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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 24, 2024

TOURMALINE BIO, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-40384**	**83-2377352**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

27 West 24th Street, Suite 702	
New York, NY	**10010**
(Address of principal executive offices)	**(Zip Code)**

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

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

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

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

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. ☐

Item 2.02 Results of Operations and Financial Condition.

On January 24, 2024, Tourmaline Bio, Inc. (the "Company") announced the commencement of an underwritten public offering of its common stock ("the Offering"). The Company will file with the Securities and Exchange Commission a preliminary prospectus supplement (the "Preliminary Prospectus Supplement") to its effective shelf registration statement on Form S-3 (File No. 333-266875) pursuant to Rule 424(b)(5) under the Securities Act of 1933, as amended (the "Securities Act"), relating to the Offering. The Company will include the following disclosure in the Preliminary Prospectus Supplement:

"We have not finalized our financial statements as of and for the year ended December 31, 2023. Based on our current estimates, we expect to report that we had approximately $203.0 million in total unrestricted cash and investments as of December 31, 2023."

Our actual financial statements as of and for the year ended December 31, 2023 are not yet available. The actual amounts that we report will be subject to our financial closing procedures and any final adjustments that may be made prior to the time our financial results for the year ended December 31, 2023 are finalized and filed with the SEC. Our independent registered public accounting firm has not audited, reviewed, compiled, or applied agreed-upon procedures with respect to the preliminary financial data. This estimate should not be viewed as a substitute for financial statements prepared in accordance with accounting principles generally accepted in the United States and it is not necessarily indicative of the results to be achieved in any future period.

The information in this Item 2.02 shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

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

The Company has attached hereto as Exhibit 99.1, 99.2 and 99.3 and incorporated by reference in this Item 8.01 (i) an updated description of the Company's business, (ii) management's discussion and analysis of financial condition and results of operations of Legacy Tourmaline as of September 30, 2023 and for the nine months ended September 30, 2023 and 2022 and as of December 31, 2022 and for the year ended December 31, 2022 and the period from September 17, 2021 (Inception) to December 31, 2021 and (iii) unaudited pro forma condensed combined financial information of Talaris Therapeutics, Inc. and Tourmaline Bio, Inc. as of September 30, 2023, for the nine months ended September 30, 2023 and for the year ended December 31, 2022 are filed herewith as Exhibit 99.3

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Description of the Business of Tourmaline Bio, Inc.
99.2	Management's Discussion and Analysis of Financial Condition and Results of Operations of Tourmaline Bio, Inc. as of September 30, 2023 and for the nine months ended September 30, 2023 and 2022 and as of December 31, 2022 and for the year ended December 31, 2022 and the period from September 17, 2021 (Inception) to December 31, 2021.
99.3	Unaudited pro forma condensed combined financial information of Talaris Therapeutics, Inc. and Tourmaline Bio, Inc. as of September 30, 2023, for the nine months ended September 30, 2023 and for the year ended December 31, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

TOURMALINE BIO, INC.

Date: January 24, 2024

By: /s/ Ryan Robinson
Name: Ryan Robinson
Title: Interim Chief Financial Officer, Vice President, Finance and Controller

TOURMALINE'S BUSINESS

Overview

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

Our initial product candidate is TOUR006, a fully human monoclonal antibody that selectively binds to interleukin-6 ("IL-6"), a key proinflammatory cytokine involved in the pathogenesis of many autoimmune and inflammatory disorders. The anti-IL-6 and anti-IL-6 receptor ("IL-6R") antibody class ("IL-6 class") has over two decades of clinical and commercial experience treating over a million patients with a variety of autoimmune and inflammatory diseases. To date, four anti-IL-6 or anti-IL-6R antibodies have been approved in the United States. These four anti-IL-6 or anti-IL-6R antibodies together generated more than $3.5 billion in global sales in 2022.

TOUR006 is a long-acting anti-IL-6 antibody which we believe has best-in-class properties including a high binding affinity to IL-6, long half-life, and low observed immunogenicity. These characteristics may allow TOUR006 to achieve substantial IL-6 pathway suppression with relatively low amounts of drug exposure, potentially enabling delivery in a convenient, low volume, infrequently administered, subcutaneous injection.

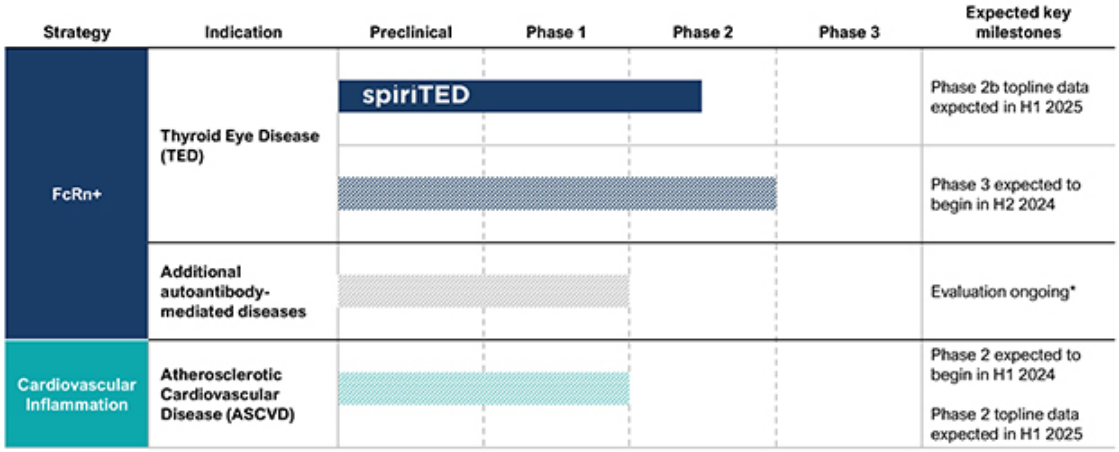
We are pursuing two strategic paths for TOUR006, the first of which we refer to as "FcRn+". Neonatal Fc receptor ("FcRn") inhibitors have emerged as a novel therapeutic class to treat autoantibody-driven diseases. However, FcRn inhibitors have significant limitations including suboptimal efficacy, lack of durable efficacy, high burden dosing profile, and an unknown long-term safety profile. We believe TOUR006 has the potential to be a superior therapy for a wide range of autoantibody-driven diseases, compared to FcRn inhibitors. We have identified thyroid eye disease ("TED") as our beachhead indication for our FcRn+ strategy. TED is an autoimmune disease characterized by autoantibody-mediated activation of the tissues surrounding the eye, causing inflammation and disfigurement which can be sight-threatening in severe cases. We have identified a substantial body of published clinical observations characterizing the beneficial off-label use of currently marketed IL-6 pathway inhibitors, namely Actemra® (tocilizumab), an anti-IL-6R monoclonal antibody, in reducing inflammation, eye-bulging, and levels of autoantibodies in patients with TED. However, no formal, industry-sponsored development effort studying the IL-6 class for the treatment of TED has been completed to date.

We are currently evaluating TOUR006 in a pivotal Phase 2b trial in first-line TED, which we refer to as the spiriTED trial. We initiated the spiriTED trial in September 2023 and expect to report topline data in the first half of 2025. Further, we expect to commence a pivotal Phase 3 trial of TOUR006 in first-line TED in 2024, with topline data expected in 2026. This second pivotal trial will replace the previously-planned open-label basket study in additional TED patient cohorts.

Our second strategic path is cardiovascular inflammation. We believe TOUR006 has the potential to transform the care of high-risk patients by targeting key inflammatory pathways driving cardiovascular disease. Atherosclerotic cardiovascular disease ("ASCVD") is a leading cause of death globally. Preventing major adverse cardiovascular events ("MACE"), such as death, nonfatal myocardial infarction or nonfatal stroke, has the potential to significantly reduce global cardiovascular disease burden. IL-6 has been identified as a promising drug target for addressing the risk of MACE in ASCVD and multiple external Phase 3 cardiovascular outcome trials investigating IL-6 blockade are ongoing. We believe that TOUR006 potentially offers a meaningfully enhanced product profile to these competitor programs with a potential for subcutaneous dosing once every three months. As previously announced in January 2024, we have reached alignment with the U.S. Food and Drug Administration ("FDA") on the ASCVD clinical development program, including a Phase 2 trial evaluating the reduction of C-reactive protein ("CRP"), a validated biomarker for inflammation, with quarterly dosing of TOUR006 in patients with elevated cardiovascular risk. This trial is targeted to commence in the first half of 2024, and we expect to report topline data in the first half of 2025. Pending successful initiation and completion, positive results from the Phase 2 trial are expected to position us to be ready in 2025 to commence a pivotal Phase 3 trial for TOUR006 in cardiovascular disease.

Our Pipeline

The following figure summarizes our current development programs:



Note: Hatched bars represent trials that have not yet commenced. The timing of regulatory submissions and clinical trial milestones are subject to change and additional discussion with the FDA

* Clinical development plan for additional indications subject to change upon indication selection and discussion with the FDA

As can be seen in the chart above, we plan to identify additional indication opportunities for TOUR006. In addition, we continue to evaluate new in-licensing and acquisition opportunities for assets that we believe have standard-of-care changing potential for patients with immune, inflammatory and other diseases.

