. Clinical trials are expensive and can take many years to complete, with a highly uncertain outcome. Failure can occur at any time during the clinical trial process and our future clinical trial results may not be successful. We may experience delays in completing our clinical trials or preclinical studies and initiating or completing additional clinical trials. We cannot be certain the ongoing and planned preclinical studies or clinical trials for ficerafusp alfa or any other future product candidates will begin on time, not require redesign, enroll an adequate number of subjects on time or be completed on schedule, if at all. We may also experience numerous unforeseen events during our clinical trials that could delay or prevent our ability to receive marketing approval or commercialize the product candidates we develop, including:

- results from preclinical studies or clinical trials may not be predictive of results from later clinical trials of any product candidate;
- the FDA, Health Canada, the EMA or other regulatory authorities, Institutional Review Boards, or IRBs, or independent ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- the FDA, Health Canada, the EMA or regulatory authorities may require us to submit additional data such as long-term toxicology studies, or impose other requirements on us, before permitting us to initiate a clinical trial;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective CROs, as the terms of these agreements can be subject to extensive negotiation and vary significantly among different CROs and trial sites;
- clinical trials of any product candidate may fail to show safety, purity or potency, or may produce negative or inconclusive results, which may cause us to decide, or regulators to require us, to conduct additional nonclinical studies or clinical trials or which may cause us to decide to abandon product candidate development programs;
- the number of patients required for clinical trials may be larger than we anticipate, or we may have difficulty in recruiting and enrolling patients to participate in clinical trials, including as a result of the size and nature of the patient population, the proximity of patients to clinical trial sites, eligibility criteria for the clinical trial, the nature of the clinical trial protocol, the availability of approved effective treatments for the relevant disease and competition from other clinical trial programs for similar indications and clinical trial subjects;
- enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or may fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our CROs and other third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that participants are being exposed to unacceptable health risks;
- any of our product candidates could cause undesirable side effects that could result in significant negative consequences, including the inability to enter clinical development or receive regulatory approval;
- the cost of preclinical or nonclinical testing and studies and clinical trials of any product candidates may be greater than we anticipate;
- we may face hurdles in addressing subject safety concerns that arise during the course of a trial, causing us or our investigators, regulators, IRBs or ethics committees to suspend or terminate trials, or reports may arise from nonclinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our product candidates;
- the supply, quality or timeliness of delivery of materials for product candidates we develop or other materials necessary to conduct clinical trials may be insufficient or inadequate; and

- we may need to change the manufacturing site and potentially the CMO for our product candidates from those that are able to produce clinical supply for our clinical trials to those with the capacity and ability to perform commercial manufacturing and/or the production of clinical material for our later stage clinical trials.

We could encounter delays if a clinical trial is suspended or terminated by us, or by the IRBs of the institutions in which such trials are being conducted, ethics committees or the Data and Safety Monitoring Board, or the DSMB, for such trial or by the FDA, Health Canada, the EMA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, Health Canada, the EMA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of marketing approval of our product candidates. The FDA, Health Canada, the EMA or other regulatory authorities may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials. Further, the FDA, Health Canada, the EMA or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials. For example, we are conducting and may in the future conduct additional "open-label" clinical trials. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. Moreover, patients selected for early clinical trials often include the most severe sufferers and their symptoms may have been bound to improve notwithstanding the new treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. For example, in our ongoing Phase 1/1b trial, objective response rate as determined using RECIST 1.1 criteria is assessed by the trial investigators who may be aware of the trial treatment, patient history or other information that could impact their choices in applying the rules and conventions of RECIST 1.1. The published literature demonstrates a consistent decrease in response rate when investigator assessed response rates are verified by independent radiology review.

Principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or other compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or a regulatory authority concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of the marketing application we submit. Any such delay or rejection could prevent or delay us from commercializing ficerafusp alfa or any future product candidates.

If we experience delays in the completion, or termination, of any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down the development and approval process for our product candidates and jeopardize our ability to commence product sales and generate revenues. Significant clinical trial delays could also allow our competitors to bring products to market before we do or shorten any periods during which we have the exclusive right to commercialize our product candidates.

Any such events would impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

Any of these occurrences may significantly harm our business, financial condition and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates or result in the development of our product candidates stopping early.

Preclinical development is uncertain. Any preclinical programs we pursue may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all.

The risk of failure for product candidates still in the discovery or preclinical stage is high. In addition, any one or more of our product candidates that have not yet entered the clinic may never advance into clinical development. In order to obtain FDA approval to market a new biologic we must demonstrate proof of safety, purity and potency, including efficacy, in humans. To meet these requirements, we will have to conduct adequate and well-controlled clinical trials. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned clinical trials in humans. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of ficerafusp alfa or any future product candidates. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA, Health Canada, the EMA or other regulatory authorities allowing clinical trials to begin.

Conducting preclinical testing is a lengthy, time-consuming and expensive process. The length of time of such testing may vary substantially according to the type, complexity and novelty of the program, and often can be several years or more per program. Delays associated with programs for which we are conducting preclinical testing and studies may cause us to incur additional operating expenses. The commencement and rate of completion of preclinical studies and clinical trials for a product candidate may be delayed by many factors, including but not limited to:

- an inability to generate sufficient preclinical or other *in vivo* or *in vitro* data to support the initiation of clinical trials;
- delays in reaching a consensus with regulatory agencies on trial design; and
- the FDA, Health Canada, the EMA or foreign regulatory authorities not permitting the reliance on preclinical or other data from published scientific literature.

We are currently conducting, and may in the future conduct, clinical trials for ficerafusp alfa or any future product candidates outside the U.S., and the FDA and comparable foreign regulatory authorities may not accept data from such trials.

We are currently conducting, and may in the future conduct, clinical trials for ficerafusp alfa or any future product candidates outside the U.S., and the FDA and comparable foreign regulatory authorities may not accept data from such trials. We are currently conducting clinical trials in the U.S. and Canada, and we expect to continue to conduct trials internationally in the future. The acceptance of data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA, Health Canada, the EMA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice, (ii) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice, or GCP, regulations, and (iii) the FDA is able to validate the data through an on-site inspection or other appropriate means. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials are subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA, Health Canada, the EMA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U.S. or the applicable jurisdiction. If the FDA, Health Canada, the EMA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time-consuming, and which may result in ficerafusp alfa or any future product candidates that we may develop being delayed or not receiving approval for commercialization in the applicable jurisdiction.

Positive results from preclinical studies and early-stage clinical trials may not be predictive of future results. Initial positive results in any of our clinical trials may not be indicative of results obtained when the trial is completed or in later stage trials.

The results of preclinical studies may not be predictive of the results of clinical trials. Preclinical studies and early-stage clinical trials are primarily designed to (i) test safety, (ii) study pharmacokinetics and pharmacodynamics and (iii) understand the side effects of product candidates at various doses and schedules, and the results of any early-stage clinical trials may not be predictive of the results of later-stage, large-scale efficacy clinical trials. In addition, initial success in clinical trials may not be indicative of results obtained when such trials are completed. There can be no assurance that any of our current or future clinical trials will ultimately be successful or support further clinical development of any of our product candidates. There is a high failure rate for drugs and biological products proceeding through clinical trials. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results.

Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval for our product candidates. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, the results of our preclinical studies may not be predictive of the results of outcomes in human clinical trials. For example, ficerafusp alfa or any future product candidates may demonstrate different chemical, biological and pharmacological properties in patients than they do in laboratory studies or may interact with human biological systems in unforeseen or harmful ways. Product candidates in later stages of clinical trials may fail to show desired pharmacological properties or produce the necessary safety and efficacy results despite having progressed through preclinical studies and initial clinical trials. Even if we are able to initiate and complete clinical trials, the results may not be sufficient to obtain regulatory approval for our product candidates. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

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

From time to time, we may publish interim data, including interim top-line results or preliminary results from our clinical trials. Interim data and results from our clinical trials are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line results also remain subject to audit, validation and verification procedures that may result in the final data being materially different from the interim and preliminary data we previously published. As a result, interim and preliminary data may not be predictive of final results and should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

Furthermore, third parties, including regulatory authorities, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could delay or prevent regulatory approval of, or limit commercial prospects for, the particular product candidate. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine to disclose. If regulatory authorities disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

Ficerafusp alfa or any future product candidates may cause undesirable side effects or have other properties when used alone or in combination with other approved products or investigational new drugs that could halt their clinical development, delay or prevent their regulatory approval, limit their commercial potential or result in significant negative consequences.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are safe, pure and potent for use in each target indication, and failures can occur at any stage of testing. As with most biological products, use of ficerafusp alfa or any future product candidates could be associated with side effects or adverse events which can vary in severity from minor reactions to death and in frequency from infrequent to prevalent. There have been serious adverse side effects reported in response to product therapeutics and bispecifics in oncology.

EGFR-targeted drugs have been observed to cause side effects, predominantly related to skin toxicity and rash, and TGF-β inhibitors have been shown to have side effects primarily related to bleeding. While we have observed these side effects during our studies, the severity of these has been minimal but additional or more severe treatment-related side effects may emerge at a later time in our trials. In addition to any potential side effects caused by the product or product candidate, the administration process or related procedures also can cause adverse side effects. If unacceptable adverse events occur, our clinical trials or any future marketing authorization could be suspended or terminated. Additionally, we may be required to repeat or conduct additional clinical trials or nonclinical studies for our product candidates beyond those that we currently contemplate. There can be no assurance that ficerafusp alfa or any future product candidates will not demonstrate unacceptable toxicities in later testing that may render it unsafe or intolerable.

If unacceptable side effects arise in the development of our product candidates, we, the FDA, the IRBs at the institutions in which our trials are conducted or the DSMB could suspend or terminate our clinical trials or the FDA, Health Canada, the EMA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

Although ficerafusp alfa and future product candidates have undergone and will undergo safety testing to the extent possible and, where applicable, under such conditions discussed with regulatory authorities, not all adverse effects of drugs can be predicted or anticipated. Antibody therapeutics and bispecifics and their method of action of harnessing the body's immune system are powerful and could lead to serious side effects that we only discover in clinical trials or during commercial marketing. Unforeseen side effects could arise either during clinical development or after our product candidates have been approved by regulatory authorities and the approved product has been marketed, resulting in the exposure of additional patients. So far, we have not demonstrated that ficerafusp alfa is safe in humans, and we cannot predict if ongoing or future clinical trials will do so. If ficerafusp alfa or any future product candidates fail to demonstrate safety and efficacy in clinical trials or do not gain marketing approval, we will not be able to generate revenue and our business will be harmed.

In addition, we intend to pursue our product candidates in combination with other therapies and may develop future product candidates in combination with other therapies, which exposes us to additional risks relating to undesirable side effects or other properties. For example, the other therapies may lead to toxicities that are improperly attributed to our product candidates or the combination of our product candidates with other therapies may result in toxicities that the product candidate or other therapy does not produce when used alone.

Even if we successfully advance our product candidates through clinical trials, such trials will likely only include a limited number of subjects and limited duration of exposure to our product candidates. As a result, we cannot be assured that adverse effects of our product candidates will not be uncovered when a significantly larger number of patients are exposed to the product candidate. Further, any clinical trial may not be sufficient to determine the effect and safety consequences of taking our product candidates over a multi-year period.

Even if we successfully develop a product candidate and it receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of treatment outweigh the risks for each potential patient, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, extensive patient monitoring, or distribution systems and processes that are highly controlled, restrictive, and more costly than what is typical for the industry. If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may limit, suspend, or withdraw their approval of the product or may refuse to approve supplemental applications for such product;
- we may be required to recall a product or change the way such product is administered to patients;
- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we may be required to implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

Any of the foregoing events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and result in the loss of significant revenues, which would materially harm our business. In addition, if one or more of our product candidates or our antibody therapeutic development approach generally prove to be unsafe, our entire technology platform and pipeline could be affected, which would also materially harm our business.

As an organization, we have limited experience designing and implementing clinical trials and we have never conducted pivotal clinical trials. Failure to adequately design a trial, or incorrect assumptions about the design of the trial, could adversely affect the ability to initiate the trial, enroll patients, complete the trial or obtain regulatory approval on the basis of the trial results, as well as lead to increased or unexpected costs and in delayed timelines.

The design and implementation of clinical trials is a complex process. We have limited experience designing and implementing clinical trials, and we may not successfully or cost-effectively design and implement clinical trials that achieve our desired clinical endpoints efficiently, or at all. A clinical trial that is not well designed may delay or even prevent initiation of the trial, can lead to increased difficulty in enrolling patients, may make it more difficult to obtain regulatory approval for the product candidate on the basis of the trial results, or, even if a product candidate is approved, could make it more difficult to commercialize the product successfully or obtain reimbursement from third-party payors. Additionally, a trial that is not well-designed could be inefficient or more expensive than it otherwise would have been, or we may incorrectly estimate the costs to implement the clinical trial, which could lead to a shortfall in funding. We also expect to continue to rely on third parties to conduct our clinical trials. Consequently, we may be unable to successfully and efficiently execute and complete clinical trials that are required for Biologics License Application, or BLA, submission and FDA approval of ficerafusp alfa or any future product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop.

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

The successful and timely completion of clinical trials in accordance with their protocols depends on, among other things, our ability to enroll a sufficient number of patients who remain in the trial until the trial's conclusion, including any follow-up period. We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the nature and size of the patient population required for analysis of the trial's primary endpoints and the process for identifying patients;
- the number and location of participating and available clinical sites or patients;
- delays in, inability, or failure to add new clinical trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new products that may be approved for the indications we are investigating;
- the availability of competing commercially available therapies;
- our ability to obtain and maintain patient informed consents for participation in our clinical trials; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion or, because they may be late-stage cancer patients, will not survive the full terms of the clinical trials.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our current and potential future product candidates. It is also likely that we may compete with competitors developing product candidates in the same therapeutic areas for clinical trial sites. This competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such sites. Moreover, because our current and potential future product candidates may represent a departure from more commonly used methods for cancer treatment, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy, rather than enroll patients in our ongoing or any future clinical trial.

Delays of difficulties in patient enrollment may result in increased costs or may affect the timing, outcome or completion of clinical trials, which would adversely affect our ability to advance the development of the product candidates we develop.

Failure to successfully develop and commercialize companion diagnostics with third party contractors for use with our product candidates could harm our ability to commercialize our product candidates.

We plan to develop, or engage third parties to develop, companion diagnostics for our product candidates where appropriate. At least in some cases, the FDA and similar regulatory authorities outside the United States may request or require the development and regulatory approval of a companion diagnostic as a condition to approving one or more of our product candidates. Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate clearance or approval prior to their commercialization. We do not have experience or capabilities in developing or commercializing diagnostics and are relying, and in the future plan to continue to rely, in large part on third parties to perform these functions.

In most cases, we will likely outsource the development, production and commercialization of companion diagnostics to third parties. By outsourcing these companion diagnostics to third parties, we become dependent on the efforts of our third-party contractors to successfully develop and commercialize these companion diagnostics. Our contractors:

- may not perform their obligations as expected;
- may encounter production difficulties that could constrain the supply of the companion diagnostic;
- may have difficulties gaining acceptance of the use of the companion diagnostic in the clinical community;
- may not commit sufficient resources to the marketing and distribution of such product; and
- may terminate their relationship with us.

We and our third-party collaborators may encounter difficulties in developing and obtaining approval for these companion diagnostics. Any delay or failure by us or third- party collaborators to develop or obtain regulatory approval of a companion diagnostic could delay or prevent approval of our related product candidates. Further, if any companion diagnostic for use with one of our product candidates fails to gain market acceptance, our ability to derive revenues from sales of such product candidate could be harmed. If our third-party contractors fail to commercialize such companion diagnostic, we may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with such product candidate or do so on commercially reasonable terms, which could adversely affect and delay the development or commercialization of such product candidate.

Risks Related to Our Dependence on and Work with Third Parties

We rely, and expect to continue to rely, on third parties, including independent clinical investigators and CROs, to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third parties, including independent clinical investigators and third-party CROs, to conduct monitor and manage data for our preclinical studies and clinical trials. We rely on these parties for execution of our preclinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities. We and our third-party contractors and CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA, the competent authorities of the member states of the EEA, and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, Health Canada, the EMA or comparable foreign regulatory authorities, who may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with the product candidate produced under FDA's current good manufacturing practice, or cGMP, regulations or similar foreign regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

Further, these principal investigators and CROs are not our employees and we will not be able to control, other than by contract, the amount of resources, including time, which they devote to our product candidates and clinical trials. If independent investigators or CROs fail to devote sufficient resources to the development of our product candidates, or if their performance is substandard, it may delay or compromise the prospects for approval and commercialization of any product candidates that we develop. In addition, the use of third-party service providers may require us to disclose our proprietary information to these parties, which could increase the risk that this information will be misappropriated.

Our CROs have the right to terminate their agreements with us in the event of an uncured material breach. In addition, some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Additionally, CROs may lack the capacity to absorb higher workloads or take on additional capacity to support our needs. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We currently and in the future may depend on other third-party collaborators for the discovery, development and commercialization of ficerafusp alfa and any of our future product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We have entered into collaborations with MSD International GmbH, or MSDIG, and MSD International Business GmbH, or MSDIB, and collectively with MSDIG, MSD and Biocon Ltd, or Biocon. In the future, we may form or seek other strategic alliances, joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to product candidates we develop. Our current and potential future collaborations involving our product candidates may pose various risks to us, including:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- collaborators may not properly enforce, maintain or defend our intellectual property rights or may use our proprietary information in a way that gives rise to actual or threatened litigation or that could jeopardize or invalidate our intellectual property or proprietary information, exposing us to potential litigation or other intellectual property proceedings;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between a collaborator and us that cause the delay or termination of the research, development or commercialization of the product candidate, or that result in costly litigation or arbitration that diverts management attention and resources;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;

- if a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated;
- collaboration agreements may restrict our right to independently pursue new product candidates; and
- the mutual termination of the Contract Transfer and License Agreement with Biocon could delay the commercialization of ficerafusp alfa.

For future collaborations, if we enter into such collaboration agreements and strategic partnerships or license our intellectual property, products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or net income that justifies such transaction. Any of the factors set forth above, among others, could delay the development and commercialization of our product candidates, which would harm our business prospects, financial condition and results of operations.

We currently have established collaborations and may seek to establish future collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

The advancement of our product candidates and development programs and the potential commercialization of ficerafusp alfa and any of our future product candidates will require substantial additional cash to fund expenses. We currently collaborate with pharmaceutical and biotechnology companies with respect to development and potential commercialization of ficerafusp alfa, and we may also do so with any future product candidates. These relationships may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders, or disrupt our management and business.

We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Whether we reach a definitive agreement for other collaborations 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 collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the progress of our clinical trials, the likelihood of approval by the FDA, Health Canada, the EMA or similar regulatory authorities outside the United States, 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 collaboration could be more attractive than the one with us for our product candidate.

Further, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for future product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view them as having the requisite potential to demonstrate safety and efficacy.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. Such exclusivity could limit our ability to enter into strategic collaborations with future collaborators. 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 collaborations 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 its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any marketing or sales 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.

We currently rely on third-party suppliers and other third parties for production of our product candidates and our dependence on these third parties may impair the advancement of our research and development programs and the development of our product candidates. Moreover, we intend to rely on third parties to produce commercial supplies of any approved product candidate and our commercialization of any of our product candidates could be stopped, delayed or made less profitable if those third parties fail to obtain approval of the FDA, Health Canada, the EMA or comparable foreign regulatory authorities following inspection of their facilities and procedures to manufacture our product candidates, fail to provide us with sufficient quantities of a product candidate or fail to do so at acceptable timing, quality levels or prices or fail to otherwise complete their duties in compliance with their obligations to us or other parties.

We rely on and expect to continue to rely on third-party CMOs for the supply of cGMP-grade clinical trial materials and commercial quantities of our product candidates and products, if approved. Reliance on third-party providers may expose us to more risk than if we were to manufacture product candidates ourselves. The facilities used by our CMOs to manufacture our product candidates must be approved by the FDA foreign regulatory authorities pursuant to inspections that will be conducted after we submit our BLA, to the FDA, or similar applications to foreign regulatory authorities. We have limited control over the manufacturing process of, and beyond contractual terms, we are completely dependent on our CMOs for compliance with cGMP, and applicable product tracking and tracing requirements, or similar foreign requirements for the manufacture of our product candidates. If our CMOs cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, Health Canada, the EMA or comparable foreign regulatory authorities, or are unable to do so in a timely manner, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities or may result in delay of our ability to obtain marketing authorization, if any, of our product candidates. In addition, we have limited control over the ability of our CMOs to maintain adequate quality control, quality assurance and qualified personnel. If the FDA, Health Canada, the EMA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. In addition, any failure to achieve and maintain compliance with these laws, regulations and standards could subject us to the risk that we may have to suspend the manufacturing of our product candidates or that obtained approvals could be revoked, which would adversely affect our business and reputation. Furthermore, third-party providers may breach existing agreements they have with us because of factors beyond our control. They may also terminate or refuse to renew their agreement because of their own financial difficulties or business priorities, at a time that is costly or otherwise inconvenient for us. If we were unable to find an adequate replacement or another acceptable solution in time, our clinical trials could be delayed or our commercial activities could be harmed. In addition, the fact that we are dependent on our collaborators, our CMOs and other third parties for the manufacture, filling, storage and distribution of our product candidates means that we are subject to the risk that the products may have manufacturing defects that we have limited ability to prevent or control. The sale of products containing such defects could adversely affect our business, financial condition and results of operations.

We rely on our CMOs to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical trials, and will rely on our existing and future collaborators to purchase from third-party suppliers the materials necessary to develop and produce our product candidates for future clinical trials and, upon approval, our products for commercialization. There are a limited number of suppliers for raw materials that we use to manufacture our product candidates and there may be a need to assess alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our product candidates for our clinical trials, and if approved, ultimately for commercial sale. Apart from contractual measures, we do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers or manufacturers paid by our collaborators. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of an product candidate to complete the clinical trial or have secured resupply capacity, any significant delay in the supply of an product candidate, or the raw material components thereof, for a planned or an ongoing clinical trial due to the need to replace a third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates.

In addition, the manufacturing of our product candidates is expensive and time-consuming, and generally requires more complex processes than those associated with small-molecule drugs. If we are successful in obtaining regulatory approval for any of our product candidates, we might have limited quantities of such product candidates available to us in connection with a potential commercial launch, and these supplies may be further limited by our ongoing clinical development activities. If our manufacturers, collaborators or we are unable to purchase or produce sufficient quantities of raw materials or of our product candidates after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates could be delayed or there could be a shortage in supply, which in either case, would impair our ability to generate revenues from the sale of our product candidates.

We rely on our manufacturers and other subcontractors to comply with and respect the proprietary rights of others in conducting their contractual obligations for us. If our manufacturers or other subcontractors fail to acquire the proper licenses or otherwise infringe third party proprietary rights in the course of completing their contractual obligations to us, we may have to find alternative manufacturers or defend against claims of infringement, either of which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

The operations of our suppliers, many of which are located outside of the United States, are subject to additional risks that are beyond our control and that could harm our business, financial condition, results of operations and prospects.

We currently rely on and engage third-party manufacturers to provide all of the drug substance and the final drug product formulation of all of our product candidates that are being used in our clinical trials and preclinical studies. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we primarily rely on one manufacturer, WuXi Biologics (Hong Kong) Limited, or WuXi Bio, for the production of product necessary to complete our ongoing clinical trials. If a replacement manufacturer became necessary in the future, we may incur added costs and delays in identifying and qualifying another manufacturer. We currently do not have any long-term supply agreements in place, though we intend to enter into such agreements as well as evaluate additional product manufacturing sources in the future. As a result of our dependence on ex-U.S. suppliers, we are subject to risks associated with doing business abroad, including:

- geopolitical tensions, political unrest, terrorism, labor disputes and economic instability resulting in the disruption of trade from foreign countries in which our products are manufactured, particularly China;
- the imposition of new laws and regulations, including those relating to labor conditions, safety standards, information and data transfer, imports, duties, taxes, and other charges on imports, as well as trade restrictions and restrictions on currency exchange or the transfer of funds, particularly new or increased tariffs imposed on imports from countries where our suppliers operate, including China, pursuant to our master supply agreement with WuXi Bio;
- greater challenges and increased costs with enforcing and periodically auditing or reviewing our suppliers' and manufacturers' compliance with cGMPs or status acceptable to the FDA, Health Canada, the EMA or comparable foreign regulatory authorities;
- reduced protection for intellectual property rights, including trade secret protection, in some countries, particularly China;
- disruptions in operations due to global, regional, or local epidemics, pandemics, public health crises or other emergencies or natural disasters;
- disruptions or delays in shipments; and
- changes in local economic conditions in countries where our manufacturers or suppliers are located.