Our Strategy

We seek to identify and develop transformative medicines that have the potential to establish new standards-of-care in areas of high unmet medical need. We plan to apply a human data-focused approach to indication selection, identifying diseases where IL-6 pathway inhibitors have been used successfully in practice despite limited formal industry development and where we believe TOUR006 can potentially bring significant improvements over existing standards of care. We also plan to leverage insights from clinical trials of competitor IL-6 pathway inhibitor programs with a goal of rapidly bringing TOUR006 into indications that have already been externally de-risked. We believe this focus on leveraging existing human data could allow us identify indications with high potential for clinical and commercial success and can maximize the value of TOUR006.

The key elements of our strategy include:

- **In our FcRn+ strategy, advance TOUR006 through clinical development in patients with TED as our beachhead indication in autoantibody-driven diseases**. Our initial product candidate, TOUR006, has the potential for a differentiated product profile for the treatment of TED based on the literature supporting IL-6 pathway inhibition in active TED, a favorable long-term safety profile of the IL-6 class observed to date, and the potentially low administrative burden offered by infrequent, subcutaneous dosing. In September 2023, we initiated our pivotal Phase 2b spiriTED trial to assess the safety and efficacy of TOUR006 for the treatment of TED, and we expect to report topline results from this trial in the first half of 2025. Further, we expect to commence a pivotal Phase 3 trial for TOUR006 in TED in 2024. Topline data from this planned Phase 3 trial are expected in 2026.
- **In our cardiovascular inflammation strategy, advance TOUR006 through clinical development in patients with ASCVD**. We believe that TOUR006 has the potential to provide a differentiated product profile for the treatment of inflammatory risk in ASCVD with the potential for subcutaneous dosing once every three months. We plan to initiate a Phase 2 clinical trial to assess the safety, pharmacokinetics (“PK”), and pharmacodynamics (“PD”) of TOUR006 for the treatment of ASCVD in the first half of 2024, with topline data expected in the first half of 2025.

- **Maximize the potential of TOUR006 in additional indications where IL-6 inhibition has shown compelling evidence of clinical benefit**. We believe that TOUR006 has broad application beyond TED and ASCVD. We aim to identify and develop in additional indications where IL-6 inhibition has shown evidence of clinical benefit, but has not entered industry-led clinical development, as well as indications where we could bring TOUR006 forward, capitalizing on external de-risking events.
- **Explore business development opportunities to selectively expand our product portfolio**. We continue to evaluate new in-licensing and acquisition opportunities for assets that we believe have standard-of-care changing potential for patients with immune, inflammatory and other diseases. We also plan to strategically evaluate potential collaborations with external parties to maximize the potential of TOUR006.

Scientific Background

Overview of Autoimmune Disorders

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

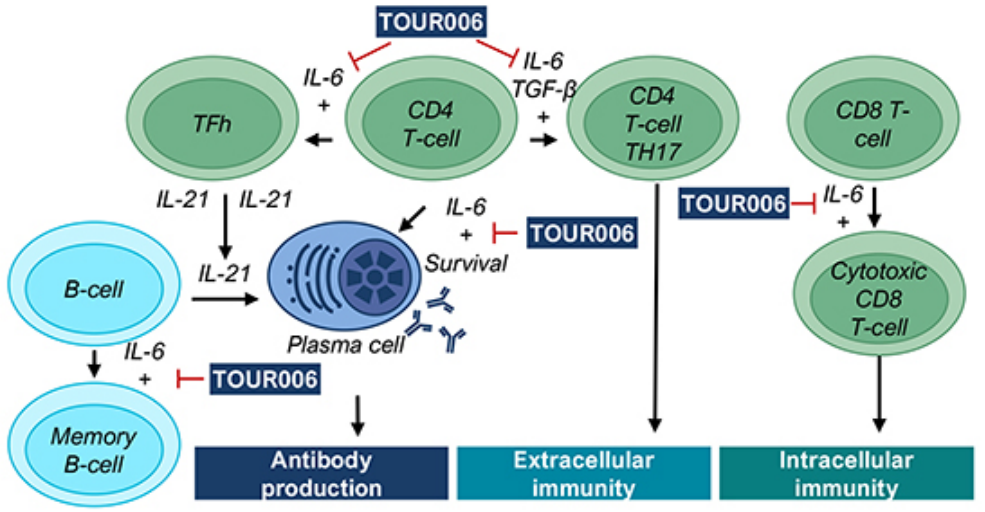
In patients with autoimmune diseases, the immune system inappropriately recognizes and attacks normal healthy tissues, resulting in inflammation, organ damage, debilitating symptoms and, in severe cases, death. To date over 80 autoimmune diseases have been documented, each with a wide range of clinical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

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

IL-6: Mechanism of Action and Overview

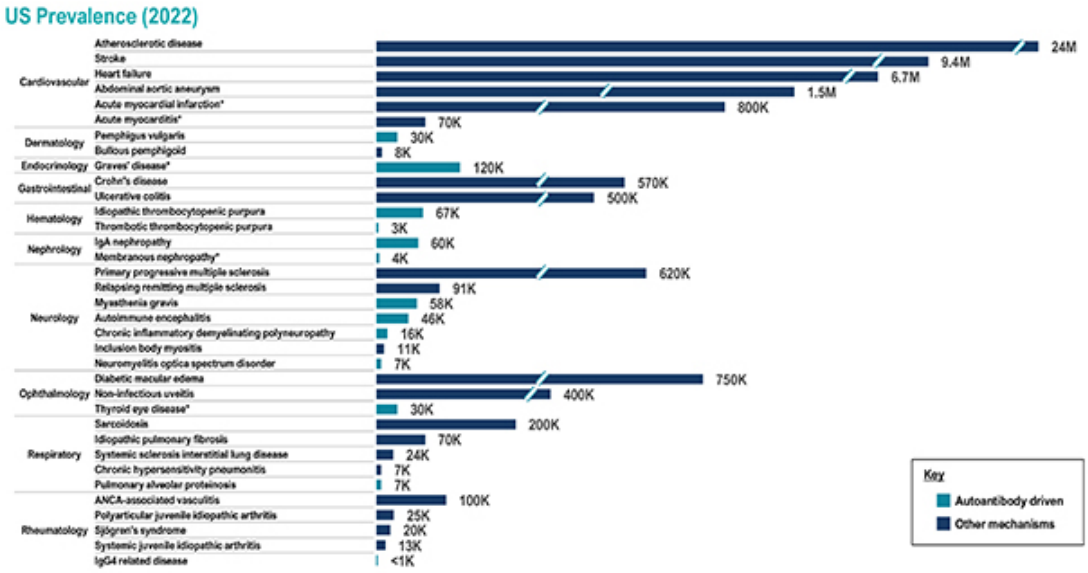
IL-6 is a pleiotropic cytokine which plays a key role in driving inflammation and cellular and humoral immune responses. In typical immunity, IL-6 is produced by various immune cells, including monocytes, macrophages, T cells, and B cells as well as fibroblasts and other non-immune cells, in response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

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



IL-6 mediates many autoimmune pathways including production of autoantibodies and proliferation of autoreactive T-cells; TOUR006 inhibits IL-6 from driving these pathways

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



* Incidence Number

Currently, there are four FDA approved therapies targeting the IL-6/IL-6R pathway: ACTEMRA® (tocilizumab), KEVZARA® (sarilumab), ENSPRYNG® (satralizumab-mwge), and SYLVANT® (siltuximab). Collectively, these therapies have been approved for nine indications: rheumatoid arthritis ("RA"), giant cell arteritis, juvenile idiopathic arthritis, polymyalgia rheumatica, cytokine release syndrome, multicentric Castleman's disease, neuromyelitis optica spectrum disorder ("NMOSD"), systemic sclerosis associated interstitial lung disease, and COVID-19. Collectively, these four anti-IL-6 or anti-IL-6R antibodies generated more than $3.5 billion in global sales in 2022.

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

Our Product Candidate: TOUR006

We licensed TOUR006, previously known as PF-04236921, from Pfizer Inc. ("Pfizer") in May 2022. TOUR006 was originally developed from a hybridoma cell line using the Medarex UltiMAb transgenic mouse platform. The UltiMAb platform produces fully human monoclonal antibodies. The IgG1 isotype of the original clone was switched by Pfizer to IgG2 to reduce Fc receptor binding, thereby creating TOUR006.

To date, TOUR006 has been tested by Pfizer in 448 subjects across six clinical trials, including over 400 autoimmune patients with RA, systemic lupus erythematosus ("SLE"), or Crohn's disease ("CD"). Across these studies, TOUR006 was generally well-tolerated, consistent with other therapies in the IL-6 class, and had low rates of anti- drug antibodies ("ADAs") in the 448 subjects tested. We seek to leverage this large existing clinical dataset for TOUR006, along with the extensive clinical experience with the IL-6 class, in our development programs. We believe this existing clinical dataset for TOUR006 serves as a basis for which the FDA will allow us to move directly into additional Phase 2 and/or pivotal trials in future selected development indications. To date, the FDA has cleared our Investigational New Drug application ("IND") to support the initiation of the ongoing pivotal Phase 2b spiriTED study, and we have reached alignment with the FDA on a Phase 2 study in patients with elevated cardiovascular risk.

Potential Benefits of TOUR006

We believe TOUR006 presents a potentially best-in-class product profile for a wide range of indications where IL-6 biology is implicated. The potential benefits of TOUR006 may include:

- **Deep and sustained suppression of the IL-6 pathway**. In preclinical studies, TOUR006 has exhibited high affinity for IL-6 (kD in the picomolar range) and, in clinical studies, has exhibited a naturally occurring terminal half-life of 47 to 58 days. TOUR006 has demonstrated meaningful suppression of IL-6 signaling at doses as low as 10mg as measured by CRP. CRP is an acute phase protein and a key downstream marker of IL-6 pathway signaling.
- **Low-volume, subcutaneous delivery**. TOUR006 is expected to be subcutaneously administered with a 1mL or lower volume, making it a potentially more convenient therapy for patients and physicians compared to agents that require intravenous infusion or high-volume subcutaneous injection or infusion.