Congress previously introduced but did not pass legislation known as the BIOSECURE Act, which would have prohibited U.S. federal agencies from entering into or renewing a government contract with a company that uses biotechnology equipment or services produced or provided by a Chinese "biotechnology company of concern" in the performance of that government contract. It would also have prohibited recipients of loan or grant funding from U.S. federal agencies from using loan or grant funds to procure, obtain or use any biotechnology equipment or services produced or provided by a Chinese "biotechnology company of concern." This legislation would have had the effect of restricting the ability of biopharmaceutical companies that enter into contracts with or receive funding from U.S. federal agencies from purchasing services or equipment from certain Chinese biotechnology companies, including those that were specifically named in the proposed BIOSECURE Act. The last version of the BIOSECURE Act introduced in the House of Representatives names WuXi Bio as a "biotechnology company of concern" and also included a grace period that would have limited the applicability of the BIOSECURE Act's prohibitions to existing contractual arrangements with named "biotechnology companies of concern" until 2032. While the BIOSECURE Act was not passed, we do not anticipate continued scrutiny on relationships with Chinese biotechnology companies, which could adversely impact WuXi Bio's operations or financial position, which, in turn, could impact its and ability to supply us with product in the future. We may also face additional manufacturing and supply-chain risks due to the evolving regulatory and legal requirements in China, or due to the deterioration of the geo-political relationship between China and the U.S., including but not limited to potential sanctions imposed by the U.S. government on WuXi Bio, or other companies in China on whom we might rely, or any of the other countries in which our products are manufactured or marketed.

These and other factors beyond our control could interrupt our suppliers' production, influence the ability of our suppliers to export our clinical supplies cost-effectively or at all and inhibit our supplier' ability to procure certain materials, any of which could delay our clinical trials or otherwise harm our business, financial condition, results of operations and prospects.

If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates or increase the product yield of its manufacturing, then our manufacturing costs may increase and commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of our product candidates, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of our product candidates. The transition to larger scale production could prove difficult. In addition, if our third-party manufacturers are not able to optimize their manufacturing processes to increase the product yield for our product candidates, or if they are unable to produce increased amounts of our product candidates while maintaining the same quality then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operations.

We may need to maintain licenses for drug substances from third parties to develop and commercialize some of our product candidates, which could increase our development costs and delay our ability to commercialize those product candidates.

Should we decide to use any cell line and raw materials in any of our product candidates that are proprietary to one or more third parties, we would need to maintain licenses to those drug substances from those third parties. If we are unable to gain or continue to access rights to these drug substances prior to conducting preclinical toxicology studies intended to support clinical trials, we may need to develop alternate product candidates from these programs by either accessing or developing alternate drug substances, resulting in increased development costs and delays in commercialization of these product candidates. If we are unable to gain or maintain continued access rights to the desired drug substances on commercially reasonable terms or develop suitable alternate drug substances, we may not be able to commercialize product candidates from these programs.

Risks Related to Government Regulation

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

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval (or maintain approval) may change during the course of a product candidate's clinical development and may vary among jurisdictions. For example, the Oncology Center of Excellence within the FDA has advanced Project Optimus, which is an initiative to reform the dose optimization and dose selection paradigm in oncology drug development to emphasize selection of an optimal dose, which is a dose or doses that maximizes not only the efficacy of a drug but the safety and tolerability as well. This shift from the prior approach, which generally determined the maximum tolerated dose, has required and will require us to continue to spend additional time and resources to further explore a product candidate's dose-response relationship to facilitate optimum dose selection in a target population. Other recent Oncology Center of Excellence initiatives have included Project FrontRunner, a new initiative with a goal of developing a framework for identifying candidate drugs for initial clinical development in the earlier advanced setting rather than for treatment of patients who have received numerous prior lines of therapies or have exhausted available treatment options, and Project Confirm, which is an initiative to promote the transparency of outcomes related to accelerated approvals for oncology indications and provide a framework to foster discussion, research and innovation in approval and post-marketing processes, with the goal to enhance the balance. We are considering these and other policy changes as they relate to our programs.

We have not obtained regulatory approval for any product candidate. Neither we nor any future collaborator is permitted to market any biological product in the U.S. until we or the future collaborator receives regulatory approval of a BLA, from the FDA. It is possible that ficerafusp alfa or any future product candidates will not obtain regulatory approval from the FDA, Health Canada, the EMA or comparable foreign regulatory authorities. Ficerafusp alfa and any future product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, Health Canada, the EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, Health Canada, the EMA or comparable foreign regulatory authorities that a product candidate has an acceptable risk-benefit profile in the proposed indication;
- we may be unable to demonstrate to the satisfaction of the FDA, Health Canada, the EMA or comparable foreign regulatory authorities that the facility in which a product candidate is manufactured meets standards designed to assure that the product candidate continues to be safe, pure, and potent;
- the results of clinical trials may not meet the level of statistical significance required by the FDA, Health Canada, the EMA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, Health Canada, the EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from clinical trials or preclinical studies;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a BLA to the FDA, Health Canada, the EMA or regulatory submissions to comparable regulatory authorities to obtain regulatory approval in such jurisdiction; and
- the FDA, Health Canada, the EMA or comparable foreign regulatory authorities may find deficiencies with or fail to approve our manufacturing processes or facility or the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies.

This lengthy approval process as well as the unpredictability of clinical trial results may result in our failing to obtain regulatory approval to market any product candidate we develop, which would significantly harm our business, results of operations and prospects. The FDA and other comparable foreign authorities have substantial discretion in the approval process and in determining when or whether regulatory approval will be granted for any product candidate that we develop. Even if we believe the data collected from future clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA, Health Canada, the EMA or any other regulatory authority.

In addition, even if we were to obtain approval, the FDA may approve any of our product candidates for fewer or more limited indications, or a more limited patient population, than we request, may grant approval contingent on the performance of costly clinical trials or other post-marketing requirements, or may approve a product candidate with a label that does not include the labeling claims we believe are necessary or desirable for the successful commercialization of such product candidates. Even if we obtain regulatory approval for our product candidates, we will be required to submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process and the FDA or comparable foreign regulatory authority may refuse to approve such applications or supplements.

In addition, the FDA, Health Canada, the EMA or comparable foreign regulatory authorities may change their policies, promulgate additional regulations, revise existing regulations or take other actions that may prevent or delay approval of our future products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy personnel, and substantial leadership, personnel and policy changes or otherwise, could prevent new or modified products from being developed, approved, or commercialized in a timely manner or at all, 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, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies 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, including substantial leadership, personnel, and policy changes, may also slow the time necessary for biological products or modifications to approved biological products to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. Currently, federal agencies in the U.S. are operating under a continuing resolution that is set to expire on September 30, 2025. Without appropriation of additional funding to federal agencies, our business operations related to our product development activities for the U.S. market could be impacted.

We may be required to suspend, repeat or terminate our clinical trials if they are not conducted in accordance with regulatory requirements, the results are negative or inconclusive or the trials are not well designed.

Clinical trials must be conducted in accordance with GCP requirements, which are regulations and guidelines enforced by the FDA, Health Canada, the EMA and comparable foreign regulatory authorities. Clinical trials are subject to oversight by the FDA, other foreign governmental agencies and IRBs or ethical committees at the trial sites where the clinical trials are conducted. In addition, clinical trials must be conducted with product candidates manufactured in accordance with applicable cGMP. Clinical trials may be suspended by the FDA, other foreign regulatory authorities, us, or by an IRB or ethics committee with respect to a particular clinical trial site, for various reasons, including:

- deficiencies in the conduct of the clinical trials, including failure to conduct the clinical trial in accordance with regulatory requirements or trial protocols;
- deficiencies in the clinical trial operations or trial sites;
- unforeseen adverse side effects or the emergence of undue risks to trial subjects;
- deficiencies in the trial design necessary to demonstrate efficacy;
- ficerafusp alfa may not appear to offer benefits over current therapies; or
- the quality or stability of ficerafusp alfa may fall below acceptable standards.

We intend to develop our product candidates in part in combination with other therapies and may develop our future product candidates in combination with other therapies, which exposes us to additional regulatory risks.

We intend to develop our product candidates in part in combination with other therapies, including ficerafusp alfa in combination with pembrolizumab as a treatment for HNSCC and SCAC, and may develop ficerafusp alfa and any future product candidates in combination with one or more currently approved cancer therapies. These combinations have not been previously tested in the clinic and may, among other things, fail to demonstrate synergistic activity, may fail to achieve superior outcomes relative to the use of single agents or other combination therapies, or may fail to demonstrate sufficient safety or efficacy traits in clinical trials to enable us to complete those clinical trials or obtain marketing approval for the combination therapy.

In addition, we did not develop or obtain regulatory approval for, and we do not manufacture or sell, any of these approved therapeutics. The other therapies we are using in combination may be removed from the market, or we may not be able to secure adequate quantities of such materials for which we have no guaranteed supply contract, and thus be unavailable for testing or commercial use with any of our approved products. The other therapies we may use in combination with our product candidates may also be supplanted in the market by newer, safer or more efficacious products or combinations of products.

Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risk that the FDA, Health Canada, the EMA or comparable foreign regulatory authorities could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially. Combination therapies are commonly used for the treatment of cancer diseases, and we would be subject to similar risks if we develop any of our product candidates for use in combination with other drugs or for indications other than cancer.

We may also evaluate ficerafusp alfa or any future product candidates in combination with one or more other cancer therapies that have not yet been approved for marketing by the FDA, Health Canada, the EMA or comparable foreign regulatory authorities. We will not be able to market and sell any product candidate we develop in combination with any such unapproved cancer therapies that do not ultimately obtain marketing approval.
If the FDA, Health Canada, the EMA or comparable foreign regulatory authorities do not approve these other biological products or revoke their approval of, or if safety, efficacy, manufacturing or supply issues arise with, the biological products we choose to evaluate in combination with any product candidate we develop, we may be unable to obtain approval of or market any such product candidate.

Even if we receive marketing approval of ficerafusp alfa, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. If we fail to comply or experience unanticipated problems with our products, we may be subject to administrative and judicial enforcement, including monetary penalties, for non-compliance and our approved products, if any, could be deemed misbranded or adulterated and prohibited from continued distribution.

Any marketing approvals that we may receive for ficerafusp alfa or any future product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or the conditions of approval or contain requirements for potentially costly post-market testing and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require implementation of a REMS as a condition of approval of any product candidate, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, if the FDA, Health Canada, the EMA or a comparable foreign regulatory authority approves a product candidate, the manufacturing processes, labeling, packaging, distribution, tracking and tracing event and deviation reporting, storage, advertising, promotion, import and export and record keeping for the product candidate will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP and GCP, for any clinical trials that we may conduct post-approval. Later discovery of previously unknown problems with any approved candidate, including adverse events of unanticipated severity or frequency, or with our or our third-party manufacturers' manufacturing processes or facilities, or failure to comply with regulatory requirements, may result in, among other things:

- suspension of, or imposition of restrictions on, the marketing or manufacturing of the product, withdrawal of the product from the market, or product recalls;
- Warning letters or untitled letters, or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications we file, or suspension or revocation of approved biologics licenses;
- product seizure or detention, monetary penalties, refusal to permit the import or export of the product, or placement on Import Alert; and
- permanent injunctions and consent decrees including the imposition of civil or criminal penalties.

Given the nature of biological products manufacturing, there is a risk of contamination. Any contamination could materially adversely affect our ability to produce product candidates on schedule and could, therefore, harm our results of operations and cause reputational damage. Some of the raw materials and other components required in our manufacturing process are derived from biologic sources. Such raw materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product or product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially and adversely affect our development and commercialization timelines and our business, financial condition, results of operations and prospects and could adversely affect our ability to meet our supply obligations.

Moreover, the FDA strictly regulates the promotional claims that may be made about drug and biological products. In particular, an approved product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling, or off-label uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. The FDA has issued guidance on the factors that it will consider in determining whether a firm's product communication is consistent with the FDA-required labeling for that product, and those factors contain complexity and potential for overlap and misinterpretation. A company that is found to have improperly promoted off-label uses of their products may be subject to significant civil, criminal and administrative penalties.

The FDA and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay marketing approval of a product. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. 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 and we may not achieve or sustain profitability.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

In addition, 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 and we may not achieve or sustain profitability.

While we intend to seek designations for our potential product candidates with the FDA and comparable foreign regulatory authorities that are intended to confer benefits such as a faster development process, there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our potential product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA and comparable foreign regulatory authorities offer certain designations for product candidates that are designed to encourage the research and development of product candidates that are intended to address conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities and priority review.

However, there can be no assurance that we will successfully obtain such designations for any potential product candidates. In addition, while such designations could expedite the development or approval process, they generally do not change the standards for approval. Even if we obtain such designations for one or more of our potential product candidates, there can be no assurance that we will realize their intended benefits. For example, we may seek fast-track designation for some of our potential product candidates. If a therapy is intended for the treatment of a serious or life-threatening condition and the therapy nonclinical or clinical data demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for fast-track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a fast-track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw fast-track designation if it believes that the designation is no longer supported by data from our clinical development program.

Additionally, we may seek a breakthrough therapy designation for some of our potential product candidates. A breakthrough therapy is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have been designated as breakthrough therapies, 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. Therapies designated as breakthrough therapies by the FDA may also be eligible for accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our potential product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our potential product candidates qualify as breakthrough therapies, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

If the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for the product candidates that we may develop. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily result in an expedited regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

We may not be able to obtain or maintain orphan drug designations for our product candidates, and we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the United States and European Union, may designate drugs for relatively small patient populations as orphan drugs. For example, the FDA may designate a product as an orphan product if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the U.S., or a patient population of greater than 200,000 individuals in the U.S. but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. We may not be able to obtain orphan drug designation for any indications for our product candidates, and we may not be able to maintain such designations if granted.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same biologic for the same indications for seven years. Even if we are able to obtain orphan drug designation or orphan drug exclusivity, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if, among other things, the FDA concludes that the later drug is clinically superior, if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. Even if we receive orphan drug designation or orphan drug exclusivity for any of our product candidates, there is no guarantee that we will enjoy the benefits of such designations or exclusivity periods.

The decision of the U.S. Court of Appeals for the 11th Circuit in *Catalyst Pharms., Inc. v. Becerra*, 14 F.4th 1299 (11th Cir. 2021) has created uncertainty regarding the scope of orphan drug exclusivity. Although the FDA subsequently announced that it intends to continue to apply its longstanding interpretation of the regulations to matters outside of the scope of the *Catalyst* order and continue tying the scope of orphan-drug exclusivity to the uses or indications for which a drug is approved, it is unclear how future litigation, legislation, agency decisions, and administrative actions will impact the scope of the orphan drug exclusivity.

While we may seek accelerated approval for some of our product candidates, we may not be able to obtain it as the sufficiency of our clinical trial results for accelerated approval are subject to the FDA's discretion.

We plan to seek approval for ficerafusp alfa under the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and generally provides a meaningful advantage over available therapies upon a determination that the product candidate has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. For more information, see the section titled "*Business-Government Regulation-Accelerated Approval.*

Under FDORA, the FDA is empowered to take action, such as issuing fines, against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. There can be no assurance that the FDA would allow any of the product candidates we may develop to proceed on an accelerated approval pathway, and even if the FDA did allow such pathway, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. Moreover, even if we received accelerated approval, any post-approval studies required to confirm and verify clinical benefit may not show such benefit, which could lead to withdrawal of any approvals we have obtained. Receiving accelerated approval does not assure that the product's accelerated approval will eventually be converted to a traditional approval.

Risks Related to Commercialization

The commercial success of ficerafusp alfa or any future product candidates will depend upon the degree of market acceptance of such product candidates by physicians, patients, healthcare payors and others in the medical community.

Ficerafusp alfa and any future product candidates may not be commercially successful. Even if ficerafusp alfa or any future product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors, or the medical community. The commercial success of ficerafusp alfa or any future product candidates will depend significantly on the broad adoption and use of the resulting product by these individuals and organizations for approved indications. The degree of market acceptance of our products will depend on a number of factors, including:

- demonstration of clinical efficacy and safety, including as compared to anymore established products;
- the indications for which ficerafusp alfa or any future product candidates are approved, if any;
- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;
- acceptance of a new drug for the relevant indication by healthcare providers and their patients;
- the pricing and cost-effectiveness of our products, as well as the cost of treatment with our products in relation to alternative treatments and therapies;
- our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government healthcare programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement;
- any restrictions on the use of our products, and the prevalence and severity of any adverse effects;
- potential product liability claims;
- the timing of market introduction of our products as well as availability, safety and efficacy of competitive drugs;
- the effectiveness of our or any current or future collaborators' sales and marketing strategies; and
- unfavorable publicity relating to the product.

If ficerafusp alfa or any future product candidates is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors or patients, we may not generate sufficient revenue from that product and may not become or remain profitable. Our efforts to educate the medical community and third-party payors regarding the benefits of our products may require significant resources and may never be successful.

The market opportunities for ficerafusp alfa or any future product candidate we develop, if approved, may be limited to those patients who are ineligible for established therapies or for whom prior therapies have failed, and may be small.

Any revenue we are able to generate in the future from product sales will be dependent, in part, upon the size of the market in the U.S. and any other jurisdiction for which we gain regulatory approval and have commercial rights. If the markets or patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, even if approved.

Cancer therapies are sometimes characterized as first-line, second-line or third-line, and the FDA often approves new therapies initially only for third-line use. When cancer is detected early enough, first-line therapy, usually chemotherapy, hormone therapy, surgery, radiation therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. The number of patients who receive second- and third-line treatment is significantly smaller than the number of patients who receive first-line treatment, and the prognosis of patients who receive second- or third-line treatment is often poorer than that of patients who receive first-line treatment.

We may initially seek approval for any other product candidates we develop as second- or third-line therapies. If we do so, for those products that prove to be sufficiently beneficial, if any, we would expect potentially to seek approval as a first-line therapy, but there is no guarantee that any product candidate we develop, even if approved, would be approved for first-line therapy, and, prior to any such approvals, we may have to conduct additional clinical trials. The number of patients who have the types of cancer or autoimmune diseases we are targeting may turn out to be lower than expected. Additionally, the potentially addressable patient population for ficerafusp alfa or any future product candidates may be limited, if and when approved. Even if we obtain significant market share for any product candidate, if and when approved, if the potential target populations are small, we may never achieve profitability without obtaining marketing approval for additional indications, including to be used as first- or second-line therapy.

If approved, our product candidates that are regulated as biological products, or biologics, may face competition from biosimilars approved through an abbreviated regulatory pathway.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, established an abbreviated pathway for the approval of biosimilar and interchangeable biologics with an FDA-licensed reference biologic product. Under the BPCIA, a reference biological product is granted 12 years of non-patent data exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. 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 develop and receive approval of a competing biologic, so long as their BLA does not rely on the reference product or sponsor's data and is not submitted as a biosimilar application. Certain changes and supplements to an approved BLA, and subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the 12-year exclusivity period. The law is complex and any new policies or processes adopted by the FDA could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of the product candidates we develop that is approved in the U.S. as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidate to be a reference product for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products will depend on a number of marketplace and regulatory factors that are still developing. The approval of a biosimilar of our product candidates could have a material adverse impact on our business due to increased competition and pricing pressure. It is also possible that payors will give reimbursement preference to biosimilars over reference biological products, even absent a determination of interchangeability.

Laws and regulations outside the United States differ, including the length and extent of patent and exclusivity protection and pathways for competition to enter the market. Other countries may have significantly shorter or longer periods of exclusivity. In addition, other countries may have different standards in determining similarity to a reference product. Any market entry of competing products to our product candidates in these other regions could adversely affect our business in those regions.

To the extent that we do not receive any anticipated periods of regulatory exclusivity for our product candidates it could adversely affect our business, financial condition, results of operations and prospects.

Obtaining and maintaining marketing approval of ficerafusp alfa and any future product candidates in one jurisdiction does not mean that we will be successful in obtaining and maintaining marketing approval of ficerafusp alfa and any future product candidates in other jurisdictions.

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

We may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which we must comply prior to marketing in those jurisdictions. Obtaining foreign marketing 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. If we fail to comply with the regulatory requirements in international markets or fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

We may enter into agreements with third parties to sell, distribute and/or market ficerafusp alfa, or any future product candidates, if we obtain regulatory approval, which may adversely affect our ability to generate revenues.

Given the development stage of ficerafusp alfa, we have no experience in sales, marketing and distribution of biotech products. However, if ficerafusp alfa, or any future product candidates that we may develop, obtains marketing approval, we might intend to develop sales and marketing capacity, either alone or with partners, or rely upon the sales and marketing capabilities of our partners. Outsourcing sales, distribution and marketing may subject us to a variety of risks, including:

- our inability to exercise direct control over sales, distribution and marketing activities and personnel;
- potential failure or inability of contracted sales personnel to successfully market our products to physicians; and
- potential disputes with third parties concerning distribution, sales and marketing expenses, calculation of royalties, and sales and marketing strategies.

If we are unable to partner with a third party that has adequate sales, marketing, and distribution capabilities, we may have difficulty commercializing ficerafusp alfa or any other product candidates which would adversely affect our business, financial condition, and ability to generate product revenues.

Off-label use or misuse of ficerafusp alfa may harm our reputation in the marketplace or result in injuries that lead to costly product liability suits.

If ficerafusp alfa is approved by the FDA, we may only promote or market ficerafusp alfa in a manner consistent with its FDA-approved labeling. We will train our marketing and sales force against promoting ficerafusp alfa for uses outside of the approved indications for use, known as "off-label uses." We cannot, however, prevent a physician from using ficerafusp alfa off-label, when in the physician's independent professional medical judgment, he or she deems it appropriate. Furthermore, the use of ficerafusp alfa for indications other than those approved by the FDA may not effectively treat such conditions. Any such off-label use of ficerafusp alfa could harm our reputation in the marketplace among physicians and patients. There may also be increased risk of injury to patients if physicians attempt to use ficerafusp alfa for these uses for which they are not approved, which could lead to product liability suits that might require significant financial and management resources and that could harm our reputation.

We are subject to export and import controls, economic sanctions and anti-corruption laws and regulations of the United States and other jurisdictions. We can face criminal liability and other serious consequences for violations of these laws and regulations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control. Export controls and trade sanctions laws and regulations may restrict or prohibit altogether the provision, sale, or supply of our products to certain governments, persons, entities, countries, and territories, including those that are the target of comprehensive sanctions or an embargo. We are also subject to anti-corruption and anti-bribery laws, including the U.S. Foreign Corrupt Practices Act of 1977, or FCPA, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, and other state and national anti-bribery laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other partners from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violation of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

If we or any third-party manufacturer we engage now or in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could have a material adverse effect on our business.

We and third-party manufacturers we engage now are, and any third-party manufacturer we may engage in the future will be, subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and waste. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our current and any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of ficerafusp alfa or products. In addition, our supply chain may be adversely impacted if any of our third-party contract manufacturers become subject to injunctions or other sanctions as a result of their non-compliance with environmental, health and safety laws and regulations.

Risks Related to Our Intellectual Property

Our ability to compete may decline if we do not adequately protect our proprietary rights.

Our commercial success depends, in part, on obtaining and maintaining patents and other forms of intellectual property rights for ficerafusp alfa, including ficerafusp alfa and any future product candidates, methods used to produce, purify, and manufacture those product candidates, and methods of utilizing the product candidates, including methods for treating patients, among other aspects of ficerafusp alfa or on licensing-in such rights. Failure to protect or to obtain, maintain, or extend adequate patent and other intellectual property rights could materially adversely affect our ability to develop and market ficerafusp alfa.

Our strategy depends in part on our ability to identify and seek patent protection for our discoveries. The patent prosecution process is time-consuming and expensive, and we and our current or future licensors, licensees 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 in all jurisdictions where protection may be commercially advantageous. It is also possible that we or our current or future licensors, licensees, 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 on them.

The standards which the United States Patent and Trademark Office, or USPTO, and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change in the future. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable. The laws of some foreign countries do not protect proprietary information to the same extent as the laws of the United States. Outside the United States, patent protection must be sought in individual jurisdictions, further adding to the cost and uncertainty of obtaining adequate patent protection outside of the United States. Accordingly, the issuance, scope, validity, enforceability, and commercial value of our and our current or future licensors', licensees' or collaborators' current and future patent rights are highly uncertain. We cannot predict whether additional patents protecting ficerafusp alfa will issue in the U.S. or in foreign jurisdictions, or whether any patents that do issue will have claims of adequate scope to provide competitive advantage. Our and our current or future licensors', licensees' or collaborators' pending and future patent applications may not result in patents being issued which protect ficerafusp alfa or other technology, in whole or in part, or which effectively prevent others from commercializing competitive products and technology. The patent examination process may require us or our current or future licensors, licensees or collaborators to narrow the scope of the claims of our or our current or future licensors', licensees' or collaborators' pending and future patent applications, which may limit the scope of patent protection that may be obtained.

We cannot assure you that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue, or have issued and even if such patents cover a product candidate, and/or other technologies, third parties may initiate opposition, interference, re-examination, post-grant review, inter partes review, litigation, nullification or derivation action in court or before patent offices, or similar proceedings challenging the validity, enforceability, scope, inventorship, or ownership of such patents, which may result in the patent claims being narrowed, invalidated, held unenforceable, or unavailable to us. Our and our current and future licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issue from such application(s), and then only to the extent the issued claims cover the technology in the relevant jurisdiction.

Patent applications in the U.S. and many foreign jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries. As such, we cannot be certain that we or our licensors were the first to make the inventions claimed in our issued patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in our patents or patent applications. As a result, we may not be able to obtain or maintain protection for certain inventions. Therefore, the enforceability and scope of our patents in the U.S. and in foreign countries cannot be predicted with certainty and, as a result, any patents that we own or license may not provide sufficient protection against competitors. We may not be able to obtain or maintain patent protection from our pending patent applications, from those we may file in the future, or from those we may license from third parties. Moreover, even if we are able to obtain patent protection, such patent protection may be of insufficient scope to achieve our business objectives.

In addition, changes in, or different interpretations of, patent laws in the U.S. and other countries may permit others to use our discoveries or to develop and commercialize ficerafusp alfa without providing any notice or compensation to us or may limit the scope of patent protection that we or our licensors are able to obtain. The laws of some countries do not protect intellectual property rights to the same extent as U.S. laws and those countries may lack adequate rules and procedures for defending our intellectual property rights.

We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.

Filing, prosecuting and defending patents on ficerafusp alfa in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. could be less extensive than those in the U.S., assuming that rights are obtained 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. As such, we will not file for patent protection in all national and regional jurisdictions in the world where such protection may be available.

Accordingly, competitors may use our and our existing or future licensors', licensees' or collaborators' technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we and our existing or future licensors, licensees or collaborators have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with ficerafusp alfa or other technologies, and our and our existing or future licensors', licensees' or collaborators' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Patent protection must be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. In addition, the legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, and the requirements for patentability differ, in varying degrees, from country to country, and the laws of some foreign countries do not protect intellectual property rights, including trade secrets, to the same extent as federal and state laws of the United States. As a result, many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. Such issues may

make it difficult for us to stop the infringement, misappropriation or other violation of our intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license. Similarly, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Furthermore, proceedings to enforce our patent rights and other intellectual property rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded to us, if any, may not be commercially meaningful, while the damages and other remedies we may be ordered to pay such third parties may be significant. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Issued patents covering ficerafusp alfa and related technology could be found invalid or unenforceable if challenged in court or before a patent office. We may become involved in lawsuits involving our intellectual property, including patents, to protect or enforce our patents, which could be expensive, time consuming and unsuccessful.

Issued patents may be challenged, narrowed, invalidated, circumvented, or otherwise encumbered by a third party. We may from time to time need to resort or become a party to litigation (or other adversarial proceeding) to enforce or defend any patents or other intellectual property rights owned by or licensed to us, or to determine or challenge the scope or validity of patents or other intellectual property rights of third parties in the U.S. and in other jurisdictions. For example, in October 2024, a complaint was filed in federal court, which among other things, alleges a claim for correction of inventorship of a number of patents, including patents alleged to be licensed to us relating to ficerafusp alfa. As enforcement of intellectual property rights is difficult, unpredictable and expensive, we may fail in enforcing our rights—in which case our competitors may be permitted to use our product without being enjoined, required to pay us any license fees, or compensate us for lost profits or reasonable royalty. In addition, litigation involving our patents carries the risk that one or more of our patents will be held invalid (in whole or in part, on a claim-by-claim basis) or held unenforceable. Such an adverse court ruling could allow third parties to commercialize technology covered by our patents we seek to enforce, such as those covering ficerafusp alfa and related methods, among other technologies, and then compete directly with us, without payment to us.

If we were to initiate legal proceedings against a third party to enforce a patent covering ficerafusp alfa or other technology, the defendant could counterclaim that our patent is invalid and/or unenforceable, which is commonplace in patent litigation in the U.S. and other foreign jurisdictions. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements for patentability, for example, lack of utility, novelty, obviousness, non-enablement or lack of written description or as constituting unpatentable subject matter. Grounds for an unenforceability assertion could be an allegation that someone substantively involved in prosecution of the patent withheld but-for material information from the USPTO or engaged in affirmatively egregious misconduct, during prosecution, with a specific intent to deceive the USPTO. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we could lose at least part, and perhaps all, of the patent protection on ficerafusp alfa or other technology. Such a loss of patent protection could have a material adverse impact on our business. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives. Patents and other intellectual property rights also will not protect ficerafusp alfa

if competitors design around our protected technology without infringing our patents or other intellectual property rights.

Even if such litigation (or other adversarial proceedings or disputes) is resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, this could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings and the legal costs associated with them, could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

If we are unsuccessful in defending against any claims by competitors or others that we are infringing upon their intellectual property rights, our business could be materially harmed.

Our commercial success will depend, in part, on our ability to operate without infringing the proprietary rights of third parties. Other entities may have or obtain patents or other proprietary rights that could limit our ability to make, use, sell, offer for sale or import a product candidate, a future approved product, or impair our competitive position. We are aware of third party issued patents and/or pending patent applications, including in the U.S., that could be alleged as covering ficerafusp alfa, irrespective of the merits of any such allegation, for example in August 2024, we received a letter alleging ficerafusp alfa infringes certain third party patents. For example, in October 2024, a complaint was filed in federal court, which among other things, alleges a claim for correction of inventorship of a number of patents, including patents alleged to be licensed to us relating to ficerafusp alfa. Although we believe that these patents are not infringed, and/or are invalid and/or unenforceable, if a court should find that they cover a product candidate and we are unable to invalidate such patents, or if licenses for them are not available on commercially reasonable terms, our business could be harmed, perhaps materially.

We believe that if such patents or patent applications were asserted against us, we would have counterclaims and defenses against such claims, including non-infringement, the affirmative defense of safe harbor designed to protect activity undertaken to obtain federal regulatory approval of a drug, including under 35 U.S.C. § 271(e) and similar foreign exceptions to infringement, and defenses concerning patent invalidity and/or unenforceability. However, if such counterclaims and defenses were not successful and such patents were successfully asserted against us such that they are found to be valid and enforceable, and infringed, unless we obtain a license to such patents, which may not be available on commercially reasonable terms or at all, we could be prevented from continuing to develop or commercialize ficerafusp alfa. We could also be required to pay substantial damages. We cannot assure you that we will ultimately prevail if any of this third-party intellectual property is asserted against us.

In the biotechnology industry, significant litigation and other proceedings regarding patents, patent applications, trademarks and other intellectual property rights have become commonplace. The types of situations in which we may become a party to such litigation or proceedings include:

- we or our collaborators may initiate litigation or other proceedings against third parties seeking to invalidate the patents held by those third parties or to obtain a judgment that our products or processes do not infringe those third parties' patents;
- if our competitors file patent applications that claim technology also claimed by us or our licensors, we or our licensors may be required to participate in interference, opposition or other proceedings to determine the priority of invention, which could jeopardize our patent rights and potentially provide a third party with a dominant patent position;
- if third parties initiate litigation claiming that our processes or products infringe their patent or other intellectual property rights, we and our collaborators will need to defend against such proceedings; and
- if a license to necessary technology is terminated, the licensor may initiate litigation claiming that our processes or products infringe or misappropriate their patent or other intellectual property rights and/or that we breached our obligations under the license agreement, and we and our collaborators would need to defend against such proceedings.

These lawsuits (or other proceedings) would be costly and could affect our results of operations and divert the attention of our management and scientific personnel. The cost of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation and proceedings more effectively than we can because of their substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

In addition, if the breadth or strength of protection provided by our or our present or future licensors', collaborators' or partners' patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize ficerafusp alfa or any future product candidates. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Third party intellectual property right holders, including our competitors, may actively bring infringement claims against us. We may not be able to successfully settle, license on commercially acceptable terms or otherwise resolve such potential infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage or continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing any approved products. If we fail in any such dispute, in addition to being forced to potentially pay damages, we or our licensees may be temporarily or permanently prohibited from commercializing our product candidates that are held to be infringing or be forced to redesign our product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

The biotechnology industry has produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform or predictable. If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid, and we may not be able to do this. Proving invalidity is difficult. For example, in the U.S., proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court. Patent litigation is costly and time consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid, we may incur substantial monetary damages, encounter significant delays in bringing ficerafusp alfa to market and be precluded from manufacturing or selling ficerafusp alfa.

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

It is also possible that in our evaluation of third-party intellectual property, we failed to identify relevant patents or applications. We cannot guarantee that any of our patent searches or analyses, including but not limited to the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third party patent and pending application in the U.S. and abroad that is relevant to or necessary for the commercialization of ficerafusp alfa in any jurisdiction.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third-party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the U.S. or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market ficerafusp alfa. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the U.S. and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Furthermore, we operate in a highly competitive field, and given our limited resources, it is unreasonable to monitor all patent applications purporting to claim broad coverage in the areas in which we are active. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover ficerafusp alfa or related technology. We cannot predict whether third parties will be able to successfully obtain claims or the breadth of such claims.

If we fail to comply with our obligations under our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are currently party to intellectual property license agreements. These license agreements impose, and we expect that future license agreements may impose, various obligations on us. For example, we have entered into patent and know-how license agreements that grant us the right to use certain technologies related to our clinical product candidate and related methods. If we fail to comply with our obligations under the licenses, the licensors may have the right to terminate their respective license agreements, in which event we might not be able to market any product that is covered by the agreements. Termination of the license agreements or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms, which could adversely affect our competitive business position and harm our business.

We may be unsuccessful in licensing or acquiring third-party intellectual property that may be required to develop and commercialize ficerafusp alfa.

We have rights, through patents that we have in-licensed or own, to the intellectual property to develop ficerafusp alfa. Because our programs may involve additional product candidates, that may require the use of intellectual property or proprietary rights held by third parties, the growth of our business may depend in part on our ability to acquire, in-license or use such intellectual property and proprietary rights. We may be unable to acquire or in-license any third-party intellectual property or proprietary rights or to do so on commercially reasonable terms. For example, we sometimes collaborate with public or private academic institutions to accelerate our research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the strategic collaboration. Regardless of such option, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us, and the institution may license such intellectual property rights to third parties, potentially blocking our ability to pursue our development and commercialization plans. The same situation may occur with a present or future development partner.

The licensing and acquisition of third-party intellectual property and proprietary rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property and proprietary rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size and greater capital resources and development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license intellectual property and proprietary rights to us.

If we are unable to successfully acquire or in-license rights to required third-party intellectual property and proprietary rights or maintain our intellectual property and proprietary rights, we may have to cease development of the relevant the relevant program, product or product candidate, which could have a material adverse effect on our business.

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

The USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent prosecution and post grant or issuance. We employ reputable law firms and other professionals to help us comply. Additionally, periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or patent applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or patent applications. We rely on our outside counsel or our agents to pay these fees when due. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If such an event were to occur, it could have a material adverse effect on our business. In addition, we may be responsible for the payment of patent fees for patent rights that we license from third parties. If any licensor of these patents does not itself elect to make these payments, and we fail to do so, we may be liable to the licensor for any costs and consequences of any resulting loss of patent rights. If we or our existing or future licensors fail to maintain the patents and patent applications covering ficerafusp alfa, our competitors might be able to enter the market, which would have an adverse effect on our business.

If we do not obtain protection under the Hatch-Waxman Amendments and similar foreign legislation for extending the term of patents covering ficerafusp alfa, our business may be materially harmed.

Patents typically have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date, not including potential patent term extensions or adjustments that may be available in the U.S., and under comparable laws applicable outside the U.S., where certain conditions are met. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering ficerafusp alfa are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive medications, including biosimilar medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours, causing our revenue from applicable products to be reduced, possibly materially, and potentially harming our ability to recover our investment in such product or obtain a reasonable return on that investment.

Depending upon the timing, duration, and conditions of FDA marketing approval of ficerafusp alfa, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced, possibly materially.

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

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously or concurrently employed at other biotechnology or pharmaceutical companies, universities, and/or research institutions and the like, including our competitors or potential competitors. We may be subject to claims that these employees, or we, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers, or that patents and applications we have filed to protect inventions of these employees, even those related to ficerafusp alfa, are rightfully owned by their former or concurrent employer.

Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize ficerafusp alfa. Such a license may not be available on commercially reasonable terms or at all.

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

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

Risks Related to Healthcare, Insurance and Legal Matters

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of ficerafusp alfa.

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

- decreased demand for any product candidate we may develop;
- withdrawal of trial participants;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and significant negative media attention;
- initiation of investigations by regulators;
- significant time and costs to defend the related litigation;
- substantial monetary awards to trial subjects or patients;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize any product candidates that we may develop.

While we currently hold trial liability insurance coverage consistent with industry standards, the amount of 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. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for ficerafusp alfa, but we may be unable to obtain commercially reasonable product liability insurance. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business and financial condition.

The successful commercialization of ficerafusp alfa or any future product candidates, if approved, will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and favorable pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our products could limit our ability to market those products and decrease our ability to generate revenue.

The availability of coverage and the adequacy of reimbursement by governmental healthcare programs including but not limited to Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as ficerafusp alfa or any future product candidates, if approved. Our ability to achieve coverage and acceptable levels of reimbursement for our products by third-party payors will have an effect on our ability to successfully commercialize those products. Accordingly, we will need to successfully implement a coverage and reimbursement strategy for any approved product candidate. Even if we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. For more information, see the section titled "*Business—Government Regulation—Pharmaceutical Coverage, Pricing and Reimbursement*."

If we participate in the Medicaid Drug Rebate Program or other governmental pricing programs, in certain circumstances, our products would be subject to ceiling prices set by such programs, which could reduce the revenue we may generate from any such products. Participation in such programs would also expose us to the risk of significant civil monetary penalties, sanctions and fines should we be found to be in violation of any applicable obligations thereunder.

Third-party payors increasingly are challenging prices charged for biopharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available. It is possible that a third-party payor may consider our products as substitutable and offer to reimburse patients only for the less expensive product. Even if we are successful in demonstrating improved efficacy or improved convenience of administration with our products, pricing of existing drugs may limit the amount we will be able to charge for our products. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us 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 our products and may not be able to obtain a satisfactory financial return on products that we may develop.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved products. In the U.S., third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for ficerafusp alfa or any future product candidates.

Obtaining and maintaining reimbursement status is time-consuming, costly and uncertain. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the U.S. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, and, in some cases, at short notice, and we believe that changes in these rules and regulations are likely. For products administered under the supervision of a physician (including products administered in the clinical setting), obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the administration of the product, or the treatment or procedure in which the product is used, may not be available, which may impact physician utilization.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of ficerafusp alfa or any future product candidates, if approved in these jurisdictions. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our products. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and other third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with the sale of any of our products due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, and prescription drugs, surgical procedures and other treatments in particular, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Government authorities currently impose mandatory discounts for certain patient groups, such as Medicare and Medicaid beneficiaries, and may seek to increase such discounts at any time. Future regulation may negatively impact the price of our products, if approved. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. In addition, the U.S. Supreme Court's July 2024 decision to overturn established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which the FDA's regulations, policies and decisions may become subject to increasing legal challenges, delays, and/or changes. 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, our product candidate may lose any marketing approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

We are subject to various U.S. federal, state and foreign healthcare laws and regulations, which could increase compliance costs, and our failure to comply with these laws and regulations could harm our reputation, subject us to significant fines and liability or otherwise adversely affect our business.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers may expose us to broadly applicable foreign, federal and state fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, and plan to market, sell and distribute any products for which we obtain regulatory approval. For more information, see the section titled "*Business—Government Regulation— Other U.S. Healthcare Laws.*"

Efforts to ensure that our current and future business arrangements with third parties will comply with applicable healthcare laws and regulations will involve ongoing 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 involving applicable fraud and abuse or other healthcare laws and regulations. Due to the breadth of these laws, the narrowness of statutory exceptions and regulatory safe harbors available, and the range of interpretations to which they are subject, it is possible that some of our current or future practices might be challenged under one or more of these laws. 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 penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government-funded healthcare programs, such as Medicare and Medicaid, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings and the curtailment or restructuring of our operations. Defending against any such actions can be costly and time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. Further, if any of the physicians or other healthcare providers or entities with whom we expect to do business are found to be noncompliant with applicable laws or regulations, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs. We plan to implement a corporate compliance program designed to identify, prevent and mitigate risk through the implementation of policies and procedures, training, and auditing and monitoring. We expect to devote resources to implement, maintain, administer and expand the compliance program as necessary. We cannot be certain, however, that our compliance program will ensure compliance with the various complex laws and regulations to which we are subject now or in the future.

Current and future healthcare reform legislation or regulation may increase the difficulty and cost for us to obtain coverage for and commercialize ficerafusp alfa, if approved, or any future product candidates and may adversely affect the prices we may set.

In the U.S. and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may reduce or limit coverage and reimbursement for newly approved drugs and biologics and affect our ability to profitably sell ficerafusp alfa or any future product candidates for which we obtain regulatory approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For more information, see the section titled "*Business—Government Regulation—Current and Future U.S. Healthcare Reform Legislation*."

Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for ficerafusp alfa and any future product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, financial condition, results of operations and prospects.

We expect that these existing laws and other federal and state healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our potential products are prescribed or administered. 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 ficerafusp alfa or any future product candidates, if approved.

Failure to comply with laws and regulations related to the protection of research subjects could result in fines, penalties, and litigation, and have a material adverse effect upon our business.

We may be subject to regulation under international, federal, state, and local laws and regulations relating to the protection of research subjects. Federally funded human-subject research in the U.S., including the collection of identifiable human biospecimens, is governed by 45 CFR Part 46, also known as the Health and Human Services Policy for Protection of Human Research Subjects or the "Common Rule." Use of biospecimens in certain other research is subject to FDA regulations for the Protection of Human Subjects and Institutional Review Boards at 21 CFR Parts 50 and 56. Research funded by the National Institutes of Health, or NIH, may be subject to grant or contract requirements, as well as NIH Certificates of Confidentiality. When collecting specimens for research in the U.S., our company and its collection sites are responsible for ensuring that specimens are collected in accordance with these regulations. In addition, other countries have their own regulations around the ethical collection of human specimens for research. While we believe that we are in compliance with these laws, we may not be aware of all such laws or may fail to properly audit and identify gaps in compliance. Similarly, we may find errors in our product candidates and processes and may fail to properly match the compliance requirements of our researchers to the compliance requirements of our suppliers. Failure of our company or our suppliers to comply with international, federal, state, and local laws and regulations could subject us to denial of the right to conduct business, fines, criminal penalties, and/or other enforcement actions which could have a material adverse effect on our business.

Risks Related to Manufacturing of Our Product Candidates

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. In addition, we may need a different CMO for manufacturing ficerafusp alfa or any future product candidates for commercial supply needs. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause ficerafusp alfa or any future product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of ficerafusp alfa and jeopardize our ability to commence sales and generate revenue.

We are subject to multiple manufacturing risks, any of which could substantially increase our costs and limit supply of ficerafusp alfa.

The process of manufacturing product therapeutics and bispecifics, including ficerafusp alfa, is complex, time-consuming, highly regulated and subject to several risks, including:

- product loss during the manufacturing process, including loss caused by contamination, equipment failure or improper installation or operation of equipment, or operator error. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our products or in the manufacturing facilities in which our products are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination; the manufacturing facilities in which our products are made could be adversely affected by equipment failures, labor and raw material shortages, natural disasters, power failures and numerous other factors; and
- any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives.

Scaling up a biopharmaceutical manufacturing process is a difficult and uncertain task and involves additional risks, including cost overruns, process scale-up, process reproducibility, stability issues, compliance with cGMPs, lot consistency and timely availability of sufficient quantity of raw materials. Even if we obtain regulatory approval for any of our product candidates, manufacturers may not be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand.

We may also make changes to our manufacturing processes at various points during development, for a number of reasons, such as controlling costs, achieving scale, decreasing processing time, increasing manufacturing success rate or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause ficerafusp alfa to perform differently and affect the results of our ongoing or future clinical trials. In some circumstances, changes in the manufacturing process may require us to perform ex vivo comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require us to show the comparability of the product used in earlier clinical phases or at earlier portions of a trial to the product used in later clinical phases or later portions of the trial.

Risks Related to Employee Matters and Managing Growth

Our ability to develop product candidates, leverage our potential and our future growth depends on attracting, hiring and retaining our key personnel and recruiting additional qualified personnel. If we are not successful in attracting, motivating and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. Additionally, we will need to grow the size of our organization, and we may experience difficulties in managing this growth.

We are highly dependent on members of our executive team. The loss of the services of any of them may adversely impact the achievement of our objectives. The loss of services of any of these individuals could delay or prevent the successful development of ficerafusp alfa, completion of our planned clinical trials or the commercialization of ficerafusp alfa.

Our success also depends upon the continued contributions of our key management and scientific personnel, many of whom have been instrumental for us and have substantial experience with developing therapies, identifying potential product candidates and building the technologies related to the clinical development of our product candidates. Given the specialized nature of dual-action biologics and our approach, there is an inherent scarcity of experienced personnel in these fields. As we continue developing our product candidates in our pipeline, we will require personnel with medical, scientific, or technical qualifications specific to each program. The loss of key personnel, in particular our scientists, would delay our research and development activities. Despite our efforts to retain valuable employees, members of our team may terminate their employment with us on short notice. The competition for qualified personnel in the biotechnology and biopharmaceutical industries is intense, and our future success depends upon our ability to attract, retain, and motivate highly skilled scientific, technical and managerial employees. We face competition for personnel from other companies, universities, public and private research institutions, and other organizations. If we hire employees from competitors or other companies, their former employers may attempt to assert that these employees or we have breached legal obligations, resulting in a diversion of our time and resources and, potentially, damages. In addition, job candidates and existing employees often consider the value of the stock awards they receive in connection with their employment. If the perceived benefits of our stock awards decline, it may harm our ability to recruit and retain highly skilled employees. If our recruitment and retention efforts are unsuccessful in the future, it may be difficult for us to implement our business strategy, which would have a material adverse effect on our business.

As our development plans and strategies develop, and as we continue operating as a public company, we expect to need additional managerial, operational, marketing, sales, financial and other personnel. Future growth would impose significant added responsibilities on members of management, including:

- managing our internal development efforts effectively, including the clinical and FDA review process for ficerafusp alfa and any other future product candidates we develop, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems and procedures.

Our future financial performance and our ability to advance development of and, if approved, commercialize ficerafusp alfa and any future product candidates we develop, will depend, in part, on our ability to effectively manage any future growth, and our management may have to divert a disproportionate amount of its attention away from day-to-day activities in order to devote a substantial amount of time to managing these growth activities.