- **Infrequent dosing**. We expect TOUR006 will be dosed once every eight weeks or possibly every three months, depending on the indication, which is supported by prior studies conducted by Pfizer as well as our pharmacokinetic-pharmacodynamic modeling.
- **Low immunogenicity**. To date, low potential for immunogenicity has been observed for TOUR006, with only two patients demonstrating evidence of treatment-emergent ADAs out of the 448 subjects dosed to date. Statistical analysis was not conducted on this observation.

TOUR006's potential profile: subcutaneous, low volume, low frequency injections

	TOUR006	Actemra (tocilizumab)		Kevzara (sarilumab)	Enspryng (satralizumab)	Sylvant (siltuximab)
Company	Tourmaline	Roche		Regeneron	Roche	EUSA
Antibody Type	Human	Humanized		Human	Humanized	Chimeric
Target	IL-6	IL-6 receptor		IL-6 receptor	IL-6 receptor	IL-6
Stage of development	In Phase 2b	Approved		Approved	Approved	Approved
Indications being pursued	TED, ASCVD	RA, GCA, PJIA, SJIA, CRS, SSc-ILD, COVID19		RA, PMR	NMOSD, AE, MG, MOGAD, TED	MCD
Black box warning	Drug not approved	Yes		Yes	No	No
Terminal half-life	47-58 days	21.5 days[1]		Up to 10 days[1]	30 days[1]	20.6 days[1]
Anti-drug antibodies	<1% of patients	1-2% of patients[1]		14-19% of patients[1]	38-73% of patients (~20% increase in drug clearance) [1]	0-2% of patients[1]
Route of admin	Subcutaneous (SC)	IV	SC	SC	SC	IV
Standard dose	≤50mg	8-12mg/kg	162mg	200mg	120mg	11mg/kg
Dosing regimen	Q8W / Q12W	Q4W	QW / Q2W	Q2W	Q4W	Q3W

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

Our FcRn+ Strategy: IL-6 Inhibition for the Treatment of Autoantibody-Driven Disorders

Autoantibody driven disorders are a type of autoimmune disease in which antibodies erroneously recognize and bind to normal cell-surface or circulating antigens. The binding of autoantibodies to their respective targets can result in inflammation, receptor activation, and further immune system attack. In some diseases, autoantibodies directed against cell surface receptors may have agonistic or antagonistic activity and aberrantly modulate signaling pathways. Approximately 2.5% of the world's population live with a disease where autoantibodies are believed to play a role. These disorders impact multiple organs and systems and include TED, Graves' disease, NMOSD, MG, and chronic inflammatory demyelinating polyneuropathy, among many others.

Therapeutic strategies that reduce autoantibody levels have been observed to produce clinical benefit in multiple indications. For example, FcRn inhibition has emerged as a novel therapeutic modality to treat patients with autoantibody driven disorders. Treatment with FcRn inhibitors results in non-disease specific depletion of circulating antibodies and has been observed to reduce autoantibody levels in patients with autoantibody driven disorders by approximately 60-70%.

Despite these advances, we believe that FcRn inhibitors may have the following limitations:

- **Limited efficacy potential due to narrow mechanism of action**. The efficacy of FcRn inhibitors is limited to their ability to reduce antibody levels, without direct effects on non-antibody mediated components of disease or ongoing active inflammation.
- **Limited durability of effect**. FcRn inhibitors do not inhibit upstream disease processes such as antibody production. As a result, their observed clinical benefit may not persist after stopping treatment. In clinical trials with FcRn inhibitors autoantibody levels have generally been observed to increase back to baseline shortly after stopping treatment, leading to symptom worsening.
- **High drug administration burden**. Because FcRn is abundantly expressed, FcRn inhibition requires high doses and frequent administration to achieve the desired target dose maintenance. VYVGART® (efgartigimod), the first FDA-approved FcRn inhibitor, is dosed in cycles of four weekly intravenous infusions. Long-term follow-up data from efgartigimod's ADAPT study in MG patients indicates patients received a median of 5 cycles in a year, with 45% of patients receiving 6 or more cycles. Recently approved subcutaneous FcRn inhibitors continue to require high administration burden. VYVGART HYTRULO® (efgartigimod and hyaluronidase) requires four weekly subcutaneous infusions of 1008mg of drug in 5.6 mL of drug volume. RYSTIGGO® (rozanolixizumab-noli) requires six weekly subcutaneous infusions of up to 840mg of drug in 6 mL.
- **Uncertain long-term safety profile**. The first FcRn inhibitor was approved in 2021 and there is therefore limited long-term experience with this drug class. FcRn inhibition results in non-specific lowering of IgG antibody levels by 60-80%, which may increase susceptibility to infection. Treatment with certain FcRn inhibitors has resulted in significant decreases in albumin, a key blood protein, which have been associated with increases in cholesterol levels, which may further impact their long-term safety profile.

Given the importance of IL-6 signaling for antibody production and plasma cell biology, we believe that IL-6 inhibition has the potential to treat autoantibody-driven disorders upstream of FcRn inhibition, although no head-to-head trial has been conducted to date. Particularly, in the four autoantibody indications where there is currently clinical evidence for both FcRn and IL-6 inhibitors— TED, MG, RA, and NMOSD— IL-6 inhibition has shown potential to outperform FcRn inhibition. Experimental models have shown that adding IL-6 to cell cultures derived from affected patients can stimulate autoantibody production. Furthermore, off-label use of IL-6 inhibitors has been observed to reduce autoantibody levels and offer clinical benefits in autoantibody-driven disorders including TED, MG, anti-neutrophil cytoplasmic antibody-associated vasculitis, and NMOSD.

In 2020, satralizumab, an anti-IL-6R monoclonal antibody, was approved for the treatment of NMOSD, a disease characterized by autoantibodies formed against aquaporin-4 ("AQP4"). This was the first approval and regulatory validation for an IL-6 targeted approach for the treatment of autoantibody-driven diseases. Subsequently, F. Hoffmann-La Roche AG ("Roche"), the developer of satralizumab, has initiated Phase 3 studies in additional autoantibody driven disorders including MG, autoimmune encephalitis, myelin oligodendrocyte glycoprotein antibody-associated disease and TED.

We believe the role of IL-6 targeted therapies has not yet been fully explored in autoantibody-mediated disorders and that there remains significant opportunity to address a variety of autoantibody-driven diseases. IL-6 inhibition has activity on other components of the immune response including the actions of pathogenic T-cells, B-cells, and macrophages. Given the pleiotropic activity of IL-6, we believe IL-6 inhibition may lead to a comprehensive suppression of disease pathophysiology, not limited to autoantibody lowering alone. We believe this approach may translate into clinical efficacy that could exceed what has been observed with treatment modalities that only lower autoantibodies.

Thyroid Eye Disease (TED) Overview

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

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

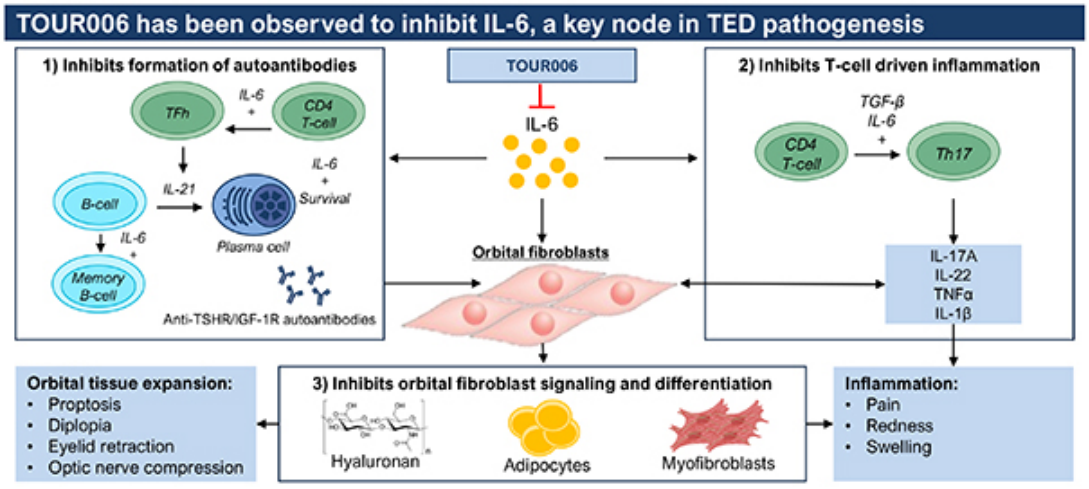
Levels of anti-TSHR antibody, specifically thyroid stimulating immunoglobulin ("TSI"), have been shown to be associated with the clinical features of TED and can influence its prognosis.

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

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

Role of IL-6 in TED

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



Current Treatment Paradigm for TED

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

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

Limitations of Current IGF-1R Treatment

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

- **High patient and physician burden**. Teprotumumab's dosing regimen requires visits to an IV infusion center once every three weeks for a total of eight visits. Generalist ophthalmologists, who typically are the front-line treaters of TED, do not usually have direct access to an IV infusion center, and patients with significant diplopia or visual impairment may have difficulty traveling to centers.
- **Significant side effects**. Teprotumumab is associated with significant, debilitating side effects including nausea, muscle spasms, hyperglycemia, and hearing impairment, the latter of which has at times been reported as possibly permanent.
- **Incomplete durability of proptosis benefit**. Long-term follow-up of patients studied in teprotumumab's Phase 3 clinical trial showed that approximately 40% of patients did not sustain their proptosis response 48 weeks after their last infusion.
- **Incomplete treatment response rates**. Clinical trials of teprotumumab observed lower response rates on other clinically important aspects of TED besides proptosis, such as improvements in diplopia or inflammatory disease activity as measured by Clinical Activity Score ("CAS").

Hearing Disturbances Associated with IGF-1R Inhibition

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

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

A recently published meta-analysis reported hearing-related disturbances occurred in 15% of patients treated with TEPEZZA, of which 45% were reported as persistent. Another publication reports that hearing disturbances began to emerge after a mean of 3.6 infusions of TEPEZZA (out of the standard eight infusions per treatment course). Furthermore, as of September 2023, 518 cases of hearing and ear-related adverse events related to TEPEZZA treatment have been captured in the FDA's Adverse Event Reporting System (FAERS) database. These events have included reports of permanent deafness.

As of January 2024, over 80 lawsuits have been filed by patients who allege suffering hearing loss due to treatment with TEPEZZA related to a failure by Horizon Therapeutics plc, now Amgen, which manufactures, promotes, and sells TEPEZZA, to adequately inform patients of the risk of hearing loss associated with the product. In July 2023, the FDA required Horizon Therapeutics plc to update TEPEZZA's label to include a warning that states, "TEPEZZA may cause severe hearing impairment including hearing loss, which in some cases may be permanent. Assess patients' hearing before, during, and after treatment with TEPEZZA and consider the benefit-risk of treatment with patients."

Clinical Experience in TED with IL-6 Inhibition

There is a large and growing body of literature documenting successful clinical experiences with IL-6 pathway inhibition, namely tocilizumab, an anti-IL-6R antibody, as an off-label treatment for TED. In over 40 investigator-led studies and retrospective analyses, spanning a total of over 340 patients with TED, IL-6 pathway inhibition was reported to offer meaningful improvement in proptosis, CAS, and/or diplopia. Substantial reductions in TSI levels have also been noted. Treatment was observed to be generally well-tolerated, with no major safety signals reported. In addition to this host of published literature, the European Group on Graves' orbitopathy ("EUGOGO") recommends tocilizumab for treatment of moderate-to-severe, steroid-resistant TED.

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

A summary of published literature reporting on the off-label use of IL-6 pathway inhibition in TED is provided in the table below. This published literature listed below may not be indicative of future clinical results for TOUR006.

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

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

TOUR006 for the Treatment of TED

We seek to establish TOUR006 as a new standard-of-care for the first-line treatment of TED. We believe TOUR006 has the potential to offer attributes of an ideal first-line therapy for TED, including:

- **Broad, deep, and durable effects**. Based on the strong evidence implicating IL-6's central role in TED, We believe TOUR006 offers the potential for meaningful and durable benefit across multiple efficacy outcome measures relevant to TED, such as proptosis, CAS, and diplopia.
- **A generally well-tolerated product without a risk of hearing loss**. Based on the extensive safety experience with IL-6 inhibitors and the available safety data to date for TOUR006, we believe that TOUR006, at the dosing regimens being evaluated, has the potential to be generally well-tolerated in TED without a risk of hearing loss.

- **An anti-inflammatory mechanism, well-suited for use early in disease**. Given the natural pathology of TED, TOUR006's anti-inflammatory mechanism may be best suited for early use in the active inflammatory phase of disease, which has a time-limited window before tissue injury and fibrosis occur.
- **A patient-centric experience**. We plan to dose TOUR006 as a subcutaneous, low-volume (≤1 mL) injection once every eight weeks, which we believe will provide substantial improvements to ease of access and ease of use over the current standard of care.

We estimate that 15,000 to 20,000 patients out of the incident population in the United States have moderate to severe, active, inflammatory TED that may be appropriate candidates for treatment with an advanced therapy such as TOUR006.

TOUR006 Clinical Program in TED

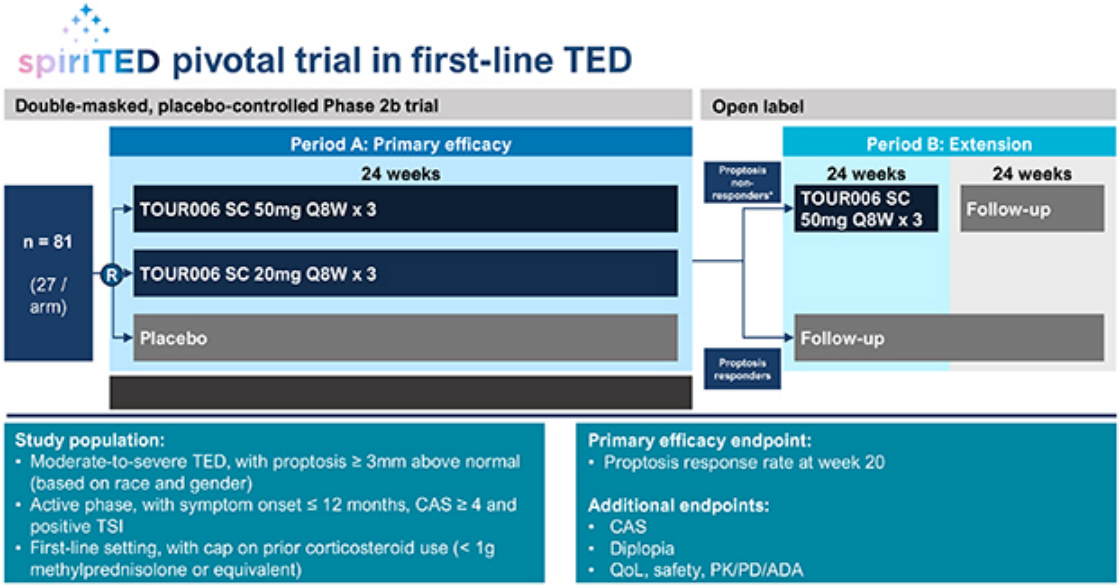
We have initiated our first pivotal trial in TED, which we refer to as the spiriTED trial. This trial is a randomized, double-masked, placebo-controlled, dose-ranging Phase 2b study in adult patients with active, moderate-to-severe TED. We are enrolling approximately 81 patients with baseline proptosis at least 3 mm greater than the normal range for race and sex, baseline CAS score of 4 or greater on the 7-point scale, and TED symptom onset of less than 12 months prior to entering the study. Patients must also have autoantibody positivity, which is defined as a TSI score greater than 130% of normal activity levels. The study protocol specifies additional inclusion and exclusion criteria.

In the Primary Efficacy Period (24-week duration), patients receive TOUR006 (20mg or 50mg) or placebo, administered subcutaneously every eight weeks at Day 1, Week 8, and Week 16. The primary endpoint of the study is the proptosis response rate at Week 20, defined as the percentage of patients who achieve at least a 2 mm reduction in proptosis from baseline in the study eye without worsening in the fellow eye and without need for rescue therapy or intervention. Additional endpoints include other efficacy outcomes (such as CAS and diplopia), safety, PK, PD, and ADA testing.

In the Extension Period, patients not experiencing a proptosis response after completing the 24-week Primary Efficacy Period will receive 50mg of TOUR006 in an open-label fashion every eight weeks for three administrations. All patients (regardless of whether they receive TOUR006) will be followed through week 72.

We expect to report topline results for spiriTED's Primary Efficacy Period in the first half of 2025.

Further, in January 2024, we announced our plans to accelerate initiation of our pivotal Phase 3 trial for TOUR006 in TED in 2024. The Phase 3 trial is expected to evaluate first-line use of TOUR006 in patients with TED. Subject to FDA and other regulatory feedback, this trial is planned to be a randomized, double-masked, placebo-controlled trial evaluating TOUR006 administration on an eight-week dosing schedule. The primary endpoint is expected to be proptosis response at week 20 following three subcutaneous (SC) administrations. Other efficacy endpoints are anticipated to include additional measures such as CAS, diplopia and quality of life ("QoL"). Topline data from this Phase 3 study are expected in 2026.



TOUR006 Phase 2b spiriTED trial design in TED. *Any patient who receives rescue therapy/intervention in Period A will not receive TOUR006 in Period B and will instead undergo follow-up only.