We currently rely, and for the foreseeable future will continue to rely, in substantial part on certain independent organizations, advisors and consultants to provide certain services. We cannot assure you that the services of independent organizations, advisors and consultants will continue to be available to us on a timely basis when needed, or that we can find qualified replacements. In addition, if we are unable to effectively manage our outsourced activities or if the quality or accuracy of the services provided by consultants is compromised for any reason, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain marketing approval of ficerafusp alfa or any future product candidates or otherwise advance our business. We cannot assure you that we will be able to manage our existing consultants or find other competent outside contractors and consultants on economically reasonable terms, or at all.

If we are not able to effectively expand our organization by hiring new employees and expanding our groups of consultants and contractors, we may not be able to successfully implement the tasks necessary to further develop and commercialize ficerafusp alfa or any future product candidates we develop and, accordingly, may not achieve our research, development and commercialization goals.

Risks Related to Ownership of Our Common Stock

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this section and elsewhere in this Annual Report on Form 10-K, these factors include:

- the commencement, enrollment, completion or results of our current or future preclinical and clinical trials for ficerafusp alfa;
- any delay in identifying and advancing a clinical candidate for our other programs;
- any delay in our regulatory filings for ficerafusp alfa and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- adverse results or delays, suspensions or terminations in future preclinical studies or clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval or potential accelerated approval of ficerafusp alfa or the failure of a regulatory authority to accept data from preclinical studies or clinical trials conducted in other countries;
- changes in laws or regulations applicable to ficerafusp alfa, including but not limited to clinical trial requirements for approvals;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- our inability to establish collaborations, if needed;
- our failure to commercialize ficerafusp alfa, if approved;
- additions or departures of key scientific or management personnel;
- unanticipated serious safety concerns related to ficerafusp alfa or any future product candidates;
- introduction of new products or services offered by us or our competitors;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our ability to effectively manage our growth;
- actual or anticipated variations in quarterly operating results;
- our cash position;
- our failure to meet the estimates and projections of the investment community or that we may otherwise provide to the public;
- publication of research reports about us or our industry, or ficerafusp alfa in particular, or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- changes in the market valuations of similar companies;
- changes in the structure of the healthcare payment systems;
- overall performance of the equity markets;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- changes in accounting practices;
- ineffectiveness of our internal controls;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the market for biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, securities class action litigation has often been instituted against companies following periods of volatility in the market price of a company's securities. This type of litigation, if instituted, could result in substantial costs and a diversion of management's attention and resources.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations.

Our quarterly and annual operating results may fluctuate significantly, due to a variety of factors, many of which are outside of our control and may be difficult to predict, including:

- the timing and cost of, and level of investment in, research, development and, if approved, commercialization activities relating to ficerafusp alfa or any future product candidates, which may change from time to time;
- the timing and status of enrollment for clinical trials;
- the cost of manufacturing ficerafusp alfa, as well as building out our supply chain, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies;
- timing and amount of any milestone, royalty or other payments due under any collaboration or license agreement;
- the timing and success or failure of preclinical studies and clinical trials for ficerafusp alfa or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- future accounting pronouncements or changes in our accounting policies;
- the timing and success or failure of preclinical studies and clinical trials for ficerafusp alfa or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners;
- the timing of receipt of approvals for ficerafusp alfa from regulatory authorities in the U.S. and internationally;
- exchange rate fluctuations;
- coverage and reimbursement policies with respect to ficerafusp alfa, if approved, and potential future drugs that compete with our products; and
- the level of demand for ficerafusp alfa, if approved, may vary significantly over time.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our future revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if any forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who covers us downgrades our stock or publishes inaccurate or unfavorable research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Our executive officers, directors, principal stockholders and their respective affiliates own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Based on the beneficial ownership of our common stock as of December 31, 2024, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially own a significant percentage of our common stock. These stockholders, if acting together, will continue to have significant influence over the outcome of corporate actions requiring stockholder approval, including the election of directors, amendment of our organizational documents, any merger, consolidation or sale of all or substantially all of our assets and any other significant corporate transaction. In addition, certain of our principal stockholders, including RA Capital and TPG LSA, have designated certain members of our board of directors. The interests of these stockholders may not be the same as or may even conflict with your interests. For example, these stockholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other stockholders, which could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company or our assets and might affect the prevailing market price of our common stock. The significant concentration of stock ownership may adversely affect the trading price of our common stock due to investors' perception that conflicts of interest may exist or arise.

Future sales of our common stock in the public market could cause our common stock price to fall.

Our common stock price could decline as a result of sales of a large number of shares of common stock or the perception that these sales could occur. These sales, or the possibility that these sales may occur, might also make it more difficult for us to sell equity securities in the future at a time and price that we deem appropriate.

In addition, in the future, we may issue additional shares of common stock, or other equity or debt securities convertible into common stock, in connection with a financing, acquisition, employee arrangement, or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause the price of our common stock to decline.

Our issuance of additional capital stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders.

We expect to issue additional capital stock in the future that will result in dilution to all other stockholders. We expect to grant equity awards to employees, directors and consultants under our stock incentive plans. We may also raise capital through equity financings in the future. As part of our business strategy, we may acquire or make investments in complementary companies, products or technologies and issue equity securities to pay for any such acquisition or investment. Any such issuances of additional capital stock may cause stockholders to experience significant dilution of their ownership interests and the per share value of our common stock to decline.

We do not currently intend to pay dividends on our common stock and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation of the value of our common stock.

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to support operations and to finance the growth and development of our business. We do not intend to declare or pay any cash dividends on our capital stock in the foreseeable future. As a result, any investment return on our common stock will depend upon increases in the value for our common stock, which is not certain.

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

Our fifth amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of not less than two-thirds of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our third amended and restated certificate of incorporation or amended and restated bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our bylaws designate certain courts as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our bylaws provide that, unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any state law claims for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of, or a claim based on, fiduciary duty owed by any of our current or former directors, officers, and employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law, our certificate of incorporation or our bylaws (including the interpretation, validity or enforceability thereof), or (iv) any action asserting a claim that is governed by the internal affairs doctrine, in each case subject to the Court of Chancery having personal jurisdiction over the indispensable parties named as defendants therein, or the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act or the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated bylaws further provide that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the U.S. shall be the sole and exclusive forum for resolving any complaint asserting a cause or causes of action arising under the Securities Act, or the Federal Forum Provision. In addition, our amended and restated bylaws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our common stock is deemed to have notice of and consented to the foregoing provisions; provided, however, that stockholders cannot and will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated bylaws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, the forum selection clauses in our amended and restated bylaws may limit our stockholders' ability to bring a claim in a forum that they find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court were "facially valid" under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the federal district courts of the U.S. may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

We may not be able to satisfy listing requirements of Nasdaq or obtain or maintain a listing of our common stock on Nasdaq.

If our common stock is listed on Nasdaq, we must meet certain financial and liquidity criteria to maintain such listing. If we violate Nasdaq's listing requirements, our common stock may be delisted. If we fail to meet any of Nasdaq's listing standards, our common stock may be delisted. In addition, our board of directors may determine that the cost of maintaining our listing on a national securities exchange outweighs the benefits of such listing. A delisting of our common stock from Nasdaq may materially impair our stockholders' ability to buy and sell our common stock and could have an adverse effect on the market price of, and the efficiency of the trading market for, our common stock. The delisting of our common stock could significantly impair our ability to raise capital and the value of your investment.

Other General Risks

Unfavorable global economic conditions could adversely affect our business, financial condition, stock price and results of operations.

The global credit and financial markets have experienced extreme volatility and disruptions (including as a result of actual or perceived changes in interest rates, inflation and macroeconomic uncertainties), which has included severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, high inflation, uncertainty about economic stability, global supply chain disruptions, and increases in unemployment rates. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of the 2024 presidential election in the United States, military conflict, including the ongoing conflicts between Russia and Ukraine, and Israel and Hamas, terrorism, or other geopolitical events. Sanctions imposed by the U.S. and other countries in response to such conflicts, including the one in Ukraine, may also continue to adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A severe or prolonged economic downturn could result in a variety of risks to our business, including a decrease in the demand for our drug candidates and in our ability to raise additional capital when needed on acceptable terms, if at all. For example, there has been proposed U.S. legislation that may restrict the ability of U.S. biopharmaceutical companies to purchase services or products from, or otherwise collaborate with, certain Chinese biotechnology companies of concern without losing the ability to contract with, or otherwise receive funding from, the U.S. government. We continue to assess the legislation as it develops to determine whether it could have an effect on our contractual relationships. Furthermore, any disruptions to our supply chain as a result of unfavorable global economic conditions, including due to geopolitical conflicts or public health crises, could negatively impact the timely execution of our ongoing and future clinical trials. In addition, current inflationary trends in the global economy may impact salaries and wages, costs of goods and transportation expenses, among other things, and recent and potential future disruptions in access to bank deposits or lending commitments due to bank failures may create market and economic instability. We cannot anticipate all of the ways in which the foregoing, and the current economic climate and financial market conditions generally, could adversely impact our business.

We, or the third parties upon whom we depend, may be adversely affected by natural disasters, public health crises or other business interruptions and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters or public health crises could severely disrupt our operations, and have a material adverse impact on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage, public health crisis or other event occurred that prevented us from conducting our clinical trials, releasing clinical trial results or delaying our ability to obtain regulatory approval for ficerafusp alfa, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time.

Our information technology systems, or those used by our CROs or other contractors or consultants, may fail or suffer cybersecurity incidents or breaches, which could adversely affect our business.

Despite the implementation of security measures, our information technology systems and data and those of our current or future CROs or other contractors and consultants are vulnerable to compromise or damage from computer hacking, computer viruses, social engineering (e.g., phishing attacks) and malware (e.g., ransomware malicious software), fraudulent activity, employee misconduct, human error, telecommunication and electrical failures, natural disasters, or other cybersecurity attacks or accidents. Future acquisitions could expose us to additional cybersecurity risks and vulnerabilities from any newly acquired information technology infrastructure. Cybersecurity attacks are constantly increasing in frequency and sophistication and are made by groups and individuals with a wide range of motives (including industrial espionage) and expertise, including by organized criminal groups, "hacktivists," nation states, and others. As a result of a continued hybrid working environment, we may also face increased cybersecurity risks due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. Further, as a company with an increasingly global presence, our systems are subject to frequent attacks, which are becoming more commonplace in the industry, including attempted hacking, phishing attempts, such as cyber-related threats involving spoofed or manipulated electronic communications, which increasingly represent considerable risk. Due to the nature of some of the attacks described herein, there is a risk that an attack may remain undetected for a period of time. Even if identified, we may be unable to adequately investigate or remediate cybersecurity incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence. While we continue to make investments to improve the protection of data and information technology, including in the hiring of IT personnel, periodic cyber security awareness trainings, and improvements to IT infrastructure and controls, and conduct regular testing of our systems, there can be no assurance that our efforts will prevent service interruptions or cybersecurity incidents or breaches.

We and certain of our service providers are from time to time subject to cyberattack attempts and cybersecurity incidents. Any cybersecurity incident could adversely affect our business, by leading to, for example, the loss of trade secrets or other intellectual property, demands for ransom or other forms of blackmail, or the unauthorized disclosure of personal or other sensitive information of our employees, clinical trial patients, customers, and others. If we were to experience a significant cybersecurity incident, it could seriously harm our development programs and our business operations. We could be subject to cybersecurity incident or breach notification requirements, regulatory actions taken by governmental authorities, litigation under laws that protect the privacy of personal information, or other forms of legal proceedings, which could result in significant liabilities or penalties, result in substantial costs and require attention from management. Further, a cybersecurity incident may disrupt our business or damage our reputation, which could have a material adverse effect on our business, prospects, operating results, share price and shareholder value, and financial condition. We could also incur substantial remediation costs, including the costs of investigating the incident, repairing or replacing damaged systems, restoring normal business operations, implementing increased cybersecurity protections, and paying increased insurance premiums.

For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If a cybersecurity breach or other incident were to result in the unauthorized access to or unauthorized use, disclosure, release or other processing of clinical trial data or personal data, it may be necessary to notify individuals, governmental authorities, supervisory bodies, the media, and other parties pursuant to privacy and security laws. Likewise, we rely on our third-party research institution collaborators for research and development of ficerafusp alfa and other third parties for the manufacture of ficerafusp alfa and to conduct clinical trials, and similar events relating to their information technology systems could also seriously harm our business. Any security compromise affecting us, our collaborators or our industry, whether real or perceived, could harm our reputation, erode confidence in the effectiveness of our security measures, and lead to regulatory scrutiny. To the extent that any disruption or cybersecurity incident or breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary or personal information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of ficerafusp alfa could be delayed, result in substantial costs and require attention from management.

We are eligible to be treated as an "emerging growth company" and a "smaller reporting company" and our election of reduced reporting requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation in this Annual Report on Form 10-K and our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In addition, as an emerging growth company, we are only required to provide two years of audited financial statements in this Annual Report on Form 10-K. We could be 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 total annual gross revenue. (ii) the date we qualify as a "large accelerated filer," which occurs when the market value of our common stock that is held by non-affiliates exceeds $700 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 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. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- providing only two years of audited financial statements in addition to any required unaudited interim financial statements and a correspondingly reduced "*Management's Discussion and Analysis of Financial Condition and Results of Operations*" disclosure in this Annual Report on Form 10-K;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In this Annual Report on Form 10-K, we have not included all of the executive compensation-related information that would be required if we were not an emerging growth company.

Even after we no longer qualify as an emerging growth company, we could still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements and reduced disclosure obligations regarding executive compensation in this Annual Report on Form 10-K and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile.

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

We are also a "smaller reporting company" as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as our common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter, or our annual revenue is less than $100.0 million during the most recently completed fiscal year and our common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, we will incur significant legal, accounting and other expenses. We are subject to the reporting requirements of the Exchange Act, which require, among other things, that we file with the Securities and Exchange Commission, or the SEC, annual, quarterly and current reports with respect to our business and financial condition. In addition, the Sarbanes-Oxley Act, as well as rules subsequently adopted by the SEC and The Nasdaq Global Select Market to implement provisions of the Sarbanes-Oxley Act, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial reporting controls and changes in corporate governance practices. Further, in July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Recent legislation permits emerging growth companies to implement many of these requirements over a longer period and up to the fifth anniversary of our initial public offering. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have an adverse effect on our business. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If we fail to establish and maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that needs to be reevaluated frequently. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with generally accepted accounting principles. We have started the process of documenting, reviewing and improving our internal controls and procedures for compliance with Section 404 of the Sarbanes-Oxley Act, which will require annual management assessment of the effectiveness of our internal control over financial reporting beginning with the Form 10-K for the year ending December 31, 2025. Any failure to implement required new or

improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an emerging growth company or a non-accelerated filer, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We could be an emerging growth company for up to five years following our initial public offering. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to restatements of our financial statements and require us to incur the expense of remediation.

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

We are subject to the periodic reporting requirements of the Exchange Act. We must design 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, 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 that breakdowns can occur because of simple error or mistake. For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make a required related party transaction disclosure. 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.

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

As of December 31, 2024, we had approximately $91.5 million of federal net operating losses, or NOLs. Federal NOLs generated in taxable years since inception, may be carried forward indefinitely, but the deductibility of such federal NOLs is limited to 80% of our taxable income. As of December 31, 2024, we had approximately $96.0 million of state NOLs. Of the state NOLs, some are of indefinite life, but most are of definite life with various expiration dates, beginning in 2039. As of December 31, 2024, we had approximately $4.1 million of federal research and development tax credit carryforwards. Federal tax credit carryforwards expire at various dates, beginning in 2040. As of December 31, 2024, we had approximately $0.6 million of state research and development tax credit carryforwards. The state tax credits, which have various carryforward rules, begin to expire in 2035.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by "5 percent shareholders" over a three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income or taxes may be limited. A corporation that experiences an ownership change will generally be subject to an annual limitation on the use of its pre-ownership change NOLs equal to the value of the corporation immediately before the ownership change, multiplied by the long-term tax-exempt rate (subject to certain adjustments). We may have experienced ownership changes in the past and may experience ownership changes as a result of our acquisitions of assets and/or subsequent shifts in our stock ownership (some of which are outside our control). There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs by federal or state taxing authorities or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities. As a result, our ability to use our pre-change NOLs and tax credits to offset future taxable income, if any, could be subject to limitations. Similar provisions of state tax law may also apply. As a result, even if we attain profitability, we may be unable to use a material portion of our NOLs and tax credits.

Changes in tax law could adversely affect our business and financial condition.

The rules dealing with U.S. federal, state and local income taxation are constantly under review by persons involved in the legislative process and by the U.S. Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have retroactive application), including with respect to net operating losses and research and development tax credits, could adversely affect us or holders of our common stock. In recent years, many such changes have been made and changes are likely to continue to occur in the future. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. We urge investors to consult with their legal and tax advisers regarding the implications of potential changes in tax laws on an investment in our common stock.

We may become involved in securities class action litigation that could divert management's attention and harm our business, and insurance coverage may not be sufficient to cover all costs and damages.

In the past, securities class action litigation has often followed certain significant business transactions, such as the sale of a company or announcement of any other strategic transaction, or the announcement of negative events, such as negative results from clinical trials. These events may also result in or be concurrent with investigations by the SEC. We may be exposed to such litigation or investigation even if no wrongdoing occurred. Litigation and investigations are usually expensive and divert management's attention and resources, which could adversely affect our business and cash resources and our ability to consummate a potential strategic transaction or the ultimate value our stockholders receive in any such transaction.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Cyber Risk Management and Strategy

- We have certain processes for assessing, identifying, and managing cybersecurity risks, which are built into our information technology function and are designed to help protect our information assets and operations from internal and external cyber threats, protect employee and clinical trial information from unauthorized access or attack, as well as secure our networks and systems. Such processes include physical, procedural, and technical safeguards, and routine review of our policies and procedures in an effort to identify risks and refine our practices. We engage certain external parties to enhance our cybersecurity oversight.

- In an effort to deter and detect cyber threats, we perform annual phishing tests with employees. We also conduct annual cybersecurity and prevention training for employees, which may cover topics such as social engineering, phishing, password protection, confidential data protection, and mobile security, and is designed to educate employees on incident reporting. We also use technology-based tools, including third-party tools and solutions, designed to mitigate cybersecurity risks and to bolster our employee-based cybersecurity programs.

- We have not identified any cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition; however, like other companies in our industry, we and our third-party vendors may, from time to time, experience threats and security incidents relating to our and our third-party vendors' information systems.

Governance Related to Cybersecurity Risks

Our Board of Directors (the "Board") has established oversight mechanisms to manage risks from cybersecurity threats. Our Audit Committee of the Board has primary responsibility for oversight of cybersecurity risk, pursuant to the Audit Committee charter, and periodically updates our board of directors on such matters.

At the management level, our cybersecurity program is managed by our Senior Director, IT, who is tasked with the operational oversight of company-wide cybersecurity strategy, policy, and standards across relevant departments to assess and help prepare us to address cybersecurity risks. Our Senior Director, IT reports to the Senior Vice President, Research & Development Strategy and Operations (SVP, R&D). Our Senior Director, IT has over twenty-five (25) years of experience in information technology, and also leverages the experience of a third-party managed systems provider. Our Senior Director, IT regularly reports to the SVP , R&D, as well as to other executive management on cyber matters, as appropriate.

Item 2. Properties

Our principal facilities consist of office space. Our corporate headquarters are currently located in Boston, Massachusetts, where we lease a total of 9,361 square feet. The lease expires on February 28, 2026, with an option to renew the lease term for three (3) years. We believe that these facilities will be adequate for our near-term needs. If required, we believe that suitable additional or alternative space would be available in the future on commercially reasonable terms.

Item 3. Legal Proceedings

We are subject to various litigation, claims and other proceedings that arise from time to time in the ordinary course of business. On October 22, 2024, a complaint was filed in federal district court in the District of Massachusetts by Y-Trap, Inc., or Y-Trap, naming as defendants us and Biocon LTD., or Biocon, captioned Y-Trap, Inc. v. Biocon LTD. and Bicara Therapeutics Inc., No. 24-cv-12678 (D. Mass.). The operative complaint alleges a claim against defendants for correction of inventorship of a number of patents, including patents alleged to be licensed to us relating to ficerafusp alfa. The complaint also alleges claims against defendants for unfair trade practices pursuant to Chapter 93A of the Massachusetts General Laws, unjust enrichment, and civil conspiracy. The complaint seeks, among other things, damages (including compensatory, enhanced, and punitive damages), an order correcting the inventorship of the patents at issue, costs and attorney's fees, and other equitable and injunctive relief. On January 31, 2025, Y-Trap filed its operative amended complaint. On February 28, 2025, Biocon and Bicara moved to dismiss all of Y-Trap's claims, which motions remain pending. We will continue to vigorously defend against this litigation.

Item 4. Mine Safety Disclosure

Not applicable.

Part II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock trades on The Nasdaq Global Market under the symbol BCAX and has been publicly traded since September 13, 2024. Prior to this time, there was no public market for our common stock.

Holders

As of March 24, 2025, we had approximately 51 holders of record of our common stock. This number does not include beneficial owners whose shares were held by nominees in street name. The actual number of holders of our common stock is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

We have never declared or paid any cash dividends on our common shares. We do not currently expect to pay any cash dividends on our common stock for the foreseeable future. Instead, we intend to retain future earnings, if any, for the future operation and expansion of our business and the repayment of debt or repurchase of common stock. Any determination to pay dividends in the future will be at the discretion of our board of directors and will depend upon our results of operations, cash requirements, financial condition, contractual restrictions, restrictions imposed by applicable laws and other factors that our board of directors may deem relevant.

Issuer Purchases of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Equity Compensation Plans

The information required by this item will be set forth in our 2025 Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

Recent Sales of Unregistered Securities

Set forth below is information regarding stock options granted by us and exercised during the period covered by this Annual Report on Form 10-K that were not registered under the Securities Act of 1933, as amended, or the Securities Act. Included is the consideration, if any, we received for such shares and options and information relating to the section of the Securities Act under which exemption from registration was claimed.

From January 1, 2024 to the closing of our initial public offering, or IPO, on September 13, 2024, we granted options to purchase an aggregate of 3,478,100 shares of common stock, with exercise prices ranging from $5.45 to $9.24 per share, to directors, employees and consultants pursuant to our 2019 Stock Option and Grant Plan, as amended, or 2019 Plan. During such period, 380,630 shares of common stock were issued for gross proceeds of $15.1 million upon the exercise of stock options pursuant to the 2019 Plan.

No underwriters were involved in the foregoing issuances of securities. The issuances of the securities described above were deemed to be exempt from registration pursuant to Section 4(a)(2) of the Securities Act as transactions by an issuer not involving a public offering or Rule 701 promulgated under the Securities Act as transactions pursuant to compensatory benefit plans. All recipients either received adequate information about us or had access, through employment or other relationships, to such information. On September 13, 2024, we filed a registration statement on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding options and all shares of our common stock otherwise issuable pursuant to our equity compensation plans.

Use of Proceeds from Initial Public Offering of Common Stock

On September 12, 2024, our Registration Statement on Form S-1, as amended (File No. 333-281722), or the Registration Statement, filed in connection with our IPO was declared effective by the SEC. Morgan Stanley & Co. LLC, TD Securities (USA) LLC, Cantor Fitzgerald & Co. and Stifel, Nicolaus & Company acted as representatives of the underwriters for this offering. On September 13, 2024, we completed our September 2024 public offering whereby we sold 20,125,000 shares of common stock at a public offering price of $18.00 per share, before underwriting discounts and expenses. The aggregate net proceeds received by us from the offering were $336.9 million, after deducting the underwriting discounts and commissions but before deducting offering costs payable by us of $4.5 million. No payments for such expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

As of December 31, 2024, none of the net proceeds have been used. The Company is in the clinical testing phase and is planning to utilize the proceeds for this process in future years.

The offering terminated after the sale of all securities registered pursuant to the Registration Statement. There has been no material change in the expected use of the net proceeds from our IPO as described in the final prospectus dated September 12, 2024 and filed with the SEC on September 13, 2024, pursuant to Rule 424(b)(4) (File No. 333-281722) of the Securities Act.

Item 6. Reserved

Not applicable.

Item 7. Management Discussion and Analysis

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our audited financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our future results of operations or financial condition, business strategy and plans and objectives of management for future operations, includes forward-looking

statements that involve risks and uncertainties and should be read together with the "Risk Factors" section of this Annual Report on Form 10-K for a discussion of important factors that could cause our actual results to differ materially from those described in or implied by these forward-looking statements contained in the following discussion and analysis. Please also see the section titled "Special Note Regarding Forward-Looking Statements."