Our Cardiovascular Inflammation Strategy

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

Atherosclerotic Cardiovascular Disease (ASCVD)

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

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

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

Current Treatment Paradigm for ASCVD

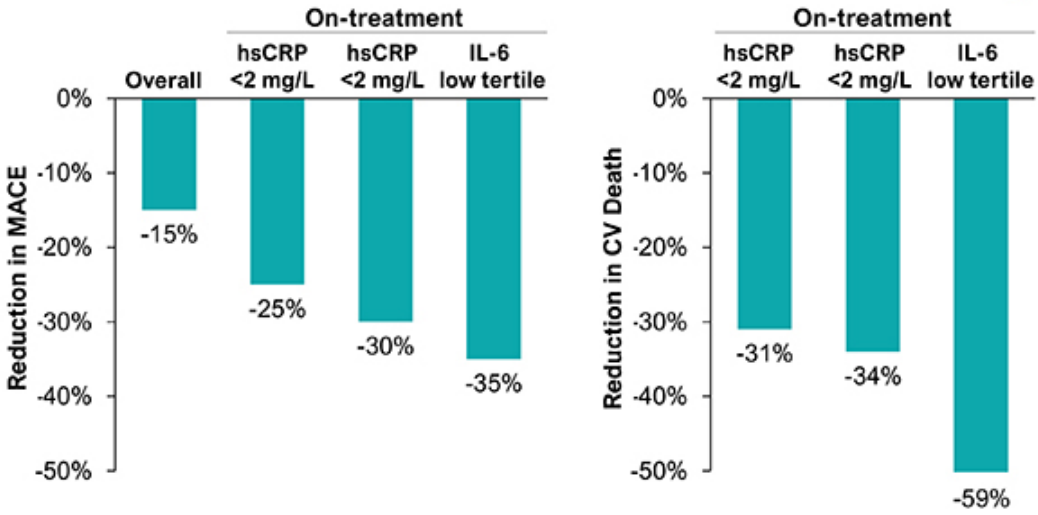
ASCVD treatment focuses on mitigating risk factors and includes lifestyle modifications, such as diet and exercise, and pharmacological interventions such as lipid lowering agents, antihypertensive agents, antiplatelet agents, and anticoagulants. In some cases, invasive procedures such as angioplasty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

Role of IL-6-driven Inflammation in ASCVD

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

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

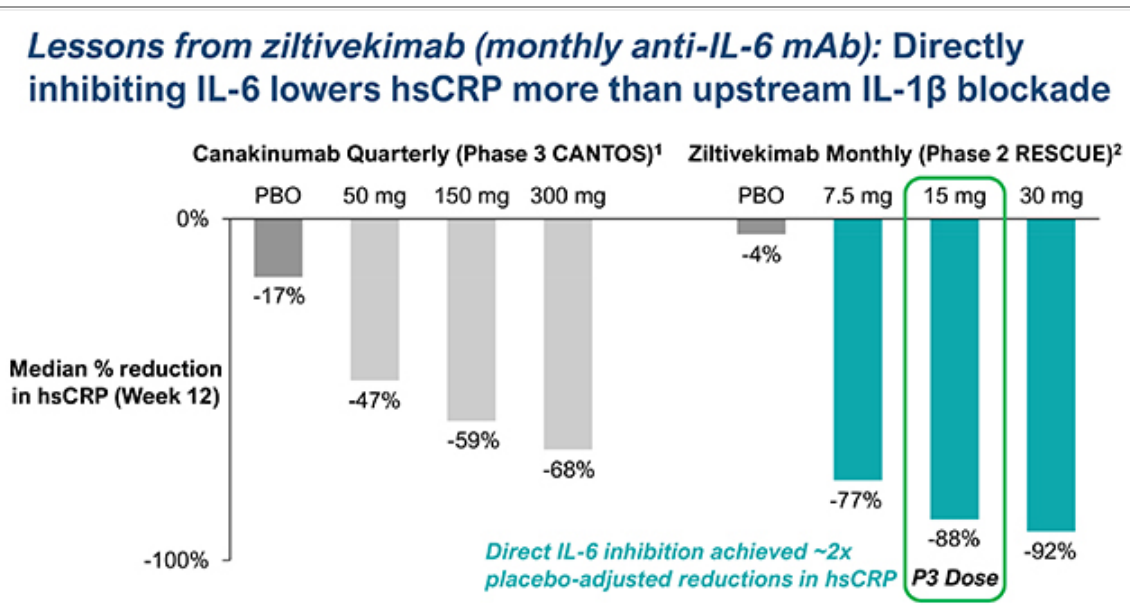
Lessons from canakinumab (anti-IL-1β mAb):
"Lower is better" for downstream biomarkers of IL-6 activity



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

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

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

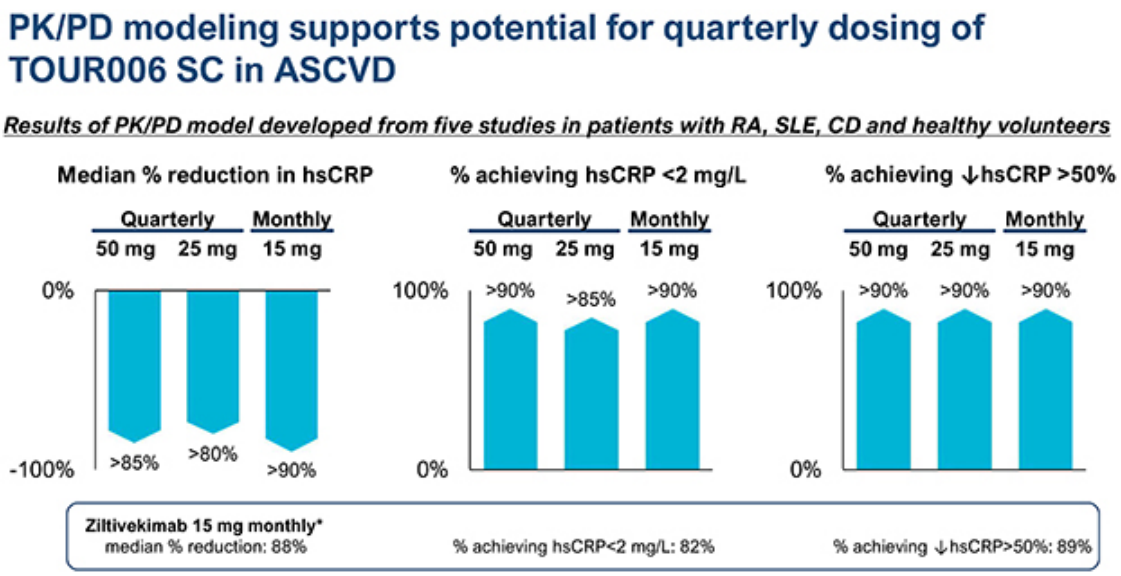


CRP reductions after treatment with canakinumab and ziltivekimab. 1. Ridker et al., NEJM (2017). 2. Ridker et al., Lancet (2021)

Multiple external Phase 3 cardiovascular outcome trials investigating IL-6 blockade are ongoing, and a positive readout from any of these trials could substantially validate the therapeutic hypothesis for IL-6 blockade in ASCVD. Novo Nordisk is currently testing ziltivekimab in four concurrent Phase 3 trials which we believe are de-risking opportunities for our own clinical development plan. For example, the ZEUS trial is testing ziltivekimab once every month in a 6,200 patient cardiovascular outcomes trial in ASCVD patients with chronic kidney disease. Topline data are expected in 2025.

TOUR006 for the Treatment of ASCVD

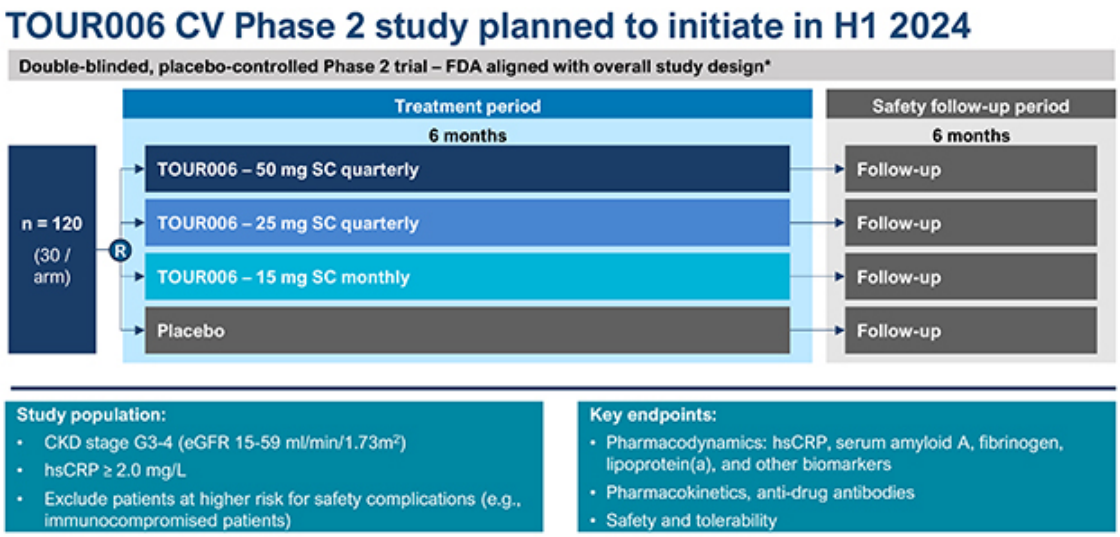
We believe TOUR006 may offer a more convenient dosing profile for IL-6 inhibitors in the treatment of ASCVD. Competitor anti-IL-6 agents under development involve either intravenous administration or a subcutaneous administration once a month. In contrast, the targeted dosing regimen for TOUR006 is subcutaneous administration once every three months supported by its PK/PD modeling as shown in the figure below. Prior Phase 1 and Phase 2 trials of TOUR006 observed consistently lower levels of CRP approximately three months following the last dose. A quarterly dosing regimen for TOUR006 would offer the potential to meaningfully improve patient convenience as well as optimize patient adherence to therapy due to the decreased drug administration burden.



ASCVD: atherosclerotic cardiovascular disease, RA: rheumatoid arthritis, SLE: systemic lupus erythematosus, CD: Crohn's disease. The PK and PK/PD models for TOUR006 were developed based on the data from 5 clinical studies (two phase 1 studies in healthy volunteers, one phase 1 study in RA, one phase 2 study in SLE, and one phase 2 study in CD). A two-compartment model with first-order absorption and linear elimination and a mechanism-based indirect response model (in a relationship on CRP) adequately described the PK and PK/PD relationships, respectively. Simulations were performed assuming an RA-like population with baseline CRP >2 mg/L to 10 mg/L. Results at Day 90 are shown. *Ridker et al., Lancet (2021). Results after 12 weeks of treatment are shown. Certain data in this slide are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross-trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein.

TOUR006 Clinical Program in ASCVD

As previously announced in January 2024, we have reached alignment with the FDA on our ASCVD clinical development program for TOUR006, including a Phase 2 trial evaluating CRP reduction, a validated biomarker for inflammation, with quarterly dosing of TOUR006 in patients with elevated cardiovascular risk. This trial is targeted to commence in the first half of 2024, with topline data expected in the first half of 2025. Pending success, the results from the Phase 2 trial are expected to position us to be ready in 2025 to commence a pivotal Phase 3 trial in cardiovascular disease.



Proposed trial design for TOUR006 Phase 2 trial in ASCVD. *Trial design to be finalized ahead of study start.

Previous Clinical Experience with TOUR006

Prior to our in-licensing of TOUR006 in May 2022, Pfizer had treated 448 study participants with TOUR006 across six clinical trials including Phase 2 studies in SLE and CD.

The following table summarizes the previous studies conducted by Pfizer:

Study Description	Subjects Who Received TOUR006	Doses tested
Single Ascending Dose PK Study in Healthy Participants	36	7, 22, 44, 112, 284, 500, 700 mg IV, single dose
Multiple Ascending Dose PK Study in Participants with Rheumatoid Arthritis Receiving Methotrexate	31	1, 10, 30, 100, 250 mg IV Q4W
Single Dose PK Study of TOUR006 Administered Subcutaneously to Healthy Participants	10	200mg SC, single dose
Phase 2 Dose-ranging Study in Participants with Moderate to Severe CD who are Anti-TNF Inadequate Responders	178	10, 50, 200 mg SC Q4W
Phase 2 Open-label Extension Study in Participants with Moderate to Severe CD	191	50, 100 mg SC Q8W
Phase 2 Dose-ranging Study in Participants with Active Generalized Systemic Lupus Erythematosus	138	10, 50, 200 mg SC Q8W

Phase 1 trial in healthy volunteers

Study design:

TOUR006 was studied by Pfizer in a first-in-human Phase 1, randomized, placebo-controlled, double-masked, single ascending dose study in healthy volunteers. A total of 48 participants were enrolled; 12 received placebo and 36 received seven different fixed intravenous doses of TOUR006: 7, 22, 44, 112, 284, 500, and 700mg. Participants were followed until their serum levels of TOUR006 were below the lower limit of quantitation ("LLOQ") and all treatment-related adverse events had resolved. The study was not powered for statistical significance.

PK/PD:

TOUR006's exposure PK increased in a dose-proportional manner across the dose range tested. Mean terminal elimination half-life was similar across dose groups, ranging from 47-58 days. A dose-dependent reduction in high-sensitivity HS-CRP ("hs-CRP") was observed. hs-CRP is an indicator of inflammation and a downstream signal of IL-6 pathway activation. Maximal hs-CRP reductions relative to baseline were observed on Day 7 or Day 14 post dose across the various dose groups. Given the low baseline levels of Free IL-6 hs-CRP in this healthy population, the full PD effect of TOUR006 was not able to be observed compared to later studies in patients with inflammatory diseases.

Safety Data:

TOUR006 in doses up to 500 mg appeared to be generally well-tolerated in this study with no dose limiting adverse effects, clinically significant laboratory abnormalities, or clinically relevant vital sign or ECG changes. During the study, three serious adverse events ("SAEs") were reported by two participants. An SAE of spontaneous abortion that was considered potentially treatment-related by the sponsor was reported in the sexual partner of a participant in the 284 mg TOUR006 arm. One participant in the 700 mg TOUR006 arm reported 2 SAEs (tonsillitis and acute pancreatitis), both of which were considered treatment-related. At least 67% of subjects in each TOUR006 group experienced at least one AE compared to 58% in the placebo group. Headache and fatigue were the most frequently reported AEs (all causalities and treatment-related). The most frequently reported treatment-related AEs by Medical Dictionary for Regulatory Activities (MedDRA) version 13.1 system organ class were infections and infestations and gastrointestinal disorders, reported by 8 and 11 subjects in the TOUR006 groups and 1 and 0 subjects in the placebo group, respectively.

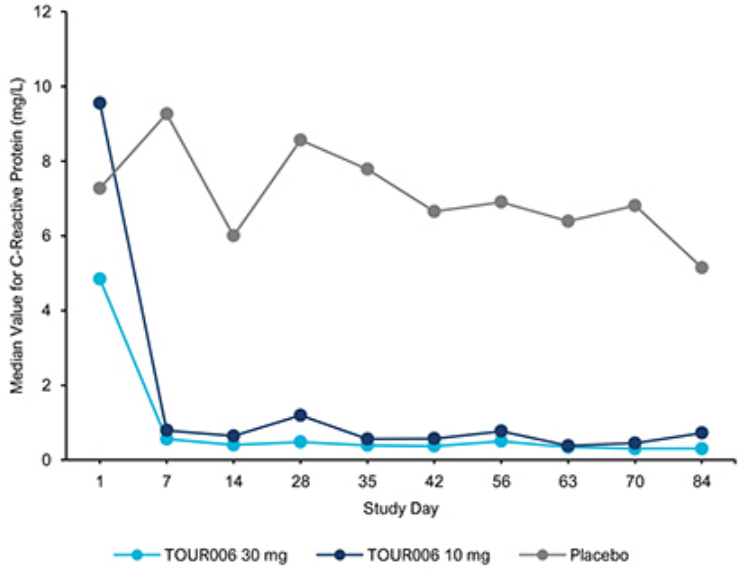
Phase 1 trial in RA patients

Trial design:

TOUR006 was studied by Pfizer in a Phase 1 randomized, placebo-controlled, double-masked, escalating dose study investigating multiple ascending doses of intravenous TOUR006 in RA patients receiving methotrexate. A total of 40 participants were treated 9 received placebo and 31 received 3 monthly IV doses of TOUR006 at a set dosing level: 1, 10, 30, 100, or 250 mg. Participants were followed until their serum levels of TOUR006 were below the LLOQ and all treatment-related AEs had resolved. The study was not powered for statistical significance.

PK/PD:

TOUR006 exposure increased approximately in proportion with dose. Accumulation of TOUR006 exposure, in terms of increases in Cmax after each 4-week dosing interval, was nearly constant from dose to dose and consistent with time-linear PK. Mean terminal elimination half-lives were 36-49 days across TOUR006 treatment groups. Greater serum CRP concentration reductions from baseline were observed in TOUR006 treatment groups compared with placebo from Day 7 to Day 84 and reductions appeared to be dose-related. Mean percent reductions from baseline were >80% (and up to 96%) in the higher TOUR006 dose groups. A single 10 mg intravenous dose of TOUR006 led to rapid and substantial decrease in CRP as shown in the figure below. Maximal reductions in CRP concentrations relative to baseline were generally observed by day 7 or day 14 across the various treatment groups. The time required for CRP levels to return to baseline appeared to increase as dose increased.



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

Safety Data:

All doses of TOUR006 tested in the study appeared to be generally well-tolerated. During the study, three participants reported five treatment-emergent SAEs: two participants in the 30 mg TOUR006 arm and one in the 100 mg TOUR006 arm. The observed SAEs were plantar fasciitis, plantar abscess, pneumonia, chest pain (all in the 30 mg arm) and road traffic accident (100 mg arm). Proportions of subjects with treatment-emergent and treatment-related AEs were similar between placebo and TOUR006 treatment groups (100.0% vs 80.6%, and 44.4% vs 51.6%, respectively). A slightly greater proportion of TOUR006-treated subjects experienced upper respiratory tract infection, increases in alanine transaminase ("ALT") and aspartate transaminase ("AST"), and leukopenia treatment-emergent adverse effects ("TEAEs"), compared with placebo-treated subjects (25.8% vs 11.1%, 12.9% vs 0%, 12.9% vs 0%, and 9.7% vs 0%, respectively). No subjects with increased ALT or AST TEAEs met study criteria for abnormal laboratory values (i.e., >3 × upper limit of normal). Of the 4 subjects with TEAEs related to either hypercholesterolemia or dyslipidemia during the study, all responded well to the addition of lipid-lowering treatment with a reduction in serum lipid levels.

Phase 1 trial in healthy volunteers for single subcutaneous dose

Trial design:

Pfizer investigated TOUR006 in a Phase 1, single center, open-label study to investigate the safety, tolerability, and PK of a single dose level of subcutaneously administered TOUR006 in 10 healthy adult participants (all male). A dose of 200 mg SC was chosen for this study (2 concurrent 100 mg doses). The study was not powered for statistical significance.

Safety Data:

There were no SAEs, deaths, dose reductions, or discontinuations due to AEs during the study. A single 200 mg total dose of TOUR006 administered SC appeared to be well-tolerated in this study.

PK:

The PK profile of TOUR006 was characterized by a prolonged absorption rate followed by a mono-exponential decline in plasma concentrations. Comparison of exposure at similar doses following IV and SC administrations indicates that SC bioavailability is relatively high. The estimated dose-normalized AUCinf following the SC dose of 262 mg.h/mL/mg was similar to the average AUCinf of 249 mg.h/mL/mg following IV administration in healthy participants across a range of doses from 7 to 700 mg in the phase 1 single ascending dose trial of IV TOUR006. The mean terminal elimination half-life was approximately 52 days.