Overview

We are a clinical-stage biopharmaceutical company committed to bringing transformative bifunctional therapies to patients with solid tumors. Our lead program ficerafusp alfa is a bifunctional antibody that combines two clinically validated targets, an epidermal growth factor receptor, or EGFR, directed monoclonal antibody with a domain that binds to human transforming growth factor beta, or TGF-β. Through this dual-targeting mechanism, ficerafusp alfa has the potential to exert potent anti-tumor activity by simultaneously blocking both cancer cell-intrinsic EGFR survival and proliferation, as well as the immunosuppressive TGF-β signaling within the tumor microenvironment, or TME. Ficerafusp alfa directs the TGF-β inhibitor into the immediate TME through the binding of EGFR on tumor cells, which we believe will lead to durable responses and an increase in overall survival, or OS, while reducing the adverse effects typically associated with systemic TGF-β inhibition. Ficerafusp alfa is initially being developed in head and neck squamous cell carcinoma, or HNSCC, where there remains a significant unmet need. We initiated a pivotal FORTIFI-HN01 Phase 2/3 trial ("FORTIFI-HN01 Phase 2/3 trial" or "FORTIFI-HN01") of ficerafusp alfa in combination with pembrolizumab as a first-line therapy in recurrent/metastatic, HNSCC excluding patients with HPV-positive oropharyngeal squamous cell carcinoma, or OPSCC, early in the fourth quarter of 2024

Since our inception in December 2018, we have not generated any revenue from product sales or other sources and have incurred significant operating losses and negative cash flows from our operations. Our primary uses of cash to date have been conducting research and development, advancing development of ficerafusp alfa, raising capital, building infrastructure, developing intellectual property, hiring personnel and providing general and administrative support for these operations. To date, we have funded our operations primarily through sale of common stock in connection with our IPO and exercise of stock options, private placements of our redeemable convertible preferred stock, and through debt financing. As of December 31, 2024, we had raised aggregate net proceeds of $687.2 million and had cash and cash equivalents of $489.7 million.

We have incurred operating losses in each year since our inception. Our net losses were $68.0 million and $52.0 million for the years ended December 31, 2024 and 2023, respectively. As of December 31, 2024, we had an accumulated deficit of $221.0 million. We expect our expenses and operating losses will increase substantially as we:

- conduct our current and future clinical trials;
- continue our research and development activities;
- utilize third parties to manufacture our product candidate and related raw materials or, should we decide to do so, build and maintain a commercial-scale current good manufacturing practice, or cGMP, manufacturing facility;
- hire additional research and development, clinical and commercial, and operational personnel;
- add quality control, quality assurance, legal, compliance, and other groups to support our operations;
- maintain, expand, enforce, defend and protect our intellectual property portfolio (including intellectual property obtained through license agreements) and provide reimbursement of third-party expenses related to our patent portfolio;
- seek regulatory approvals for ficerafusp alfa or any future product candidates for which we successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize ficerafusp alfa or any future product candidates for which we may obtain marketing approval;
- make any payments due under potential license agreements and any potential milestones, royalties or other payments due under any future in-license or collaboration agreements; and incur additional costs associated with being a public company.

Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our planned clinical trials, manufacturing and research and development activities.

Based upon our current operating plans, we believe that our existing cash and cash equivalents, will be sufficient to fund our operations and capital expenditure requirements into the first half of 2029. Without additional funding, we believe that we will have sufficient funds to meet our obligations within the next twelve months from the date of issuance of our consolidated financial statements. See the section titled “Use of Proceeds.” We do not expect to generate any revenue from product sales unless and until we successfully complete development and obtain regulatory approval for ficerafusp alfa or future product candidates, which will not be for at least the next several years, if ever. If we obtain regulatory approval for ficerafusp alfa or any of our future product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, until such time as we can generate significant revenue from sales of our product candidate, if ever, we expect to finance our cash needs through equity offerings, debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. See the section titled “Liquidity and Capital Resources” below. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidate that we would otherwise prefer to develop and market ourselves.

Components of Results of Operations

Revenue

We currently have no products approved for sale, and we have not generated any revenue to date. In the future, we may generate revenue from collaboration or license agreements we may enter into with respect to our product candidate, as well as product sales from any approved product, which approval we do not expect to occur for at least the next several years, if ever. Our ability to generate product revenue will depend on the successful development and eventual commercialization of ficerafusp alfa and any future product candidates we pursue. If we fail to complete clinical development of or to obtain regulatory approval for ficerafusp alfa or any future product candidates, our ability to generate future revenues, and our results of operations and financial position would be adversely affected.

Operating Expenses

Research and Development (including Research and Development—Related Party)

Research and development expenses (including related party research and development) have primarily consisted of external and internal costs associated with our research and development activities, including the development of our bifunctional ficerafusp alfa antibody therapies to treat solid tumors, and the clinical development of our product candidate. Our research and development expenses include:

- external expenses, including expenses incurred under arrangements with third parties, such as sponsored research agreements, consultants and our scientific advisors;
- the cost to obtain licenses to intellectual property;
- personnel-related costs, including salaries, bonuses, benefits, and stock-based compensation for employees engaged in research and development functions;
- costs for laboratory supplies, research materials and reagents; and
- the cost of developing and validating our manufacturing process for use in our future clinical trials.

Most of our research and development expenses have been related to the development of ficerafusp alfa. We use our personnel and infrastructure resources across the breadth of our research and development activities, which are directed toward identifying and developing our product candidate.

We expense all research and development costs in the periods in which they are incurred. Costs for certain research and development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors, related parties and third-party service providers.

We plan to substantially increase our research and development expenses for the foreseeable future as we continue with the development of ficerafusp alfa and any other product candidates we may determine to pursue. Due to the inherently unpredictable nature of pre-clinical and clinical development, we cannot determine with certainty the timing of the initiation, duration or costs of future clinical trials and pre-clinical studies of product candidates. The timelines and costs associated with research and development activities are uncertain and can vary significantly for any product candidate we pursue, and development programs are inherently unpredictable nature of clinical development. We anticipate we will make determinations as to which programs to pursue and how much funding to direct to each current program on an ongoing basis in response to clinical results, regulatory developments, and ongoing assessments as to each program's commercial potential.

Research and development activities are central to our business model. Therapeutic candidates in later stages of clinical development generally have higher development costs than those in earlier stages, primarily due to the increased size and duration of later-stage clinical trials. As a result, we expect that our research and development expenses will increase substantially over the next several years as we expect to (i) advance ficerafusp alfa into late-stage clinical trials, (ii) develop ficerafusp alfa for other potential indications and (iii) expand our manufacturing efforts.

Our future development costs may vary significantly based on various factors such as timely and successful completion of clinical trials, positive results from our future clinical trials, receipt of marketing approvals from applicable regulatory authorities, establishment of arrangements with third parties, intellectual property updates, and continued acceptable safety, tolerability and efficacy profile of any product candidates that we may develop following approval. Any changes in the outcome of any of these variables with respect to the development of our therapeutic candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these therapeutic candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time to complete clinical development of that therapeutic candidate. We may never obtain regulatory approval for any of our therapeutic candidates, and, even if we do, drug commercialization takes several years and millions of dollars in development costs.

General and Administrative

General and administrative expenses consist primarily of personnel-related costs, including salaries, bonuses, benefits, and stock-based compensation charges for those individuals in executive, legal, finance, human resources, facility operations, and other administrative functions. Other significant costs include legal fees relating to intellectual property and corporate matters, professional fees for auditing, accounting, tax and consulting services, office and information technology costs, insurance costs, and facilities, depreciation and other general and administrative expenses, which include rent and maintenance of facilities and utilities.

We anticipate that our general and administrative expenses will increase for the foreseeable future to support our increased research and development activities. We also anticipate increased expenses related to audit, accounting, legal, regulatory, and tax-related services associated with maintaining compliance with our Nasdaq and Securities and Exchange Commission, or SEC, requirements, director and officer insurance premiums, and investor relations costs associated with operating as a public company.

Other (Expenses) Income

Interest income

Interest income consists primarily of interest income earned on cash and cash equivalents. We expect our interest income will increase as we invest the cash received from the offering of common stock in 2024 and our sales of Series B and C redeemable convertible preferred stock in 2023.

Change in fair value of Series B convertible preferred stock tranche rights liability

Freestanding financial instruments that permit the holder to acquire shares that are either puttable by the holder, redeemable or contingently redeemable are required to be reported as liabilities in the consolidated financial statements. We present such liabilities on the balance sheets at their estimated fair values. Changes in fair value of the Series B convertible preferred stock tranche rights liability were recognized in the consolidated statements of operations. See the section titled “Series B Tranche Rights” below for additional details.

Income Taxes

The Company’s provision for income taxes is not material for the years ended December 31, 2024 and 2023.

Since our inception, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in each year or our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items.

Results of Operations

Comparison of the Years Ended December 31, 2024 and 2023

The following table summarizes our results of operations for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,		
	2024	**2023**	**Change**
Operating expenses			
Research and development - related party	$ 8,216	$ 9,244	$ (1,028)
Research and development	55,403	21,373	34,030
General and administrative	18,770	9,272	9,498
Total operating expenses	82,389	39,889	42,500
Loss from operations	(82,389)	(39,889)	(42,500)
Other (expenses) income			
Interest income	14,581	1,314	13,267
Change in fair value of Series B preferred stock tranche rights liability	—	(13,405)	13,405
Total other income (expense)	14,581	(12,091)	26,672
Net loss before income taxes	(67,808)	(51,980)	(15,828)
Income tax expense	(187)	(5)	(182)
Net loss	$ (67,995)	$ (51,985)	$ (16,010)

Research and Development Expenses (including Research and Development—Related Party)

Research and development expenses increased by $33.0 million from $30.6 million for the year ended December 31, 2023, to $63.6 million for the year ended December 31, 2024. The following table summarizes our research and development expenses for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,		
	2024	2023	Change
Research	$ 2,732	$ 1,387	$ 1,345
Manufacturing and process development	23,411	11,835	11,576
Clinical operations and development	27,146	13,495	13,651
Research and development personnel cost and other (including stock-based compensation)	10,330	3,900	6,430
Total research and development expenses	$ 63,619	$ 30,617	$ 33,002

The increase in research and development expenses for the year ended December 31, 2024 compared to the year ended December 31, 2023 was primarily due to:

- approximately $11.6 million in increased manufacturing and process development cost driven by additional batch manufacturing of drug substance;
- approximately $13.7 million in increased clinical operations and development expenses driven by costs associated with initiation of our pivotal FORTIFI-HN01 Phase 2/3 trial and continued patient enrollment on our ongoing Phase 1/1b trials;
- approximately $6.4 million in increased personnel related costs, including stock-based compensation, driven by higher number and value of stock options granted and an increase in the size of our workforce to support clinical development, manufacturing and research and increased professional service expenses as we continue to build out our clinical operations and development functions; and
- Research expenses increased by $1.3 million due to preparation for the upcoming FORTIFI-HN01 Phase 2/3 trial.

The table below summarizes our research and development expenses by program (in thousands):

	Year Ended December 31,		
	2024	2023	Change
Direct external program expenses:			
ficerafusp alfa	$ 53,926	$ 25,423	$ 28,503
BCA 300	—	947	(947)
BCA 400/600	—	8	(8)
Internal and unallocated expenses:			
Personnel related costs (including stock-based compensation)	9,693	3,847	5,846
Other	—	392	(392)
Total	$ 63,619	$ 30,617	$ 33,002

The increase in research and development expenses by program for the years ended December 31, 2024, compared to the year ended December 31, 2023 was primarily due to:

- approximately $28.5 million in increased costs for our ficerafusp alfa program, driven by manufacturing costs and clinical operation and development costs associated with our FORTIFI-HN01 Phase 2/3 trial design and continued patient enrollment in our Phase 1/1b dose expansion cohorts; and
- approximately $5.8 million in increased personnel cost, driven by an increase in the size of our workforce to support clinical development, manufacturing and research and increased professional service expenses as we continue to build out our clinical operations and development functions.

These increases were partially offset by approximately $0.9 million in decreased costs for our BCA 300 program, which was paused in 2023.

General and Administrative Expenses

General and administrative expenses increased by $9.5 million from $9.3 million for the year ended December 31, 2023, to $18.8 million for the year ended December 31, 2024. The following table summarizes our general and administrative expenses for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,		
	2024	2023	Change
General and administrative personnel costs (including stock-based compensation)	$ 12,545	$ 5,820	$ 6,725
Professional fees	3,696	2,061	1,635
Facility costs, IT, office expense and other	2,529	1,391	1,138
Total general and administrative expenses	$ 18,770	$ 9,272	$ 9,498

The increase in general and administrative expenses for the year ended December 31, 2024 compared to the year ended December 31, 2023 was primarily due to:

- approximately $6.7 million in increased personnel related costs, including stock-based compensation, driven by an increase in the size of our workforce and by a higher number and value of stock options granted;
- approximately $1.6 million in increased professional service expenses associated with higher legal, accounting and other expenses as we continue to build out our general and administrative functions to support advancing of our clinical trials and operating a publicly traded company; and
- approximately $1.1 million in increased information technology expenses and related miscellaneous expenses.

Other (Expense) Income

Interest income

Interest income for the years ended December 31, 2024 and 2023 was $14.6 million and $1.3 million, respectively. The increase was primarily due to an increase in cash equivalents from the sale of common stock and private sale of preferred stock.

Change in fair value of Series B convertible preferred stock tranche rights liability

Change in fair value of Series B convertible preferred stock tranche rights liability for the years ended December 31, 2024 and 2023 was none and $13.4 million, respectively. The loss was primarily due to the increase in fair value of the Series B convertible preferred shares sold in connection with tranched milestone closings during the year ended December 31, 2023.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception in December 2018, we have not generated any revenue from any sources and have incurred significant operating losses and negative cash flows from operations. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of ficerafusp alfa or any future product candidates we elect to pursue. Further we expect to incur additional costs associated with operating as a public company. From our inception in December 2018 through December 31 2024, we have received aggregate net proceeds of $687.2 million from the sale of our common stock in connection with the IPO and exercise of stock options, sale of our redeemable convertible preferred stock in private placements and debt financing.

Future Funding Requirements

As of December 31, 2024, we had cash and cash equivalents of $489.7 million. Based upon our current operating plans, we believe that our existing cash and cash equivalents, will be sufficient to fund our operations and capital expenditure requirements into the first half of 2029. However, 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. Additionally, the process of testing our product candidate in clinical trials is costly, and the timing of progress and expenses in these trials is uncertain. We will need to raise substantial additional capital in the future.

Our future capital requirements will depend on many factors, including but not limited to:

- the type, number, scope, progress, expansions, results, costs, and timing of, clinical trials of ficerafusp alfa and future product candidates;
- the costs and timing of manufacturing for ficerafusp alfa and any future product candidates and commercial manufacturing thereof;
- the costs, timing, and outcome of regulatory review of ficerafusp alfa and any future product candidates;
- the terms and timing of establishing and maintaining licenses and other similar arrangements;
- the legal costs of obtaining, maintaining, and enforcing our patents and other intellectual property rights (including intellectual property obtained through license agreements);
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company;
- the costs associated with hiring additional personnel and consultants as our clinical activities increase;
- the costs and timing of establishing or securing sales and marketing capabilities if ficerafusp alfa or any future product candidate is approved;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third- party payors and adequate market share and revenue for any approved products; and
- costs associated with any products or technologies that we may in-license or acquire.

Until such time, if ever, as we can generate substantial product revenue to support our cost structure, we expect to finance our cash needs through equity offerings, debt financings, or other capital sources, potentially including collaborations, licenses, and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. To the extent that we raise additional capital through the sale of equity 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, such as incurring additional debt, making capital expenditures, or declaring dividends. If we raise funds through collaborations, or other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or current or future product candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. Our failure to raise capital or enter into such other arrangements when needed could have a negative impact on our financial condition and on our ability to pursue our

business plans and strategies. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our current or future product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Cash Flows

Comparison of the Years Ended December 31, 2024 and 2023

The following table sets forth a summary of the net cash flow activity for the years ended December 31, 2024 and 2023 (in thousands):

	Year Ended December 31,	
	2024	2023
Net cash used in operating activities	$ (74,751)	$ (45,628)
Net cash provided by (used in) investing activities	(9)	(586)
Net cash provided by financing activities	334,031	272,496
Net increase in cash and cash equivalents	$ 259,271	$ 226,282

Operating Activities

For the year ended December 31, 2024, net cash used in operating activities was $74.8 million resulting from our net loss of $68.0 million and a net increase in our operating assets and liabilities of $14.1 million partially offset by non-cash charges of $7.4 million, which consists primarily of stock-based compensation.

For the year ended December 31, 2023, net cash used in operating activities was $45.6 million resulting from our net loss of $52.0 million and a net increase in our operating assets and liabilities of $9.6 million partially offset by non-cash charges of $16.0 million, which consisted primarily of $13.4 million change in the fair value of Series B preferred stock tranche rights liability and $1.9 million of stock-based compensation expenses.

Investing Activities

Net cash used in investing activities was $0.0 million during the year ended December 31, 2024 as compared to $0.6 million during the year ended December 31, 2023. The decrease in net cash used in investing activities was due to a decrease in purchases of property and equipment.

Financing Activities

Net cash provided by financing activities was $334.0 million during the year ended December 31, 2024. The positive net cash provided by financing activities was primarily due to the net proceeds of $332.4 million raised from the sale of our common stock in fiscal 2024

Net cash provided by financing activities was $272.5 million during the year ended December 31, 2023. which consisted primarily of the net proceeds from our Series B and Series C raises.

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2024 (in thousands):

	Payment Due by Period			
	Total	Less than 1 Year	1-3 years	4-5 years
Operating lease commitments	$ 745	$ 639	$ 106	$ —
Total	$ 745	$ 639	$ 106	$ —

We enter into contracts in the normal course of business with contract research organizations for clinical trials, with contract manufacturing organizations, or CMOs, for clinical supplies manufacturing and with other vendors for supplies and other products and services for operating purposes. These agreements generally provide for termination at the request of either party generally with less than one-year notice and, therefore, we believe that our non-cancellable obligations under these agreements are not material. We do not currently expect any of these agreements to be terminated and did not have any non-cancellable obligations under these agreements as of December 31, 2024 and 2023.

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under rules and regulations of the SEC.

Critical Accounting Polices and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which are prepared in accordance with generally accepted accounting principles in the U.S., or GAAP. The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, costs, and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements and accompanying notes. We base our estimates and assumptions on historical experience and other factors that we believe to be reasonable under the circumstances. We evaluate our estimates and judgments on an ongoing basis. We base our estimates on historical experience, known trends and events, and on various other factors that we believe 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. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in Note 2 titled "Summary of Significant Accounting Policies" to our consolidated financial statements appearing elsewhere in this Form 10-K, we believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Accrued Research and Development Expenses

We are required to estimate our expenses resulting from obligations under contracts with vendors and consultants, in connection with conducting research and development activities. The financial terms of these contracts are subject to negotiations, which vary from contract to contract and may result in payment flows that do not match the periods over which materials or services are provided under such contracts. We reflect research and development expenses in our consolidated financial statements by matching those expenses with the period in which services are provided. We account for these expenses according to the progress of the clinical studies as measured by the timing of various aspects of the study or related activities. We determine accrual estimates through review of the underlying contracts along with preparation of financial models taking into account discussions with research and other key personnel as to the progress of studies, or other services being conducted. During the course of a study, we adjust our rate of expense recognition if actual results differ from our estimates.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Series B Tranche Rights

Freestanding financial instruments that permit the holder to acquire shares that are either puttable by the holder, redeemable or contingently redeemable are required to be reported as liabilities in the consolidated financial statements. We present such liabilities on the balance sheets at their estimated fair values. Changes in fair value of the liability are calculated each reporting period, and any change in value is recognized in the consolidated statements of operations.

The Company's Series B convertible preferred stock financing included tranche rights, or the Series B Tranche Rights, to purchasers who participated in the initial Series B convertible preferred stock issuance. The Series B Tranche Rights were determined to be a "freestanding financial instrument" as defined in the ASC Master Glossary as they were legally detachable and separately exercisable. Management assessed the freestanding financial instrument under ASC 480, Distinguishing Liabilities from Equity, and determined that such rights should be accounted for as a liability at fair value given they imposed a contingent obligation on the Company to issue additional Series B convertible preferred shares that would be contingently redeemable. The Series B Tranche Rights were revalued at each reporting period until settlement, with changes in the fair value recorded in the consolidated statements of operations.

Common Stock Valuation

Due to the absence of an active market for our common stock prior to the offering of common stock completed on September 13, 2024, we utilized methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants' Audit and Accounting Practice Guide: Valuation of Privately-Held Company Equity Securities Issued as Compensation to estimate the fair value of our common stock. In determining the exercise prices for options granted, we considered the fair value of the common stock as of the grant date. The fair value of our common stock was determined by our board of directors using a variety of factors, including: valuations of our common stock performed with the assistance of independent third-party valuation specialists; our stage of development and business strategy, including the status of research and development efforts of our product candidate, and the material risks related to our business and industry; our business conditions and projections; our results of operations and financial position, including our levels of available capital resources; the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies; the lack of marketability of our common stock as a private company; the prices of our preferred stock sold to third party investors, and the rights, preferences and privileges of our preferred stock relative to those of our common stock; the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering or a sale given prevailing market conditions; trends and developments in our industry; the hiring of key personnel and the experience of management; and external market conditions affecting the life sciences and biotechnology industry sectors. Significant changes to the key assumptions underlying the factors used could result in different fair values of our common stock at each valuation date.

Valuation Methodologies

Our common stock valuations were prepared in accordance with the guidelines in the AICPA Practice Aid, which prescribes several valuation approaches for determining the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its capital structure and specifically the common stock.

Prior to the IPO our common stock valuations were prepared using (i) the back-solve method to calculate the total equity value and the option-pricing method, or OPM, to allocate the total equity value and (ii) probability weighted expected return method or PWERM.

The back-solve method derives the implied equity value for one type of equity security from a contemporaneous transaction involving another type of security. We used the back-solve method to calculate the total equity value of our company as we had recently completed redeemable convertible preferred stock financings that should be considered in estimating the fair value of our equity per the AICPA Practice Aid. The OPM method allows for the allocation of a company's equity value among the various equity capital owners (preferred and common shareholders). The OPM uses the preferred shareholders' liquidation preferences, participation rights, dividend policy, and conversion rights to determine how proceeds from a liquidity event shall be distributed among the various ownership classes at a future date.

The PWERM method involved the estimation of future potential outcomes for the Company, as well as values and probabilities associated with each respective potential outcome. The common stock per share value determined using this approach was ultimately based upon probability-weighted per share values resulting from the various future scenarios, which included an IPO scenario or continued operation as a private company scenario.

Following the closing of the initial public offering, the fair value of our common stock has been determined based on the quoted market price of our common stock.

Stock-Based Compensation

Stock-based compensation expense represents the cost of the grant date fair value of equity awards recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis. We estimate the fair value of stock option awards using the Black-Scholes option pricing model and recognize forfeitures as they occur.

The Black-Scholes option pricing model requires the use of subjective assumptions, including the risk-free interest rate, the expected stock price volatility, the expected term of stock options, the expected dividend yield, and the fair value of the underlying common stock on the date of grant. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require judgment to develop. See Note 10 titled "Stock-based Compensation" to our consolidated financial statements included elsewhere in this Form 10-K for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted for the years ended December 31, 2024, and 2023, respectively.

For awards that vest based solely on achievement of a service condition, the Company recognizes expense on a straight-line basis over the period during which the award holder provides such services. The Company recognizes forfeitures as they occur and reverses any previously recognized compensation cost associated with forfeited awards. The Company accounts for share-based compensation for awards granted to nonemployees in a similar fashion to the way it accounts for share-based compensation awards to employees.