Phase 2 trial in SLE patients

Trial design:

TOUR006 was investigated by Pfizer in SLE through a Phase 2 randomized controlled trial, and results from this study have been published in a peer-reviewed medical journal. This Phase 2 trial was a multicenter, randomized, placebo-controlled, dose-ranging, double-masked, clinical study evaluating patients with active, generalized SLE. Participants were randomized to subcutaneous doses of TOUR006: 10, 50, and 200 mg or placebo in a 1:1:1:1 ratio. The study included a 24-week treatment period and a 28-week follow-up period. Participants received study treatment on Day 1, Week 8, and Week 16. A total of 183 participants received at least 1 dose of study treatment (45 participants in the 10 mg TOUR006 group, 47 participants in the 50 mg TOUR006 group, 46 participants in the 200 mg TOUR006 group, and 45 participants in the placebo group). The primary endpoint of the study was the proportion of patients achieving a response on the SLE Responder Index (SRI-4) criteria at Week 24. The study was designed with 80% power to detect a 25% difference in the SRI-4 response rate between TOUR006 and placebo using a one-sided alpha of 0.05.

Safety:

Safety data results from this study supported the use of 10 and 50mg doses of TOUR006. During the double-masked treatment period, the most commonly reported TEAEs (excluding infections or injection site reactions (“ISRs”)) across all treatment groups were headache (8.7%), nausea (8.2%), and diarrhea (6.6%), and the most frequently reported infectious TEAEs were upper respiratory tract infection (13.7%), cystitis (5.5%), and pharyngitis/laryngitis (5.5%). A total of 15 participants across the study experienced at least 1 ISR: 8 participants in the 50 mg TOUR006 arm, 3 participants in the placebo arm and 2 participants each in the 10 mg and 200 mg TOUR006 arms. More subjects experienced SAEs in the placebo (5 subjects, 11.1%) and 200 mg (5 subjects, 10.9%) groups compared to the 10 mg (2 subjects, 4.4%) and 50 mg groups (1 subject, 2.1%). There were 4 deaths in the study (1 in the 10 mg arm and 3 in the 200 mg arm). Causes of death were suspected pulmonary embolism in the 10 mg arm, and cardio-respiratory arrest, sepsis with pulmonary embolism, and disseminated tuberculosis in the 200 mg arm. In the interest of the safety of participants in the study, dosing in the 200 mg arm was prematurely terminated, based on an unblinded recommendation from the internal review committee for this study.

SLE has an elevated risk of serious complications, such as infection and thromboembolism. This risk is further amplified in patients who have higher severity of inflammation and/or are in the midst of an active disease flare, as the patients in this study were. Additional confounding data was introduced from a high rate of concomitant medication use, such as systemic corticosteroids which may increase the risk for complications including infection and thromboembolism. Additionally, the 200 mg TOUR006 arm had a disproportionately higher rate of comorbidities at baseline, such as SLE-associated cardiorespiratory involvement and neuropsychiatric involvement. Despite these confounding factors, we do not intend to pursue treatment with a 200 mg dose of TOUR006.

Efficacy Data:

The study did not meet the primary endpoint for efficacy on SRI-4, though the 10 mg TOUR006 treatment arm did see a numerically positive signal with a 60% response rate compared to 40% in the placebo arm (p=0.076). A p-value (“p”) represents the probability that the observed treatment effect or larger would have occurred assuming the drug had no effect compared to placebo. The 10 mg TOUR006 treatment arm achieved a statistically significant response rate on the BILAG-Based Composite Lupus Assessment (BICLA) (p=0.026). There were statistically significant trends in the 10 mg TOUR006 and 50 mg TOUR006 treatment arms on reduction of severe flares.

PK/PD:

TOUR006 exposure increased dose-proportionally and mean terminal half-life ranged between 40-44 days. Dose proportional CRP reductions were observed and serum CRP levels were continuously suppressed from week 2 through week 24 in the treatment period. Median percentages of change of CRP were 2.5%, -56.0%, -80.0%, and -93.0% at Week 24 in the placebo, 10, 50, and 200 mg TOUR006 treatment groups, respectively.

Phase 2 trials in Crohn's Disease patients

Trial design:

TOUR006 was investigated by Pfizer in CD through a Phase 2 randomized controlled trial and a companion open-label extension ("OLE") trial. Results from these studies have been published in a peer-reviewed medical journal. The Phase 2 trial was a multi-center, parallel, dose-ranging, randomized, double-masked, placebo-controlled study evaluating patients with moderate to severe CD who were inadequate responders to anti-tumor necrosis factor ("TNF") therapy. Participants were randomized to subcutaneous doses of TOUR006: 10, 50, 200 mg or placebo in a 1:1:1:1 ratio. Participants received study treatment on Day 1 and Day 28 of the 12-week induction period. The primary endpoint of induction study was the proportion of patients achieving a ≥70-point reduction in CD Activity Index ("CDAI") score ("CDAI-70"). The induction study was designed with 78% probability to detect a greater CDAI-70 response rate for TOUR006 versus placebo at Weeks 8 or 12, assuming a 25% difference in CDAI-70 response rates between TOUR006 and placebo and assuming the family-wise error rate was controlled at one-sided 0.05 using the Bonferroni method for two time points. After completing the induction period, participants could either enter the 28-week follow-up period or enter the OLE study. 247 participants received at least 1 dose of study treatment (67 participants in the 10 mg TOUR006 group, 71 participants in the 50 mg TOUR006 group, 40 participants in the 200 mg TOUR006 group, and 69 participants in the placebo group). Due to safety concerns from results of the SLE study, dosing of the 200 mg arm was prematurely terminated. The OLE study included a 48-week treatment period and a 28-week follow-up period. In the OLE, 191 participants received TOUR006 on Day 1 and every 8 weeks through Week 40. All participants received subcutaneous 50 mg TOUR006 on Day 1. Dose escalation to 100 mg was allowed for non-responders starting at 8 weeks; if such an individual did not experience a response within 8 weeks after this dose escalation, they were discontinued from the active treatment period. Responders who subsequently relapsed were also eligible for dose escalation to 100 mg. The OLE study was not powered for statistical significance.

Safety:

Safety results from this study supported the use of 10 mg, 50 mg, and 100 mg TOUR006. At least 1 TEAE and at least 1 SAE were reported by 86.6% and 14.6%, respectively, of all participants during the first 12 weeks of the study. The most common TEAEs across all participants during this treatment period were CD (11.7%), abdominal pain (11.3%), nasopharyngitis (9.3%), and headache (8.5%). ISRs were infrequent, and there was no apparent imbalance in rates across treatment arms. There was 1 death in the 50 mg TOUR006 arm due to respiratory failure secondary to pneumonia following post-operative complications of colectomy in a participant with chronic obstructive pulmonary disease, which was assessed as unrelated to study treatment by the investigator. The most common SAEs across treatment arms were CD (15 participants), condition aggravated (6 participants), anal fistula and anal abscess (3 participants each), and abdominal pain (2 participants), and all other SAEs were experienced by only 1 participant across treatment arms; there were no apparent imbalances in the incidences of SAEs across treatment arms.

Across the 191 participants in the OLE, the median drug exposure was 378 days. At least 1 TEAE was reported by 89.5% of participants during the treatment period and 74.2% of participants during the follow-up period. At least 1 SAE was reported by 30.4% of participants during the treatment period and 20.6% of participants during the follow-up period. The most frequently reported TEAEs during the treatment period were CD (27.7%), abdominal pain (16.2%), and nasopharyngitis (12.0%). The incidence of ISRs during the treatment period was 4.7% and 11.0% of 50 mg TOUR006-treated participants and 100 mg TOUR006-treated participants respectively. The most common SAEs were worsening of CD (26 participants), followed by condition aggravated (13 participants). During the follow-up period, the most common TEAEs were worsening of CD (19.4%) and abdominal pain (7.7%). The most common SAEs were worsening of CD (17 participants) and condition aggravated (5 participants). No participants died during the OLE study in either the treatment period or follow-up period.

PD and Efficacy Data:

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

The CDAI-70 response rates for the 50 mg TOUR006 arm were significantly greater than placebo at Week 8 (49.3% vs 30.6%, one-sided $p < 0.05$) and Week 12 (47.4% vs 28.6%, one-sided $p < 0.05$) and met the primary endpoint. The primary endpoint was not met for the 10 mg dose of TOUR006. Due to halting of dosing in the 200mg TOUR006 arm, efficacy analysis was not conducted for this treatment group.

Immunogenicity:

Across the six studies described above, limited immunogenicity has been observed to date. Across the 448 healthy volunteers and patients treated with TOUR006, two study participants had samples that were confirmed ADA positive following TOUR006 treatment. Both participants' ADAs were confirmed positive for neutralizing antibodies. Neither of the two participants experienced any AE or SAE that could be related to ADAs and no discernable impact on PK was observed. Two additional participants had samples at baseline that were confirmed ADA positive but without any increase in ADA titer following TOUR006 treatment.