Emerging Growth Company and Smaller Reporting Company Status

The Jumpstart Our Business Startups Act of 2012, or JOBS, permits an "emerging growth company" such as us to take advantage of an extended transition to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected not to "opt out" of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (i) irrevocably elect to "opt out" of such extended transition period or (ii) no longer qualify as an emerging growth company. There are other exemptions and reduced reporting requirements provided by the JOBS Act that we are currently evaluating. For example, as an "emerging growth company," we are exempt from Sections 14A(a) and (b) of the Securities Exchange Act of 1934, as amended, which would otherwise require us to (1) submit certain executive compensation matters to shareholder advisory votes, such as "say-on-pay," "say-on-frequency," and "golden parachutes;" and (2) disclose certain executive compensation related items such as the correlation between executive compensation and performance and comparisons of our chief executive officer's compensation to our median employee compensation. We also intend to rely on an exemption from the rule requiring us to provide an auditor's attestation report on our internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We will continue to remain an "emerging growth company" until the earliest of the following: (1) the last day of the fiscal year following the fifth anniversary of the date of the completion of our IPO; (2) the last day of the fiscal year in which our total annual gross revenue is equal to or more than $1.235 billion; (3) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (4) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

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

Recent Accounting Pronouncements

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 titled "Summary of Significant Accounting Policies" to our consolidated financial statements included elsewhere in this Form 10-K.

Item 7A. Quantitative and Qualitative Disclosure

Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

As of December 31, 2024, we had $489.7 million in cash and cash equivalents, which consisted of cash and money market funds. Our cash and cash equivalents are primarily maintained in accounts with multiple financial institutions in the U.S. At times, we may maintain cash and cash equivalent balances in excess of Federal Deposit Insurance Corporation limits. We do not believe that we are subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, we believe an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investment portfolio.

Inflation Risk

Inflation generally affects us by increasing our cost of labor and research and development contract costs. We do not believe inflation has had a material effect on our results of operations during the periods presented.

Foreign Currency Exchange Risk

We are exposed to foreign exchange rate risk. Our headquarters is located in the U.S., where the majority of our general and administrative expenses and research and development costs are incurred in U.S. dollars. While we are subject to fluctuations in foreign currency rates in connection with these arrangements, to date, these fluctuations have not been significant. Based on our expected volumes with these vendors and employees in fiscal year 2024, a movement of 10% in the exchange rates would not have a material effect on our results of operations or financial condition.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements, together with the reports of our independent registered public accounting firm, appear beginning on page 146 of this Annual Report for the year ended December 31, 2024.

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

We maintain disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure. In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and management necessarily applies judgement in evaluating the benefits of possible controls and procedures relative to their costs.
Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of December 31, 2024. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2024.

Management's Annual Report on Internal Controls Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the SEC for newly public companies. Additionally, our independent registered accounting firm will not be required to opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act, and our unaffiliated market capitalization exceeds $700 million.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended December 31, 2024 that have materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

a. None.

b. Rule 10b5-1 Trading Plans

The following table describes for the three months ended December 31, 2024 each trading arrangement under which the Company's directors or officers adopted, materially modified, or terminated any contract, instruction, or written plan for the purchase or sale of Company securities that was intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) or any non-Rule 10b5-1 trading arrangement.

Name (Title)	Action Taken (Date of Action)	Type of Trading Arrangement	Nature of Trading Arrangement	Duration of Trading Arrangement	Aggregate Number of Securities
Lara Meisner (Chief Legal Officer)	Adoption (November 13, 2024)	Rule 10b5-1 trading arrangement	Sale	Until the earlier of a) September 30, 2025; b) the first date on which all trades have been executed or all trading orders related to such trades have expired; and c) the date on which the plan holder gives notice to terminate the plan.	Up to 144,611 shares

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 10 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item 11 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and, other than the information required by Item 402(v) of Regulation S-K, is incorporated herein by reference.

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

The information required by this Item 12 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

Our independent public accounting firm is KPMG LLP, Boston, Massachusetts, United States, PCAOB Auditor ID [185].

The information required by this Item 14 will be included in our Definitive Proxy Statement to be filed with the SEC with respect to our 2025 Annual Meeting of Stockholders and is incorporated herein by reference.

Part IV

Item 15. Exhibits, Financial Statement Schedules.

(a) Financial Statements

- For a list of the financial statements included herein, see Index to the Consolidated Financial Statements on page 145 of this Annual Report on Form 10-K, incorporated into this Item by reference.
- Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

(b) Exhibits

The exhibits filed as part of this Annual Report on Form 10-K are set forth on the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

Not applicable.

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors
Bicara Therapeutics Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Bicara Therapeutics Inc. and subsidiary (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit), and cash flows for the years then ended, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated 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 the years then ended, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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 consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ KPMG LLP

We have served as the Company's auditor since 2021.

Boston, Massachusetts
March 27, 2025

BICARA THERAPEUTICS INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except shares and per share data)

	December 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 489,711	$ 230,440
Prepaid expenses and other assets	12,822	633
Total current assets	502,533	231,073
Property and equipment, net	155	202
Right of use asset – operating lease	690	613
Other assets	6,618	2,094
Total assets	$ 509,996	$ 233,982
Liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 3,893	$ 2,142
Accounts payable – related party	615	1,044
Accrued expenses and other current liabilities	12,875	8,053
Accrued expenses and other current liabilities – related party	—	3,561
Operating lease liability – current portion	607	285
Total current liabilities	17,990	15,085
Operating lease liability – net of current portion	131	372
Other liabilities	—	17
Total liabilities	18,121	15,474
Commitments and Contingencies:		
Series Seed redeemable convertible preferred stock, $0.0001 par value, 0 and 81,790,144 authorized; issued and outstanding as of December 31, 2024 and December 31, 2023, respectively (liquidation preference of $0 and $81,790 as of December 31, 2024, and December 31, 2023, respectively)	—	81,525
Series B redeemable convertible preferred stock, $0.0001 par value, 0 and 105,595,101 shares authorized; issued and outstanding as of December 31, 2024 and December 31, 2023, respectively (liquidation preference of $0 and $108,235 as of December 31, 2024 and December 31, 2023, respectively);	—	121,148
Series C redeemable convertible preferred stock, $0.0001 par value, 0 and 119,599,872 shares authorized; issued and outstanding as of December 31, 2024 and December 31, 2023, respectively (liquidation preference of $0 and $165,000 as of December 31, 2024 and December 31, 2023, respectively)	—	164,604
Total redeemable convertible preferred stock	—	367,277
Stockholders' equity (deficit):		
Preferred stock $0.0001 par value, 10,000,000 shares authorized; 0 shares issued and outstanding as of December 31, 2024 and December 31, 2023	—	—
Common stock, $0.0001 par value, 500,000,000 and 365,000,000 shares authorized; 54,444,180 and 711,895 shares issued and 54,440,013 and 640,386 shares outstanding as of December 31, 2024 and December 31, 2023, respectively	7	2
Additional paid-in capital	712,884	4,250
Accumulated deficit	(221,016)	(153,021)
Total stockholders' equity (deficit)	491,875	(148,769)
Total liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)	$ 509,996	$ 233,982

See accompanying notes to consolidated financial statements

BICARA THERAPEUTICS INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands except shares and per share data)

	Year Ended December 31,	
	2024	**2023**
Operating expenses		
Research and development - related party	$ 8,216	$ 9,244
Research and development	55,403	21,373
General and administrative	18,770	9,272
Total operating expenses	82,389	39,889
Loss from operations	(82,389)	(39,889)
Other (expenses) income		
Interest income	14,581	1,314
Change in fair value of Series B preferred stock tranche rights liability	—	(13,405)
Total other income (expense)	14,581	(12,091)
Net loss before income taxes	(67,808)	(51,980)
Income tax expense	(187)	(5)
Net loss	$ (67,995)	$ (51,985)
Net Loss per share, basic and diluted	$ (4.05)	$ (89.61)
Weighted-average number common shares outstanding, basic and diluted	16,805,524	580,109

See accompanying notes to consolidated financial statements

BICARA THERAPEUTICS INC.
CONSOLIDATED STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands except shares)

	Seed Series Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Series C Redeemable Convertible Preferred Stock		Common Equity		Additional Paid in Capital	Accumulated Deficit	Total Stockholders Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
December 31, 2022	81,790,144	$ 81,525	—	$ —	—	$ —	504,544	$ 2	$ 2,231	$ (101,036)	$ (98,803)
Issuance of Series B redeemable convertible preferred stock, net of offering cost, expenses, and discount	—	—	105,595,101	107,101	—	—	—	—	—	—	—
Issuance of Series C redeemable convertible preferred stock, net of offering cost and expenses	—	—	—	—	119,599,872	164,604	—	—	—	—	—
Settlement of Series B preferred stock tranche rights liability, upon issuance of milestone shares	—	—	—	14,047	—	—	—	—	—	—	—
Issuance of common stock upon exercise of stock options	—	—	—	—	—	—	29,149	—	120	—	120
Vesting of restricted common stock	—	—	—	—	—	—	106,693	—	—	—	—
Stock-based compensation	—	—	—	—	—	—	—	—	1,899	—	1,899
Net loss	—	—	—	—	—	—	—	—	—	(51,985)	(51,985)
December 31, 2023	81,790,144	$ 81,525	105,595,101	$ 121,148	119,599,872	$ 164,604	640,386	$ 2	$ 4,250	$ (153,021)	$ (148,769)
Issuance of common stock, net of offering cost, expenses and discount	—	—	—	—	—	—	20,125,000	2	332,427	—	332,429
Conversion of convertible preferred stock into common stock upon initial public offering	(81,790,144)	(81,525)	(105,595,101)	(121,148)	(119,599,872)	(164,604)	33,210,876	3	367,150	—	367,153
Issuance of common stock upon exercise of stock options	—	—	—	—	—	—	416,555	—	1,660	—	1,660
Vesting of restricted common stock	—	—	—	—	—	—	47,196	—	—	—	—
Stock-based compensation	—	—	—	—	—	—	—	—	7,397	—	7,397
Net loss	—	—	—	—	—	—	—	—	—	(67,995)	(67,995)
December 31, 2024	—	$ —	—	$ —	—	$ —	54,440,013	$ 7	$ 712,884	$ (221,016)	$ 491,875

See accompanying notes to consolidated financial statements

BICARA THERAPEUTICS INC.
CONSOLIDATED STATEMENT OF CASH FLOWS
(in thousands)

	Year Ended December 31,	
	2024	**2023**
Operating activities:		
Net loss	$ (67,995)	$ (51,985)
Adjustments to reconcile net loss to cash used in operating activities:		
Change in fair value of Series B preferred stock tranche rights liability	—	13,405
Stock-based compensation	7,397	1,899
Depreciation	56	19
Non-cash loss on equipment impairment	—	568
Non-cash lease expense	(77)	90
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	(16,850)	(914)
Accounts payable and accrued expenses	6,627	3,792
Accounts payable and accrued expenses – related party	(3,990)	(12,455)
Operating lease liabilities	81	(47)
Net cash used in operating activities	(74,751)	(45,628)
Investing activities:		
Purchase of property and equipment	(71)	(586)
Proceeds from sale of property and equipment	62	—
Net cash provided by (used in) investing activities	(9)	(586)
Financing activities:		
Proceeds from issuance on common stock, net of issuance costs	332,427	—
Proceeds from issuance of preferred stock and preferred stock tranche rights, net	—	272,347
Proceeds from exercise of options	1,604	149
Net cash provided by financing activities	334,031	272,496
Net increase in cash and cash equivalents	259,271	226,282
Cash and cash equivalents at beginning of period	230,440	4,158
Cash and cash equivalents at end of period	$ 489,711	$ 230,440
Supplemental disclosure of cash flow information:		
Non-cash investing and financing activities:		
Settlement of Series B preferred stock tranche rights, upon issuance of milestone shares	$ —	$ 14,047
Right-of-use asset obtained in exchange for lease liability	$ 413	$ 703
Vesting of early exercise stock options	$ 68	$ 68

See accompanying notes to consolidated financial statements

1. Description of Business, Organization, and Liquidity

Bicara Therapeutics Inc. ("Bicara" or the "Company") was incorporated in the state of Delaware in December 2018 and is a clinical-stage biopharmaceutical company based in Boston, Massachusetts. The Company is committed to bringing transformative bifunctional therapies to patients with solid tumors. Its lead program ficerafusp alfa is a bifunctional antibody that combines a clinically validated epidermal growth factor receptor directed monoclonal antibody with a domain that binds to human transforming growth factor beta.

Since inception, the Company has operated in the preclinical and clinical stages and has devoted substantially all of its time and efforts to performing research and development activities, raising capital, and recruiting management and technical staff to support these operations. The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry including, but not limited to, risks associated with the successful research, development and manufacturing of product candidates, competition from other companies, dependence on key personnel, protection of intellectual property, compliance with government regulations and the ability to secure additional capital to fund operations. Current and future programs will require significant research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel, and infrastructure. Even if our product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

The Company historically has funded its operations from the issuance of common stock in connection with its initial public offering ("IPO"), redeemable convertible preferred stock and through debt financing.

In 2023, the Company issued 105,595,101 shares of Series B preferred stock with par value $0.0001 per share (the "Series B Preferred Stock") and purchase price of $1.025 per share for net proceeds of $107.7 million after deducting expenses paid by the Company. The Company additionally issued 119,599,872 shares of Series C preferred stock with par value of $0.0001 per share (the "Series C Preferred Stock") and purchase price of $1.3796 per share for net proceeds of $164.6 million after deducting expenses paid by the Company. During 2023, the Company raised net proceeds of $272.3 million from the issuance of redeemable convertible preferred stock. The Company expects that its cash and cash equivalents as of December 31, 2024 of $489.7 million will be sufficient to fund the operating expenditures and capital expenditure requirements necessary to advance its research efforts and clinical trials for at least one year from the date of issuance of these consolidated financial statements.

The Company has incurred operating losses since inception and expects such losses and negative operating cash flows to continue for the foreseeable future. As of December 31, 2024, the Company had cash of $489.7 million and an accumulated deficit of $221.0 million.

During 2024, the Company completed an IPO, through which it issued 20,125,000 shares of common stock with par value of $0.0001 per share and a purchase price of $18.00 per share. The Company raised net proceeds of $332.4 million from the issuance of common stock.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements are prepared in conformity with accounting principles generally accepted in the U.S. ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB"). The accompanying consolidated financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the ordinary course of business.

The Company's consolidated financial statements include the financial position, results of operations and cash flows of Bicara. The Company's consolidated financial statements are denominated in U.S. dollars. The consolidated financial statements include the accounts of the Company and its wholly owned, controlled subsidiary. All intercompany transactions and balances have been eliminated in consolidation.

Reverse Stock Split

In September 2024, the Company effected a 1-for-9.2435 reverse stock split of its common stock. On the effective date of the reverse stock split, (i) each 9.2435 shares of outstanding common stock were reduced to one share of common stock; (ii) the number of shares of common stock into which each outstanding option to purchase common stock is exercisable were proportionately reduced on a 9.2435-to-1 basis; and (iii) the exercise price of each outstanding option to purchase common stock were proportionately increased on a 1-to-9.2435 basis. All the share numbers, share prices, and exercise prices have been adjusted, on a retroactive basis, to reflect this 1-for-9.2435 reverse stock split. Additionally, the authorized, issued and outstanding shares of redeemable convertible preferred stock and their related per share amount, other than the conversion price per share, was not adjusted as a result of the reverse stock split.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenue, expenses and the related disclosure of contingent assets and liabilities as of and during the reporting period. The Company bases its estimates on historical experience when available and on other assumptions that management believes are reasonable under the circumstances. Significant estimates and assumptions reflected in these consolidated financial statements include but are not limited to: the estimated costs of research and development activities, the fair value of tranche right liabilities, and the fair values of common stock and stock awards and associated stock- based compensation expense. The Company assesses estimates on an ongoing basis; however, actual results could materially differ from those estimates.

Redeemable Convertible Preferred Stock

The Company recorded shares of redeemable convertible preferred stock at their respective fair values on the dates of issuance, net of issuance costs. The Company applied the guidance in ASC 480-10-S99-3A, SEC Staff Announcement: Classification and Measurement of Redeemable Securities, and therefore classified the Series Seed, Series B and Series C convertible preferred stock as mezzanine equity. The convertible preferred stock was recorded outside of stockholders' deficit because, in the event of certain deemed liquidation events considered not solely within the Company's control, such as a merger or consolidation and sale, lease or transfer of all or substantially all of the Company's assets, the convertible preferred stock would have become redeemable at the option of the holders. In the event of a change of control of the Company, proceeds received from the sale of such shares would have been distributed in accordance with the corresponding liquidation preferences. The Company did not adjust the carrying values of the convertible preferred stock to the deemed liquidation values of such shares since a liquidation event was not probable at any of the reporting dates prior to the IPO, which was executed in the third quarter of 2024 and resulted in the conversion to common shares.

Series B Tranche Rights

Freestanding financial instruments that permit the holder to acquire shares that are either puttable by the holder, redeemable or contingently redeemable are required to be reported as liabilities in the consolidated financial statements. We present such liabilities on the balance sheets at their estimated fair values. Changes in fair value of the liability are calculated each reporting period, and any change in value are recognized in the consolidated statements of operations.

The Series B Preferred Stock issuance as described in Note 9 Redeemable Convertible Preferred Stock to these consolidated financial statements, included tranche rights ("Series B Tranche Rights") to purchasers who

participated in the initial Series B Preferred Stock issuance. The Series B Tranche Rights were determined to be a "freestanding financial instrument" as defined in the ASC Master Glossary as they are legally detachable and separately exercisable. Management assessed the freestanding financial instrument under ASC 480, Distinguishing Liabilities from Equity, and determined that such rights should be accounted for as a liability at fair value given they impose an obligation on the Company to issue shares that are contingently redeemable. The Series B Tranche Rights were revalued at each reporting period until settlement, with changes in the fair value recorded in the consolidated statements of operations.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under U.S. GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. A framework is used for measuring fair value utilizing a three-tier hierarchy that prioritizes the inputs to valuation techniques used to measure fair value. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—defined as observable inputs, such as quoted prices unadjusted in active markets for identical assets or liabilities;
- Level 2—defined as inputs other than quoted prices included in Level 1 that are either directly or indirectly observable; and
- Level 3—defined as significant unobservable inputs in which little or no market data exists, therefore, requiring an entity to develop its own assumptions

The carrying amounts of the Company's financial assets (which include cash) and liabilities (which include accounts payable) approximate fair value because of the short maturity of these instruments and have been classified as Level 1. The Series B Tranche Rights are classified as Level 3 financial liabilities (Refer to Note 3 Fair value measurement to these consolidated financial statements for more details).

Cash and Cash Equivalents

The Company's cash and cash equivalents are held in standard checking accounts and money market funds at two financial institutions. The Company considers all highly liquid investments with a maturity date of 90 days or less at the date of purchase to be cash equivalents.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist of cash and cash equivalents. At times, the Company's cash deposits may be in excess of insured limits. Company has not experienced any losses on its deposits of cash and does not have off-balance sheet concentrations of credit risk.

Long-Lived Assets

The Company states property and equipment at cost, net of accumulated depreciation. The Company capitalizes major improvements and expenses maintenance and repairs as incurred. The Company recognizes depreciation on a straight-line basis over the estimated useful lives of the related assets, which are as follows:

	Estimated useful life
Computers and equipment	3 years
Furniture and fixtures	3 years

Upon retirement or sale of property and equipment, as applicable, the cost and related accumulated depreciation are removed from the balance sheets and the resulting gain or loss is reflected in operations. The Company recorded no loss and a $0.6 million loss for the years ended December 31, 2024 and 2023, respectively, for property that was abandoned and written off. The Company evaluates long-lived asset impairments every year under ASC 360, noting no impairments for the years ended December 31, 2024 and 2023, respectively, except as described above.

Leases

ASC 842, Leases, requires lessees to recognize right-of-use assets and lease liabilities on the balance sheet for all leases with a term of greater than 12 months regardless of classification. Operating lease right-of-use assets and liabilities are recognized at the commencement date based on the present value of lease payments over the lease term discounted using an appropriate incremental borrowing rate. The incremental borrowing rate is based on the estimated interest rate for borrowing over a term similar to that of the lease payments at commencement of the lease. The operating lease expense for the operating leases is recognized on a straight-line basis over the lease term. The Company has elected the practical expedient to not separate lease and non-lease components of contracts.

Research and Development Expense

Research and development costs are expensed as incurred in accordance with ASC 730, Research and Development ("ASC 730"). Research and development expenses include costs directly attributable to the conduct of research and development programs, including compensation costs, which includes salaries and benefits, stock-based compensation expense and the cost of services provided by outside contractors.

The Company capitalizes advance payments for goods or services that will be used or rendered for future research and development activities and recognizes expense as the related goods are delivered or services are performed. The Company also records expenses and accruals for estimated costs of research and development activities, including third party contract services for clinical research and contract manufacturing. The Company bases its estimates on the best information available at the time. Costs for certain research and development activities are recognized based on the pattern of performance of the individual arrangements, which may differ from the pattern of billings incurred, and are reflected in the consolidated financial statements as prepaid expenses or as accrued research and development expenses.

The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows to the Company's vendors. Billing terms and payments are reviewed by management to ensure estimates of outstanding obligations are appropriate as of period end. Tracking the progress of completion for clinical trial and contract manufacturing activities performed by third parties allows the Company to record the appropriate expense and accruals under the terms of the agreements. During the years ended December 31, 2024 and 2023, the Company incurred $63.6 million and $30.6 million, respectively, relating to research and development expenses. The Company recorded accrued liabilities of $9.4 million and $9.6 million for clinical trial and contract manufacturing expenses as of December 31, 2024 and 2023, respectively.

General and Administrative Expense

General and administrative expenses consist primarily of salaries and related benefits, including share-based compensation expense, related to the Company's executive, finance and other support functions. Other general and administrative expenses include professional fees for legal, auditing, tax, consulting services, investor relations, IT and office expenses, rent and insurance.

Stock-Based Compensation

The Company accounts for stock-based employee and nonemployee compensation awards in accordance with provisions of ASC 718, Compensation—Stock Compensation ("ASC 718"). ASC 718 requires the recognition of stock-based compensation expense, using a fair-value based method, for costs related to all stock-based compensation awards. We use the Black-Scholes option-pricing model to determine the fair value of options. The Black-Scholes option-pricing model requires the use of judgment to develop input assumptions, some of which are highly subjective, including: (i) the fair value of our common stock on the date of grant; (ii) the expected term of the award; (iii) the expected volatility; (iv) the risk-free interest rate; and (v) expected dividends. In applying these assumptions, we consider the following factors:

Fair Value of Common Stock: The grant date fair value of stock awards granted under its 2019 Stock Option and Grant Plan are determined using the fair market value of the Company's common stock on the date of grant, as set forth in the applicable plan document. Prior to the Initial Public Offering ("IPO") and due to the absence of an active market for the Company's common stock, the Company utilized methodologies in accordance with ASC 820, Fair Value Measurement. The estimated fair value of the common stock has been determined at each grant date based upon a variety of factors, including the illiquid nature of the common stock, recent transactions involving the Company's stock, the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event. Among other factors are the Company's financial position and historical financial performance, the status of clinical developments, the composition and ability of the current research and management team, an evaluation or benchmark of the Company's competition, and the current business climate in the marketplace. Significant changes to the key assumptions underlying the factors used could result in different fair values of common stock at each valuation date. For the most recent valuation of common stock prior to the IPO, the Company used valuation methods to estimate future potential outcomes for the Company, as well as values and probabilities associated with each respective potential outcome. The common stock per share value determined using this approach was ultimately based upon probability-weighted per share values resulting from the various future scenarios, which included an IPO scenario or continued operation as a private company scenario.

After the IPO, the Company utilized its publicly quoted stock price on grant date as the fair value of common stock.

Expected Term: The expected term represents the period that the options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The expected life is applied to the stock option grant group as a whole as we do not expect substantially different exercise or post-vesting termination behavior among our employee population.

Expected Volatility: We used an average historical stock price volatility of comparable public companies within the biotechnology and pharmaceutical industry that were deemed to be representative of future stock price trends due to absence of an active market for the Company's common stock.

Risk-Free Interest Rate: We based the risk-free interest rate over the expected term of the options based on the constant maturity rate of U.S. Treasury securities with similar maturities as of the date of the grant.

Expected Dividend: We have not paid and do not anticipate paying any dividends in the near future. Therefore, the expected dividend yield was zero.

For awards that vest based solely on achievement of a service condition, the Company recognizes expense on a straight-line basis over the period during which the award holder provides such services. The Company recognizes forfeitures as they occur and reverses any previously recognized compensation cost associated with forfeited awards. The Company accounts for share-based compensation for awards granted to nonemployees in a similar fashion to the way it accounts for share-based compensation awards to employees.

Income Taxes

The Company accounts for income taxes in accordance with ASC 740, Income Taxes ("ASC 740"), which requires that deferred tax assets and liabilities be recognized using enacted tax rates for the effect of temporary differences between the book and tax bases of recorded assets and liabilities. Under ASC 740, the asset and liability method is used in accounting for income taxes. Deferred tax assets and liabilities are determined based on the differences between financial reporting and the tax basis of assets and liabilities and are measured using the enacted tax rates and law that will be in effect when the differences are expected to reverse. ASC 740 also requires that deferred tax assets be reduced by a valuation allowance if it is more likely than not that some or all of the deferred tax assets will not be realized. The Company evaluates annually the realizability of the deferred tax assets by assessing the valuation allowance and by adjusting the amount of such allowance, if necessary. The factors used to assess the likelihood of realization include forecast of future taxable income and available tax planning strategies that could be implemented to realize the net deferred tax assets. In 2024 and 2023, the Company recorded a full valuation allowance for the deferred tax assets based on the historical loss and the uncertainty regarding the ability to project future taxable income. In future periods if the Company is able to generate income, the Company may reduce or eliminate the valuation allowance.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit would more likely than not be realized assuming examination by the taxing authority. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. At December 31, 2024 and 2023, the Company had no liability for income tax associated with uncertain tax positions. The Company would recognize any corresponding interest and penalties associated with its income tax positions in income tax expense. There was no income tax interest or penalties incurred during the years ended December 31, 2024 and 2023.

Comprehensive Loss

Comprehensive loss consists of net loss and changes in equity during a period arising from transactions and other equity and circumstances, of which we have none. Our comprehensive loss equals our net loss for all periods presented.

Net Loss Per Common Share

Net loss per common share is computed using the two-class method required due to the participating nature of the redeemable convertible preferred stock. Although the redeemable convertible preferred stock are participating securities, such securities do not participate in net losses and therefore do not impact the Company's net loss from continuing operations per share calculation as of December 31, 2024 and 2023.

Basic net loss per common share is determined by dividing the net loss applicable to common shareholders by the weighted average common shares outstanding during the period. Outstanding common stock options, unvested restricted stock awards and redeemable convertible preferred shares are excluded from the calculation of diluted net loss per share when their effect would be anti-dilutive.

The following potentially dilutive securities have been excluded from the computations of diluted weighted average shares outstanding as they would be anti-dilutive:

	As of December 31,	
	2024	2023
Options and restricted stock awards outstanding	7,748,972	4,897,868
Series Seed redeemable convertible preferred stock	—	8,848,387
Series B redeemable convertible preferred stock	—	11,423,688
Series C redeemable convertible preferred stock	—	12,938,801

Amounts in the table above reflect the common stock equivalents of the noted instruments.

Segments

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources.

Recent Accounting Pronouncements

New Accounting Pronouncements Issued and Adopted as of December 31, 2024

Accounting Standards Update (ASU) 2023-07, Segment Reporting (Topic 280): Improvements to Reportable Disclosures, which requires that an entity report segment information in accordance with Topic 280, Segment Reporting. The amendment in the ASU is intended to improve reportable segment disclosure requirements primarily through enhanced disclosures about significant segment expenses. The Company adopted this ASU in December 2024 on a retrospective basis to all periods presented and it did not have a material impact on the Company's consolidated financial statements.

Accounting Pronouncements Issued and Not Adopted as of December 31, 2024

Accounting Standards Update 2023-09—Income Taxes (Topic 740): Improvements to Income Tax Disclosures, or ASU 2023-09. ASU 2023-09 focuses on income tax disclosures around effective tax rates and cash income taxes paid. The standard largely follows the proposed ASU issued earlier in 2023 with several important modifications and clarifications. ASU 2023-09 is effective for public entities for annual periods beginning after December 15, 2024 and for all other business for annual periods beginning after December 15, 2025. Early adoption is permitted, and the Company is evaluating the impact of this guidance on the consolidated financial statements and related disclosures.

Accounting Standards Update 2024-03, Disaggregation of Income Statement Expenses (DISE). This new guidance requires all public entities to incorporate disclosures about specific types of expenses included in the expense captions presented on the face of the income statement as well as disclosures about selling expenses. The standard is effective prospectively for fiscal years beginning after December 15, 2026, and interim reporting periods beginning after December 15, 2027. Early adoption and retrospective application are permitted. We are currently evaluating the impact that ASU 2024-03 will have on our consolidated financial statements.

The Company reviewed additional recent accounting pronouncements and concluded they are either not applicable or that the Company does not expect adoption to have a material effect on the consolidated financial statements.

3. Fair Value Measurements

The following tables present information about the Company's financial assets that have been measured at fair value as of December 31, 2024 and 2023 (in thousands):

Description	Level 1	Level 2	Level 3	December 31, 2024
Assets:				
Money market funds included within Cash and cash equivalent	$ 485,168	$ —	$ —	$ 485,168
Total	$ 485,168	$ —	$ —	$ 485,168

Description	Level 1	Level 2	Level 3	December 31, 2023
Assets:				
Money market funds included within Cash and cash equivalent	$ 230,088	$ —	$ —	$ 230,088
Total	$ 230,088	$ —	$ —	$ 230,088

The Company estimated the fair value of the Series B Tranche Rights at the time of issuance and subsequently remeasured them at each reporting period and prior to settlement. The fair value of the Series B Tranche Rights was determined using a contingent forward model, which considered as inputs the estimated fair value of the Series B Preferred Stock as of each valuation date, the risk-free interest rate, probability of achievement and estimated time to tranche closing. The most significant assumptions in the contingent forward model impacting the fair value of the Series B Tranche Rights are the fair value of the Company's Series B Preferred Stock, probability of achievement, and time to the tranche closing as of each measurement date. The Company determined the fair value per share of the underlying Series B Preferred Stock by taking into consideration the most recent sales of its preferred units, results obtained from third-party valuations and additional factors the Company deems relevant.

The following table sets forth a summary of the changes in fair value of the Level 3 Series B Tranche Rights for the year ended December 31, 2023 (in thousands):

	Tranche Rights Liability
Balance as of December 31, 2022	$ —
Fair value recognized upon the issuance of preferred stock tranche rights	642
Change in fair value of preferred stock tranche rights	13,405
Settlement of the preferred stock tranche rights	(14,047)
Balance as of December 31, 2023	$ —

The following assumptions were used in the estimation of the fair value of the Series B Tranche Rights, on closing dates of Series B financing tranches (as defined in Note 9):

	November 3, 2023 Milestone Closing	September 8, 2023 Milestone Closing	March 2, 2023 Initial Closing
Preferred share price	$ 1.23	$ 1.23	$ 1.01
Expected term (in years)	—	—	0.5
Risk-free rate	—	—	5.2 %
Probability of achievement	100.0 %	100.0 %	95.0 %

4. Leases

On August 16, 2023, the Company entered into a 2.5 years lease for 4,617 square feet of office space in Boston, Massachusetts. In October, 2024, the Company amended its original lease agreement to lease an additional 4,744 square feet of office space (the "Amended Lease") in order to expand the Company's headquarters to 9,361 square feet of office space. The base rent under the Amended Lease is approximately $0.6 million per year. The Amended Lease did not extend the original lease end date under the original lease term. The lease requires a security deposit totaling $0.1 million, which the Company has met with cash on deposit.

The Company recorded rent expense of $0.4 million and $0.5 million for the years ended December 31, 2024 and 2023, respectively. Rent expense incurred prior to entering into the above lease agreement was based on a month-to-month agreement.

The minimum aggregate future lease commitments are as follows (in thousands):

	Amount
2025	$ 639
2026	132
Total minimum lease payments	771
Less: imputed interest	(33)
Present value of lease liability	$ 738
Other information:	
Weighted-average remaining lease term (in years)	1.17 years
Weighted-average discount rate	8.32 %

5. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following (in thousands):

	December 31, 2024	December 31, 2023
Accrued research and development expenses	$ 9,397	$ 6,035
Accrued bonus and payroll related expenses	3,083	1,742
Accrued professional fees	158	184
Accrued other	237	92
Total	$ 12,875	$ 8,053

6. Accrued Expenses and Other Current Liabilities—Related Party

Accrued expenses and other current liabilities—related party consisted of the following (in thousands):

	As of December 31,	
	2024	2023
Accrued research - related party (Note 12)	$ —	$ 3,561

7. Commitments and Contingencies

Legal Matters

From time to time, the Company is involved in lawsuits, arbitrations, claims, investigations and proceedings, consisting of intellectual property, commercial, employment and other matters, which arise in the ordinary course of business. The Company makes provisions for liabilities when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated.

The Company does not have contingency reserves established for any litigation liabilities as of December 31, 2024, or December 31, 2023.

On October 22, 2024, a complaint was filed in federal district court in the District of Massachusetts by Y-Trap, Inc. ("Y-Trap") naming as defendants us and Biocon LTD. ("Biocon"), captioned Y-Trap, Inc. v. Biocon LTD. and Bicara Therapeutics Inc., No. 24-cv-12678 (D. Mass.). The operative complaint alleges a claim against defendants for correction of inventorship of a number of patents, including patents alleged to be licensed to us relating to ficerafusp alfa. The complaint also alleges claims against defendants for unfair trade practices pursuant to Chapter 93A of the Massachusetts General Laws, unjust enrichment, and civil conspiracy. The complaint seeks, among other things, damages (including compensatory, enhanced, and punitive damages), an order correcting the inventorship of the patents at issue, costs and attorney's fees, and other equitable and injunctive relief. On January 31, 2025, Y-Trap filed its operative, amended complaint. On February 28, 2025, Biocon and Bicara moved to dismiss all Y-Trap's claims, which motions remain pending. We will continue to vigorously defend against this litigation.

8. Common Stock

The Company has 500,000,000 shares of Common Stock authorized for issuance with par value $0.0001 per share. As of December 31, 2024 and 2023, 54,444,180 and 711,895 shares were issued, net of share repurchased and cancellation, respectively and 54,440,013 shares and 640,386 shares, net were outstanding, respectively.

The Company has reserved 5,881,181 shares of Common Stock for issuance to officers, directors, employees and consultants pursuant to the 2019 Stock Option and Grant Plan. As of December 31, 2023, of the 640,386 shares outstanding, 87,404 shares relate to the exercises of stock options, 437,203 shares relate to vesting of RSAs issued under the 2019 Stock Option and Grant Plan, 115,757 shares of Common Stock are held by Biocon Limited and its affiliates ("Biocon") and were awarded by the Company in 2020 and the remaining balance was issued to an investor.

In September 2024, the Company completed an IPO. As part of the IPO, the Company received net proceeds of $332.4 million after deducting underwriting discounts, commissions and other offering expenses paid by the Company, totaling $29.8 million from the issuance of 20,125,000 shares.

Prior to the IPO, the Company issued shares of convertible redeemable preferred shares, which consisted of Seed Series, Series B and Series C of preferred stock. Each tranche was subject to automatic conversion to common stock per the terms of the initial agreement. Prior to the IPO, there were 81,790,144, 105,595,101 and 119,599,872 shares outstanding in Seed Series, Series B and Series C tranches of preferred stock, respectively. These shares were converted into 33,210,876 shares of common stock upon completion of the IPO.

9. Redeemable Convertible Preferred Stock

On December 23, 2020, the Company issued to Biocon 40,000,000 shares of Seed Series Preferred Stock ("Seed Series") with a par value of $0.0001 per share and purchase price of $1.00 per share, in exchange for net proceeds of $40.0 million. On April 26, 2022, the Company authorized for issuance an additional 50,940,144 shares of Seed Series Preferred Stock with par value of $0.0001 per share and price of $1.00 per share. On March 2, 2023, the Company reduced the total number of its authorized Seed Series Preferred Stock to 81,790,144.

In March 2022, as part of the first close of the Company's Seed Series extension financing, the Company entered into several SAFEs, pursuant to which the Company received approximately $5.4 million in exchange for its agreement to issue to certain investors shares of its preferred stock upon the occurrence of the Seed Series extension financing at $1.00 per share. On April 26, 2022, the Company issued 5,350,000 shares of Seed Series Preferred Stock with par value of $0.0001 per share and a $1.00 per share price to settle the $5.4 million in SAFEs, of which 4,000,000 shares of Seed Series Preferred Stock were issued to two investors controlled by a board member, who is also a relative of the Chief Executive Officer, and 350,000 shares of Seed Series Preferred Stock held by relatives of the Chief Executive Officer.

In July 2022, as part of the second close of the Company's Seed Series extension financing, the Company sold an additional 3,000,000 shares of Seed Series Preferred Stock to the two investors controlled by a board member, who is also a relative of the Chief Executive Officer, referred to above increasing their ownership to 7,000,000 shares of Seed Series Preferred Stock.

On March 2, 2023, the Company issued 37,073,162 shares of Series B Preferred Stock at a price of $1.025 per share (the "Initial Series B Closing") for proceeds of $37.8 million.

The Company was also obligated to sell up to 68,521,939 additional shares (the "Milestone Shares") of Series B Preferred Stock to the same purchasers at the same purchase price as the Initial Series B Closing the Series B Tranche Rights. The sale of Milestone Shares (the "Milestone Closings") was contingent upon the Company's achievement of certain milestones. In addition, if elected by a purchaser, the Company was obligated to sell Milestone Shares prior to achievement of the milestones (the "Voluntary Closings"). The Series B Tranche Rights are considered a freestanding instrument classified as a liability under ASC 480. The initial fair value of the liability was determined to be $0.6 million. Refer to Note 3 Fair Value Measurements to these consolidated financial statements for further details. Share issuances pursuant to exercise of the Series B Tranche Rights under such Milestone Closings occurred on September 8 and November 3, 2023 in the amounts of 39,024,386 and 29,497,553, respectively, for net proceeds of $69.9 million. Upon completion of the Milestone Closings, such tranche liabilities of $8.0 million and $6.0 million on September 8, 2023 and November 3, 2023, respectively, were settled to redeemable convertible preferred stock on the consolidated balance sheets. The Voluntary Closings were not exercised by the purchasers in 2023, and this right has expired.

On December 6, 2023, the Company issued 119,599,872 shares of Series C Preferred Stock at a price of $1.3796 per share in exchange for aggregate net proceeds of $164.6 million. The Company additionally executed various side letters where certain purchasers have the right to tender all owned shares back to the Company for an aggregate purchase price of $1.00 (the "Put Option"). The Put Option has no accounting implications as it is considered immaterial.

The Seed Series Preferred Stock, Series B Preferred Stock and Series C Preferred Stock are collectively referred to as the "Preferred Stock". As of December 31, 2023 and until they were converted to common shares on September 13, 2024, the Preferred Stock had the following rights, preferences, and privileges:

Conversion Rights

The holders of the Preferred Stock had rights to convert the shares of Preferred Stock into shares of Common Stock (the "Conversion Rights") at the applicable original issue price ("Conversion Price") with a conversion ratio ("Conversion Ratio") of 9.2435:1. All outstanding shares of the Preferred Stock were converted automatically into 33,210,876 shares of Common Stock immediately prior to the closing of the sale of shares of Common Stock to the public on September 13, 2024.

Liquidation Preference

Series B and Series C Preferred Stock - In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, the shareholders of outstanding Series B Preferred Stock and Series C Preferred Stock were entitled to be paid out of the assets of the Company available for distribution to its stockholders and in case of a Deemed Liquidation Event (defined as a merger or consolidation in which the Company was a constituent party, or the sale, lease, transfer, exclusive license or other disposition by the Company of all or substantially all the assets), the holders of the Series B and Series C Preferred Stock would have been entitled to be paid out of the consideration payable to stockholders or out of the available proceeds of the Company, before the Seed Series and common stockholders, an amount per share (the "Liquidation Amount") equal to the greater of: (a) the applicable original issue price, plus any dividends declared but unpaid, or (b) such amount per share amount as would have been payable on the conversion of all Series B Preferred Stock and Series C Preferred Stock (as applicable) into Common Stock immediately prior to such liquidation, dissolution, winding up or Deemed Liquidation Event. If the amount to be paid as Liquidation Amount was insufficient, then all Series B and Series C preferred stockholders would have shared the assets available for distribution in proportion of their shareholding.

Seed Series Preferred Stock - The Seed Series preferred stockholders had priority over the common stockholders, with a liquidation preference equal to the greater of (a) the Seed Series original issue price, plus any dividends declared but unpaid thereon, or (b) such amount per share as would have been payable on the conversion of all shares of Seed Series Preferred Stock into Common Stock immediately prior to such liquidation, dissolution, winding up or Deemed Liquidation Event. If upon any such liquidation, dissolution or winding up of the Company or Deemed Liquidation Event, and after the payment of all preferential amounts required to be paid to the holders of the Series B Preferred Stock and Series C Preferred Stock, the assets of the Company available for distribution to its stockholders was insufficient to pay the holders of shares of Seed Series Preferred Stock the full amount to which they would have been entitled, the holders of shares of Seed Series Preferred Stock would have shared ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares of Seed Series Preferred Stock held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

Redemption

The Preferred Stock was not redeemable except in the event of a Deemed Liquidation Event. As redemption by the holders was not within the control of the Company, all the outstanding convertible preferred stock was classified as temporary equity in the balance sheets.

Dividends

Series B and Series C Preferred Stock - The holders of then outstanding shares of Series B Preferred Stock and Series C Preferred Stock were entitled to receive, only when, as and if declared by the board of directors of the Company, dividends at the rate of eight percent (8%) of the applicable original issue price for each share of Series B Preferred Stock or Series C Preferred Stock, prior and in preference to any declaration or payment of any other dividend on shares of Seed Series Preferred Stock or Common Stock (other than dividends on shares of Common Stock payable in shares of Common Stock) during the same calendar year. The Company was not to declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Company unless the holders of the Series B Preferred Stock and Series C Preferred Stock then outstanding first received a dividend on each outstanding share of Series B Preferred Stock or Series C Preferred Stock at the same rate and same time on an as-converted basis. No dividends have been declared or paid as of December 31, 2024.

Seed Series Preferred Stock – The Company could not declare, pay or set aside any dividends on shares of Common Stock unless the holders of the Seed Series Preferred Stock then outstanding were to first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock at the same rate and same time on an as-converted basis. No dividends have been declared or paid as of December 31, 2024.

Voting Rights

The holders of the Preferred Stock had the same voting rights as the holders of the Common Stock, on an as-converted basis. As of December 31, 2024, the board of directors of the Company was comprised of ten members.

Protective Provisions

At any time when shares of Preferred Stock were outstanding, the Company would not do any of the following without the written consent or affirmative vote of at least 65% of the outstanding Preferred Stock holders, including at least one holder of Series C Preferred Stock who did not hold shares of any other class or series of Preferred Stock: 1) liquidate, dissolve or wind-up the business and affairs of the Company, or effect any merger or consolidation or any other Deemed Liquidation Event; 2) amend, alter or repeal any provision of the Certificate of Incorporation or Bylaws of the Company in a manner that adversely affects the powers, preferences or rights of the Preferred Stock; 3) create, issue, or reclassify any capital stock unless the same ranks junior to the Preferred Stock with respect to its rights, preferences and privileges; 4) cause or permit any of its subsidiaries to, without approval of the board of directors, sell, issue, sponsor, create or distribute any digital tokens, cryptocurrency or other blockchain-based assets; 5) purchase or redeem or pay or declare any dividend or make any distribution on, any

shares of capital stock of the Company other than as expressed with the Preferred Stock agreements; 6) create, issue, or authorize the issuance of any debt security or create any lien or security interest or incur other indebtedness for borrowed money; 7) create, or hold capital stock in, any subsidiary that is not wholly owned by the Company, or permit any subsidiary to create or issue any shares, or sell, transfer or otherwise dispose of any capital stock; 8) create, adopt, amend, terminate or repeal any equity (or equity-linked) compensation plan; or 9) increase or decrease the authorized number of directors constituting the board of directors.

Additional protective provisions for certain classes of shares included the following:

Series B Preferred Stock - For so long as at least 52,797,551 shares of Series B Preferred Stock were outstanding, the Company would not do any of the following without the written consent or affirmative of at least 60% of the Series B holders: a) waive or otherwise forego any adjustment in the Series B Conversion Price; b) create, or authorize the creation of, or issue or obligate itself to issue shares of, or reclassify, any capital stock unless the same ranks junior to the Series B Preferred Stock with respect to its rights, preferences and privileges; or c) amend, modify, change or waive the liquidation amount applicable to the Series B Preferred Stock.

Series C Preferred Stock - For so long as at least 71,759,924 shares of Series C Preferred Stock were outstanding, the Company would not do any of the following without the written consent or affirmative of at least 60% of the Series C holders: a) waive or otherwise forego any adjustment in the Series C Conversion Price; b) effect the conversion of the Series C Preferred Stock to Common Stock in a Qualified IPO; c) create, or authorize the creation of, or issue or obligate itself to issue shares of, or reclassify, any capital stock unless the same ranks junior to the Series C Preferred Stock with respect to its rights, preferences and privileges; or d) amend, modify, change or waive the liquidation amount applicable to the Series C Preferred Stock.

10. Stock-Based Compensation

Stock Option and Grant Plans

In 2019, the board of directors adopted, and the Company's shareholders approved, the 2019 Stock Option and Grant Plan (the "2019 Plan") under which the Company may grant equity-based incentive awards to the Company's employees, officers, directors, consultants and other key persons of the Company and its affiliates upon whose judgement, initiative, and efforts the Company largely depends for the successful conduct of its business.

The following are awards that are authorized to be issued:

- Stock Options including Incentive Stock Options ("ISO") or Non-Qualified Stock Options ("NQSO");
- Restricted Stock Awards ("RSA");
- Unrestricted Stock Awards ("URSA"); and
- Restricted Stock Units ("RSU")

Under the 2019 Plan, as amended, the Company is authorized to issue up to 8,856,245 shares of Common Stock. For the year ended December 31, 2024, the Company has issued RSAs, ISOs and NQSOs under the 2019 Plan. The terms of equity award agreements, including vesting requirements, were determined by the board of directors and are subject to the provisions of the 2019 Plan. Equity awards granted to employees and non-employees generally vest over a four-year period but may be granted with different vesting terms. Certain options provide for early vesting.

RSAs were issued under individual RSA agreements (the "Award Agreements"). The Award Agreements dictate vesting terms and once vested, the recipients' restricted stock may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of except as specifically provided in the respective Award Agreement.

Stock options granted to employees and non-employees expire no more than 10 years from the date of grant and are generally service based. A limited number of awards contain performance-based vesting criteria and for such awards

that are deemed probable of vesting, the Company records expense in the period in which such determination is made through any estimated remaining vested period.

In 2024, in connection with the Company's IPO, the board of directors adopted, and the Company's shareholders approved the 2024 Stock Option and Grant Plan (the "2024 Plan") under which the Company may grant equity-based incentive awards to the Company's employees, officers, directors, consultants and other key persons of the Company and its affiliates upon whose judgement, initiative, and efforts the Company largely depends for the successful conduct of its business.

Under the 2024 Plan, the Company is authorized to issue up to 2,453,616 shares of Common Stock, plus on January 1, and on each January 1 thereafter, the number of shares of stock reserved and available for issuance under the 2024 Plan shall automatically be cumulatively increased by 5% of the outstanding shares on the immediately preceding December 31 or such lesser number of shares as approved by the Company. Through December 31, 2024, the Company has issued 289,707 ISOs and NQSOs under the 2024 Plan. The terms of equity award agreements, including vesting requirements, were determined by the board of directors and are subject to the provisions of the 2024 Plan. Equity awards granted to employees and non-employees generally vest over a four-year period but may be granted with different vesting terms. Certain options provide for early vesting.

Stock options granted to employees and non-employees expire no more than 10 years from the date of grant and are generally service based. A limited number of awards contain performance-based vesting criteria and for such awards that are deemed probable of vesting, the Company records expense in the period in which such determination is made through any estimated remaining vested period.

Stock-Based Compensation Expense

The Company recognized total stock-based compensation expense for non-employees and employees in its statements of operations as follows (in thousands):

	Year Ended December 31,	
	2024	**2023**
Research and development	$ 2,084	$ 381
General and administrative	5,313	1,518
Total	$ 7,397	$ 1,899

Restricted Stock Awards

A summary of RSA award activity for non-employees and employees of the Company is as follows:

	Number of Shares	**Weighted-Average Grant Date Fair Value**
Balance as of December 31, 2023	47,199	$ 4.07
Granted	—	—
Vested	(47,199)	4.07
Repurchased/forfeited	—	—
Balance as of December 31, 2024	—	

There were no unvested RSAs and unrecognized compensation costs as of December 31, 2024.

Stock Options

Stock-based compensation, measured at the grant date based on the fair value of the award, is typically recognized ratably over the requisite service period, using the straight-line method of expense attribution. When utilizing the Black-Scholes option-pricing model to determine the grant date fair value of stock options granted to employees or non-employees, we used the following weighted average assumptions:

	Year Ended December 31,	
	2024	**2023**
Risk-free interest rate	3.8 %	3.2 %
Expected term (in years)	6.1	6.1
Expected annual dividend yield	— %	— %
Expected volatility	90.8 %	81.7 %
Fair Value of common stock	$5.45 - $24.43	$3.79 - $5.45

Using the Black-Scholes option pricing model, the weighted-average grant date fair value of stock options granted during the years ended December 31, 2024 and 2023 was $7.46 and $3.33 per share, respectively.
A summary of options award activity for non-employees and employees of the Company is as follows:

	Shares	**Weighted-Average Exercise Price**	**Weighted Average - Remaining Contractual Life (years)**	**Aggregate Intrinsic Value[(1)] (in thousands)**
Outstanding at December 31, 2023	4,850,669	$ 4.53		
Granted	3,767,807	9.76		
Exercised	(416,569)	3.83		
Canceled	(163,228)	4.04		
Outstanding as of December 31, 2024	8,038,679	$ 7.02	9.1	$ 84,052
Exercisable as of December 31, 2024	1,366,377	$ 5.14	8.5	$ 16,777
Exercisable and expected to vest as of December 31, 2024	8,038,679		9.1	

(1) The aggregate intrinsic values is calculated as the difference between the exercise price of the underlying options and the fair value of the Company's common stock on December 31, 2024 for the options that were in the money.

The Company had 6,672,302 unvested stock options outstanding as of December 31, 2024. As of December 31, 2024, total unrecognized compensation costs of $34.5 million related to unvested stock options are expected to be recognized as expense over a weighted average period of 3 years.

On September 5, 2024, the Company's board of directors adopted, and its stockholders approved, the 2024 Employee Stock Purchase Plan (the "ESPP"), which became effective September 5, 2024. The ESPP initially reserves and authorizes the issuance of up to 507,383 shares of our common stock to participating employees. The ESPP provides that the number of shares reserved and available for issuance will automatically increase on January 1, 2025 and each January 1 thereafter through January 1, 2034, by the least of (i) 1,014,766 shares of common stock, (ii) 1% of the sum of (A) the number of shares of our common stock issued and outstanding on the immediately preceding December 31, and (B) the number of shares of common stock issuable pursuant to the exercise of any outstanding, pre-funded warrants to acquire such common stock for a nominal exercise price on the immediately preceding December 31, or (iii) such number of shares of common stock as determined by the administrator of the ESPP. The number of shares reserved under the ESPP is subject to adjustment in the event of a stock split, stock dividend, or other change in our capitalization. There has been no activity on this plan to date and no stock-based compensation expense was recognized during the year ended December 31, 2024.

11. Income Taxes

The provision for income taxes is as follows (in thousands):

	As of December 31,	
	2024	**2023**
Current income taxes		
Federal	$ —	$ —
State	180	5
Total current income taxes	180	5
Deferred income taxes		
Federal	—	—
State	—	—
Total deferred income taxes	—	—
Total tax expense	$ 180	$ 5

	As of December 31,	
	2024	**2023**
Deferred tax assets		
Net operating losses	25,269	21,651
Tax credit carryforwards	4,570	1,510
Intangibles	1,528	1,633
Capitalized R&D (Section 174)	26,292	12,585
Stock compensation	1,335	307
Lease liability	195	174
Other	10	8
Total gross deferred tax asset	59,199	37,868
Deferred tax liabilities - ROU asset	(182)	(163)
Valuation allowance	(59,017)	(37,705)
Net deferred tax asset	—	—

The Company has had net operating losses ("NOLs") since inception. As of December 31, 2024, and December 31, 2023, the Company has federal net operating loss carryforwards of $91.5 million and $80.4 million, respectively, all of which can be carried forward indefinitely. The Company also has federal research and development tax credit carryforwards of $4.1 million and $1.3 million, respectively, available to reduce future tax liabilities, which expire at various dates beginning in 2040.

The Company has state net operating loss carryforwards of $96.0 million and $75.6 million as of December 31, 2024 and December 31, 2023, respectively, to reduce future state taxable income. These state NOLs carryforwards will start expiring in 2039. The Company also has state research and development tax credit carryforwards of $0.6 million and $0.3 million, respectively as of December 31, 2024 and 2023, available to reduce future state tax liabilities, which expire at various dates beginning in 2035.

Under the provisions of the Internal Revenue Code, certain substantial changes in the Company's ownership may result in a limitation on the amount of NOL carryforwards and research and development credit carryforwards that may be utilized annually to offset future taxable income and taxes payable. The Company has not determined whether a limitation has occurred.

As required by ASC 740, management has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which principally comprise NOL carryforwards, research and development credit carryforwards and an IPR&D license. Management has determined that it is more likely than not that the Company will not recognize the benefits of its federal and state deferred tax assets, and as a result, a valuation allowance of $59.0 million and $37.7 million has been established as of December 31, 2024, and 2023, respectively. The change in the valuation allowance was $21.3 million for the year ended December 31, 2024. The primary reason for the difference between the income tax expense recorded by the Company and the amount of income tax expense at statutory income tax rates was the change in the valuation allowance.

As of December 31, 2024 and 2023, the Company had no unrecognized tax benefits. The Company has not as yet conducted a study of its research and development credit carryforwards. This study 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 credits, 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 balance sheets or statements of operations if an adjustment were required.

Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as income tax expense in the accompanying statements of operations. As of December 31, 2024 and 2023, the Company has no accrued interest related to uncertain tax positions. In many cases, the Company's uncertain tax positions are related to years that remain subject to examination by relevant tax authorities. Since the Company is in a loss carryforward position, it is generally subject to examination by the U.S. federal, state, and local income tax authorities for all tax years in which a loss carryforward is available.

Net operating loss 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. 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. Subsequent ownership changes may further affect the limitation in future years. The Company has not conducted a Section 382 and 383 study for the year ended December 31, 2024.

	As of December 31,	
	2024	2023
Income tax computed at federal statutory tax rate	21.0 %	21.0 %
State taxes, net of federal benefit	6.7 %	4.1 %
Change in valuation allowance	(31.3)%	(19.1)%
General business credit carryovers	4.1 %	1.0 %
Permanent differences	(0.5)%	(5.6)%
Other	0.1 %	(1.4)%
Total	— %	— %

12. Significant Agreements - Related Parties

The Company entered into a master services agreement on December 15, 2020 (the "Master Services Agreement") with Biocon. Pursuant to the terms of the master service agreement, Biocon provided services related to research and development, clinical trials, regulatory interactions and manufacturing. The Company did not incur any expenses under the Master Services Agreement during the years ended December 31, 2024 and 2023. As of December 31, 2024 and 2023, the Company owed $0.6 million and $1.6 million, respectively, which were classified in accrued expenses-related party on the balance sheets.

On July 23, 2019, the Company entered into a manufacturing agreement with a wholly-owned subsidiary of Biocon, Biocon Biologics Limited ("BBL") formerly Biocon Biologics India Limited, which is valid for 5 years unless earlier terminated by one of the parties. Additionally, the Company entered into a material transfer agreement on August 17, 2023, a quality agreement on October 12, 2023, a service agreement on October 18, 2023 and a manufacturing agreement on December 15, 2023 (the "BBL Agreements"). Pursuant to the terms of the BBL Agreements, BBL manufactures and supplies specified quantities of products to Bicara to be utilized in research and development and manufacturing as per purchase orders executed from time to time between the two parties. For the years ended December 31, 2024 and 2023, the Company incurred $1.0 million and $1.2 million research and development expenses, respectively, under the BBL Agreements. As of both December 31, 2024 and 2023, the Company owed $0.0 million.

The Company additionally entered into a manufacturing agreement with a wholly-owned subsidiary of Biocon, Syngene International Limited ("Syngene"), on July 17, 2019, and subsequently amended, along with a master contract services agreement on July 24, 2020 (the "Syngene Agreements"). Pursuant to the terms of the Syngene Agreements, Syngene manufactures and supplies specified quantities of products to Bicara to be used in research and development as per purchase orders executed from time to time between the two parties and performs additional contract research services under the master contract services agreement. The manufacturing agreement is valid for 6 years unless earlier terminated by one of the parties, while the master contract services agreement carried a term of 2 years. On December 16, 2024, the Company entered into an additional master contract services agreement with Syngene, whereby Syngene agreed to provide the Company with dedicated research laboratories and personnel ("Dedicated Center Agreement"). The Dedicated Center Agreement has a term of 4 years, unless earlier terminated by one of the parties.

For the years ended December 31, 2024 and 2023 the Company incurred $7.2 million and $8.4 million of research and development expenses, respectively, under the Syngene Agreements. As of December 31, 2024, and 2023, the Company owed $0.6 million and $2.9 million, respectively, relating to these incurred costs, of which $0.6 million and $1.0 million, respectively, were classified in accounts payable-related party and $0.0 million and $1.9 million, respectively, were classified in accrued expenses-related party on the balance sheets.

On July 1, 2021, the Company entered into a master service agreement with a wholly-owned subsidiary of Biocon, Biofusion Therapeutics Limited ("Biofusion") (the "Biofusion Agreement"), which was terminated upon acquisition of Biofusion by Syngene on August 2, 2022. Pursuant to the terms of the Biofusion Agreement, Biofusion provided research and development services. As of December 31, 2022, the Company owed $7.7 million in connection with services provided by Biofusion, which were classified in accrued expenses-related party on the balance sheet, of which $4.1 million were incurred in 2022. The Company paid the full amount on March 21, 2023.

In September 2021, the Company entered into a full recourse promissory note (the "Promissory Note") with our Chief Financial Officer ("CFO"), pursuant to which the Company loaned $0.3 million, plus interest accruing at rate of 0.86% per annum (or if higher, the applicable federal rate as of the date of the Promissory Note), due by the earliest to occur of (i) December 31, 2025, (ii) the date of certain transfers of the collateral pledged under the Promissory Note, (iii) upon the day prior to the date a change in the Company's or the CFO's status would cause the loan to be deemed prohibited under applicable law, (iv) upon the date prior to the Company's filing of a registration statement for an initial public offering or a change of control, (v) upon acceleration of the Promissory Note in accordance with its terms or (vi) the date three months following the CFO's termination of employment with the Company. As part of the Promissory Note, the CFO pledged 66,676 shares of restricted Common Stock as collateral under the terms of a security agreement. There has been immaterial interest income from the Promissory Note. The CFO repaid the full amount in June 2024. As of December 31, 2023, the Company recorded $0.1 million within prepaid expenses and other assets, and $0.1 million within other assets on the balance sheet.

13. Significant Agreements

IQVIA

On October 15, 2019, the Company entered into a master clinical contract services agreement with IQVIA RDS Inc ("IQVIA"), which was amended in December 2023 to include global clinical trials. Pursuant to the terms of the agreement, as amended, IQVIA will provide the Company with certain global clinical-development related services and laboratory services under separately executed statements of work ("SOWs"). In June 2021, the Company entered into an SOW with IQVIA for lab and clinical development services, to be invoiced on a monthly basis based on work performed by IQVIA. Under this SOW, Bicara agreed to provide IQVIA with an initial upfront payment of $1.8 million, of which $1.0 million was a refundable deposit and $0.8 million for investigator grant payment in advance. In December 2022, Bicara entered into an authorized to proceed agreement ("ATP") with IQVIA. Under the ATP, Bicara agreed to provide IQVIA with an additional refundable deposit of $0.9 million, which was paid in March 2023. Both the initial deposit and the ATP deposit will be held on account and reconciled against final invoices. As of December 31, 2024 and 2023, the refundable deposit balance was $1.9 million. For the years ended December 31, 2024 and 2023 the Company incurred $15.1 million and $11.4 million in expenses, respectively, and paid $15.5 million and $6.8 million, respectively, to IQVIA. As of December 31, 2024 and 2023, the Company had $0.5 million and $1.6 million classified in accounts payable, respectively, and $6.0 million and $4.7 million classified in accrued expenses and other current liabilities on the balance sheets.

On December 18, 2024, the Company entered into a second SOW for lab and clinical development services with IQVIA, which was incorporated into the master clinical contract services agreement and part of the Company's FORTIFI-HN-01 Phase 2/3 clinical trial ("FORTIFI-HN01 Phase 2/3 trial" or "FORTIFI-HN01"). Services will be invoiced on a monthly basis based on work performed by IQVIA. Under this SOW, Bicara agreed to provide IQVIA with an initial upfront payment of $12.8 million, of which $7.3 million was for an investigator grant payment, $4.5 million was a deposit for services and $1.0 million was a deposit for pass through costs. The deposits will be held on account with an incremental return starting the month after 75% of the budgeted costs has been paid by the Company. IQVIA is eligible to receive potential additional payments and it is subject to potential penalties based on certain milestone targets. As of December 31, 2024, $5.5 million had been incurred related to the second SOW, which is part of the FORTIFI-HN01 Phase 2/3 trials.

Clinical Trial Collaboration And Supply Agreement with MSD

On May 19, 2022, we entered into a Clinical Trial Collaboration and Supply Agreement, or the MSD Agreement, with MSD International GmbH, or MSDIG, and MSD International Business GmbH, MSDIB, and collectively with MSDIG, MSD. Pursuant to the MSD Agreement, we provide ficerafusp alfa and MSD provides pembrolizumab to be used in combination in a clinical trial sponsored by us. The clinical trial is a First-in-Human, Phase 1/1b, Open-label, Multicenter Study intended to characterize the safety, tolerability and recommended dose of single agent ficerafusp alfa and combination ficerafusp alfa plus pembrolizumab. To facilitate such collaboration activities and information exchange and pursuant to the MSD Agreement, we and MSD created a joint development committee with an equal number of representatives from each party.

Pursuant to the MSD Agreement, all clinical data resulting from the portion of the clinical trial involving the combination of ficerafusp alfa and pembrolizumab is jointly owned by both us and MSD. We own all clinical data resulting from the part of the clinical trial involving ficerafusp alfa alone or in combination with other treatments that are not pembrolizumab, and MSD owns all clinical data resulting from the part of the clinical trial involving pembrolizumab alone or in combination with other treatments that are not ficerafusp alfa. There are no accounting considerations for this agreement.

14. Defined Contribution Plan

The Company currently maintains a tax-qualified 401(k) retirement savings plan for our employees. All eligible employees are able to participate in the plan beginning one month after their first day of employment. Under our defined contribution plan, employees may elect to defer a percentage of their compensation per year, subject to a maximum limit prescribed by tax law, and the Company match a portion of their eligible contributions. The Company provided matching discretionary contributions under the 401(k) plan of $0.2 million and $0.1 million, respectively, for the years ended December 31, 2024 December 31, 2023.

15. Segment Reporting

The Company has one reportable segment relating to research and development of its product. The segment does not currently generate revenues as it is currently conducting clinical trials and has not commercialized.

The Company's Chief Operating Decision Maker (the "CODM"), its Chief Executive Officer, manages the Company's operations on an integrated basis for the purposes of allocating resources. When evaluating the Company's financial performance, the CODM regularly reviews total expenses and expenses by function and the CODM makes decisions using this information on a global basis. The CODM monitors performance at the consolidated level such that the measure of segment loss is consolidated net loss and the measure of reportable segment assets is reported on the balance sheet as total assets.

The table below is a summary of the segment profit or loss, including significant segment expenses (in thousands):

	Year Ended December 31,	
	2024	2023
Expenses		
Clinical operations and development	$ 27,146	$ 13,495
Manufacturing and process development	23,411	11,835
Research and development personnel cost and other (including stock-based compensation)	10,330	3,900
Research	2,732	1,387
Total research and development	63,619	30,617
General and administrative personnel costs (including stock-based compensation)	12,545	5,820
Professional fees	3,696	2,061
Facility costs, IT, office expense and other	2,529	1,391
Total general and administrative expenses	18,770	9,272
Total operating expenses	82,389	39,889
Operating loss	(82,389)	(39,889)
Interest income	14,581	1,314
Change in fair value of Series B preferred stock tranche rights liability	—	(13,405)
Total other income (expense)	14,581	(12,091)
Net income before losses	(67,808)	(51,980)
Income tax expense	(187)	(5)
Segment and consolidated net loss	$ (67,995)	$ (51,985)

Included within General and administrative personnel costs are depreciation expense, which is disclosed on the Statement of Cash Flows.

Exhibit Number	Exhibit Description
3.1	Fifth Amended and Restated Certificate of Certificate of Incorporation of the Registrant ((incorporated by reference to Exhibit 3.1 to the Registrant's Form 8-K (File No. 001-42271) filed on September 16, 2024).
3.2	Third Amended and Restated Bylaws of the Registrant ((incorporated by reference to Exhibit 3.2 to the Registrant's Form 8-K (File No. 001-42271) filed on September 16, 2024).
4.1	Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-281722) filed on September 6, 2024).
4.2	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated December 6, 2023. (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1 (File No. 333-281722) filed on August 22, 2024).
4.3*	Description of Securities
10.1#	2019 Stock Option and Grant Plan, as amended, and form of award agreements thereunder. (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1/A (File No. 333-281722) filed on August 22, 2024).
10.2#	2024 Stock Option and Incentive Plan and form of award agreements thereunder (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1/A (File No. 333-281722) filed on September 6, 2024).
10.3#	2024 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1/A (File No. 333-281722) filed on September 6, 2024).
10.4#	Form of Indemnification Agreement between the Registrant and each of its directors and executive officers (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1/A (File No. 333-281722) filed on September 6, 2024).
10.5#	Senior Executive Cash Incentive Bonus Plan (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1 (File No. 333-281722) filed on August 22, 2024).
10.6#	Form of Executive Employment Agreement (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1 (File No. 333-281722) filed on August 22, 2024).
10.7#	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1 (File No. 333-281722) filed on September 6, 2024).
10.8	First Amendment to Office Lease Agreement Office Lease Agreement by and between Columbia Property Trust, Inc. and the Registrant, dated as of October 1, 2024 (incorporated by reference to Exhibit 10.7 of the Registrant's Quarterly Report on Form 10-Q (File No. 001-42271) filed on November 12, 2024).
10.9†	Contract Transfer and License Agreement, by and between the Registrant and Biocon Limited, dated October 1, 2019 (incorporated by reference to Exhibit 10.9 of the Registrant's Registration Statement on Form S-1 (File No. 333-281722) filed on August 22, 2024).
10.10†	Clinical Trial Collaboration and Supply Agreement, by and between the Registrant and MSD International GmbH and MSD International Business GmbH, dated May 19, 2022 (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1 (File No. 333-281722) filed on August 22, 2024).
10.11	Office Lease Agreement by and between Columbia Property Trust, Inc. and the Registrant, dated as of August 16, 2023 (incorporated by reference to Exhibit 10.11 of the Registrant's S-1 (File No. 281722) filed on August 22, 2024).
19.1*	Insider Trading Policy.
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 of the Registrant's Registration Statement on Form S-1 (File No. 333-281722) filed on August 22, 2024).
23.1*	Consent of KPMG LLP, independent registered public accounting firm (filed herewith)

31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
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#	Compensation Clawback Policy (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1 (File No. 333-281722) filed on August 22, 2024).
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
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 Calculation Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)

* Filed herewith

** The certification furnished in Exhibit 32.1 hereto is deemed to accompany this Annual Report on Form 10-K and will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended. Such certification will not be deemed to be incorporated by reference into any filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that the Registrant specifically incorporates it by reference.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10) of Regulation S-K.

\# Indicates a management contract or any compensatory plan, contract or arrangement

SIGNATURES

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

Bicara Therapeutics Inc.

/s/ Claire Mazumdar

Claire Mazumdar

Chief Executive Officer (Principal Executive Officer)

Dated: March 27, 2025

POWER OF ATTORNEY AND SIGNATURES

Each person whose individual signature appears below hereby authorizes and appoints Claire Mazumdar Ph.D., M.B.A., Ryan Cohlhepp, Pharm.D. and Ivan Hyep, and each of them, with full power of substitution and resubstitution and full power to act without the other, as his or her true and lawful attorney-in-fact and agent to act in his or her name, place and stead and to execute in the name and on behalf of each person, individually and in each capacity stated below, and to file any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing, ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue thereof.

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 and in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Claire Mazumdar Claire Mazumdar, Ph.D.	Chief Executive Officer and Director (Principal Executive Officer)	March 27, 2025
/s/ Ivan Hyep Ivan Hyep	Chief Financial Officer (Principal Financial Officer & Principal Accounting Officer)	March 27, 2025
/s/ Ryan Cohlhepp Ryan Cohlhepp	President and Chief Operations Officer, and Director	March 27, 2025
/s/ Michael Powell Michael Powell, Ph.D.	Director, Chairperson	March 27, 2025
/s/ Christopher Bowden Christopher Bowden, MD	Director	March 27, 2025
/s/ Kate Haviland Kate Haviland	Director	March 27, 2025
/s/ Nils Lonberg Nils Lonberg, Ph.D.	Director	March 27, 2025
/s/ Kiran Mazumdar-Shaw Kiran Mazumdar-Shaw	Director	March 27, 2025
/s/ Carolyn Ng Carolyn Ng, Ph.D.	Director	March 27, 2025
/s/ Scott Robertson Scott Robertson	Director	March 27, 2025
/s/ Jake Simson Jake Simson, Ph.D.	Director	March 27, 2025

EXECUTIVE OFFICERS

Claire Mazumdar, Ph.D., M.B.A.
Chief Executive Officer

Ryan Cohlhepp, Pharm.D.
President and Chief Operating Officer

Ivan Hyep, M.B.A
Chief Financial Officer

David Raben, M.D.
Chief Medical Officer

Lara Meisner, J.D.
Chief Legal Officer

BOARD OF DIRECTORS

Claire Mazumdar, Ph.D., M.B.A.
Chief Executive Officer, Bicara Therapeutics Inc.

Ryan Cohlhepp, Pharm.D.
President and Chief Operating Officer, Bicara Therapeutics Inc.

Kiran Mazumdar-Shaw
Executive Chairperson, Biocon Limited

Jake Simson, Ph.D.
Partner, RA Capital Management, L.P.

Scott Robertson, M.B.A.
Chief Financial Officer and Chief Business Officer, Star Therapeutics LLC.

Nils Lonberg, Ph.D.
Executive in Residence, Canaan Partners.

Christopher Bowden, M.D.
Chief Medical Officer, Remix Therapeutics, Inc

Carolyn Ng, Ph.D.
Partner and Managing Director, TPG Life Sciences Innovations.

Kate Haviland, M.B.A.
President and Chief Executive Officer, Blueprint Medicines Corporation.

Michael Powell, Ph.D.
Executive Partner and Venture Advisor, Omega Funds.

CORPORATE INFORMATION

Corporate Headquarters
116 Huntington Avenue, Suite 703
Boston, MA 02116

Transfer Agent
Computershare Trust Company, N.A.
150 Royall Street
Canton, MA 02021

Form 10-K
The Company's Annual Report on Form 10-K for the year ended December 31, 2024, as filed with the SEC on March 27, 2025, except for exhibits, is printed as part of this 2024 Annual Report. Additional copies are available without charge upon written request.

Please address all requests to: Bicara Therapeutics Inc.
Attention: Corporate Secretary,
116 Huntington Avenue, Suite 703
Boston, MA 02116

Independent Registered Public Accounting Firm
KPMG LLP
Boston, MA

Investor Relations
IR@bicara.com

Visit us on the web: https://www.bicara.com