License Agreement with Pfizer

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

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

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

As additional consideration for the license, we are obligated to pay Pfizer up to $128.0 million upon the achievement of specific development and regulatory milestones. We are also obligated to pay Pfizer up to $525.0 million upon the first achievement of specific sales milestones. We are also obligated to pay Pfizer a marginal royalty rate in the low-double digits (less than 15%), subject to specified royalty reductions. The royalty term, on a Product-by-Product and country-by-country basis, begins on the first commercial sale of such Product and expires upon the later of twelve years following the date of the first commercial sale or the expiration of regulatory exclusivity protecting such Product. In the event we complete a Significant Transaction (as defined in the Pfizer License Agreement), we will be obligated to pay Pfizer a one-time payment in the low-eight digits (up to $20.0 million); the amount of such payment is based on the timing of the transaction. No such milestone or royalty amounts have been paid to date.

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

License Agreement with Lonza

In May 2022, we entered into a license agreement (the "Lonza License Agreement") with Lonza Sales AG ("Lonza"), pursuant to which we obtained a worldwide, non-exclusive, sublicensable (subject to certain conditions) license under certain know-how to market, sell, offer for sale, distribute, import and export products containing TOUR006 ("Product"). We also obtained a non-exclusive, sublicensable (subject to certain conditions) license under certain licensed know-how to use, develop, and manufacture (including have manufactured in accordance with the terms of the Lonza License Agreement) Product at premises approved by Lonza.

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

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

The Merger

On October 19, 2023, we, formerly known as Talaris Therapeutics, Inc., completed the previously announced merger transaction in accordance with the terms and conditions of the Agreement and Plan of Merger, dated as of June 22, 2023 (the "Merger Agreement"), by and among us, Tourmaline Bio, Inc. ("Legacy Tourmaline") and Terrain Merger Sub, Inc., our direct wholly owned subsidiary ("Merger Sub"), pursuant to which Merger Sub merged with and into Legacy Tourmaline, with Legacy Tourmaline surviving as our direct wholly owned subsidiary and the surviving corporation of the merger (the "Merger"). Following the completion of the Merger, we began conducting the business conducted by Legacy Tourmaline.

On October 19, 2023, in connection with and prior to the completion of the Merger, we effected a 1-for-10 reverse stock split of our common stock (the "Reverse Stock Split"), Legacy Tourmaline changed its name from "Tourmaline Bio, Inc." to "Tourmaline Sub, Inc.", and we changed our name from "Talaris Therapeutics, Inc." to "Tourmaline Bio, Inc."

Under the terms of the Merger Agreement, immediately prior to the effective time of the Merger, each share of Legacy Tourmaline's Series A preferred stock was converted into one share of Legacy Tourmaline's common stock. At the effective time of the Merger, we issued an aggregate of approximately 15,877,090 shares of our common stock to Legacy Tourmaline's stockholders, based on an exchange ratio of 0.7977 (without giving effect to the Reverse Stock Split) shares of our common stock for each share of Legacy Tourmaline common stock outstanding immediately prior to the Merger, including those shares of common stock issued upon conversion of the Legacy Tourmaline Series A preferred stock and those shares of Legacy Tourmaline common stock issued in the Legacy Tourmaline pre-closing financing transaction (the "Pre-Merger Financing Transaction") which closed on October 19, 2023, immediately prior to the closing of the Merger (but excluding shares to be canceled pursuant to the Merger Agreement and excluding any dissenting shares).

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

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

Sales and Marketing

We do not currently have our own marketing, sales or distribution capabilities. In order to commercialize TOUR006 or any future product candidate, if approved for commercial sale, we would have to develop a sales and marketing infrastructure or make arrangements with third parties to perform these services for it. We may opportunistically seek strategic collaborations to maximize the commercial opportunities for TOUR006 or any future product candidates inside and outside the United States.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of TOUR006. Furthermore, there is limited capacity at contract manufacturers that operate under the current good manufacturing practice ("cGMP") requirements of the FDA to meet our timelines and production needs. We currently rely and intend to continue to rely on contract development and manufacturing organizations ("CDMOs"), for both drug substance and drug product. Currently, we contract with two well-established third-party manufacturers, one for the manufacture of our drug substance and another for the manufacture of our drug product. We may engage additional third-party manufacturers to support any clinical trials for TOUR006 as well as commercialization of TOUR006, if approved, in the United States or other jurisdictions. In addition, as our production needs increase, we intend to recruit additional experienced personnel to manage the CDMOs producing our product candidate and other product candidates or products that we may develop in the future.

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

Competition

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

IL-6

There are four FDA-approved products that block IL-6 or IL-6R, including tocilizumab (ACTEMRA®), siltuximab (SYLVANT®), sarilumab (KEVZARA®), and satralizumab-mwge (ENSPRYNG®).

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

Competition in TED

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

- Roche is developing satralizumab, currently being evaluated in ongoing Phase 3 studies
- Viridian is developing VRDN-001, a monoclonal antibody targeting IGF-1R, delivered by intravenous infusion, currently in a Phase 3 study. Viridian has announced VRDN-003 as its lead follow-on anti-IGF-1R antibodies to be delivered by subcutaneous administration with a pivotal study expected to start in 2024.
- Acelyrin, Inc. is developing lonigutamab (VB-421), a monoclonal antibody targeting IGF-1R, delivered by subcutaneous administration, currently in a Phase 1 study.
- Sling Therapeutics, Inc. is developing linsitinib, a small molecule IGF-1R inhibitor, currently being evaluated in an ongoing Phase 2b trial.
- Innovent Biologics, Inc. is developing IBI311, a monoclonal antibody targeting IGF-1R, delivered by intravenous infusion, currently in a Phase 3 study in China only.
- Minghui Pharmaceutical, Inc. is developing MHB018A, a monoclonal antibody targeting IGF-1R, delivered by subcutaneous administration, currently in a Phase 1a healthy volunteer study, with plans to develop in TED.
- Lirum Therapeutics, Inc. is developing LX-101, an IGF-1 bound to methotrexate, currently in Phase 1 oncology studies, but with plans to develop in TED.
- argenx is developing efgartigimod, an antibody fragment targeting FcRn expected to be studied in a registrational trial.
- Immunovant and Harbour BioMed are developing batoclimab (IMVT-1401/HBM9161), a monoclonal antibody targeting FcRn, currently being evaluated in ongoing Phase 3 trials.
- Lassen is developing LASN01, a monoclonal antibody targeting IL-11R, currently being evaluated in a Phase 1 study.

- Regeneron is collaborating with the Massachusetts Eye and Ear Infirmary to study aflibercept, a soluble decoy receptor that binds vascular endothelial growth factor-A ("VEGF"-A), VEGF-B and placental growth factor, in a Phase 2 trial.
- Kriya Therapeutics, Inc. is developing a gene therapy program, currently in preclinical studies.
- Crinetics Pharmaceuticals, Inc. is developing a TSHR antagonist, currently in preclinical studies.
- Septerna, Inc. is developing a TSHR negative allosteric modulator, currently in preclinical studies.

Competition in ASCVD

Several classes of therapies are routinely used for the treatment of ASCVD, including statins, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, aspirin, and anti-platelet agents. These therapies are largely once-daily, oral therapies. Recently, low-dose colchicine (LoDoCo®), a broad anti-inflammatory medicine, and bempedoic acid (Nexletol®), another lipid lowering agent, were approved for the treatment of ASCVD. Both are once-daily, oral medicines. Additionally, agents with longer dosing intervals inhibiting proprotein convertase subtilisin/kexin type 9 ("PCSK9") have recently been approved. These agents include alirocumab (Praluent®), evolocumab (Repatha®), and inclisiran (Leqvio®). We are not aware of any targeted, anti-inflammatory therapies approved for ASCVD.

We are aware of two IL-6 antibodies currently being developed for the treatment of ASCVD. Novo Nordisk is developing ziltivekimab, a monoclonal antibody targeting IL-6, for the treatment of ASCVD in patients with chronic kidney disease as well as in patients with a recent myocardial infarction. CSL Behring is developing clazakizumab, a monoclonal antibody targeting IL-6, for the treatment of ASCVD in patients with end-stage kidney disease.

Intellectual Property

We pursue a layered intellectual property strategy, including patents, trademarks, and trade secret rights, to protect our TOUR006 platform, and our use in treating the targeted indications.

Our future commercial success depends, in part, on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; to defend and enforce our patents and other intellectual property; to preserve the confidentiality of our trade secrets; and to operate without infringing, misappropriating or violating the valid and enforceable patents and other intellectual property rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products, or from developing competing diagnostic technologies, may depend on the extent to which we have rights under valid and enforceable patents, trade secrets or other intellectual property rights that cover these activities. We cannot be sure that patents will issue with respect to any of the pending patent applications or, with respect to any patent applications that we may file or license in the future, nor can we be sure that any of the patents we do obtain will be commercially useful in protecting any products that we ultimately attempt to commercialize, or any method of making or using such products. Moreover, we may be unable to obtain patent protection for certain of our indications. See the section titled "Risk Factors—Risks Related to Our Intellectual Property" in our Quarterly Report for the period ended September 30, 2023, filed with the SEC on November 14, 2023, for a more comprehensive description of risks related to our intellectual property.

Patents

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

Our patent portfolio currently includes solely owned provisional patent application filings in the United States, international patent applications and non-provisional patent applications in Taiwan covering the use of TOUR006 for treating specified ocular and inflammatory indications. Given our pre-commercial state of development, we cannot be certain that any of the patent application filings in our portfolio will provide meaningful protection for any drug or indication we ultimately attempt to commercialize. Non-provisional filings in the United States and other jurisdictions that claim the benefit of the provisional filings would have a presumptive twenty-year term extending into 2043 or 2044.

We intend to pursue patent protection, whether through in-licensing or our own development, for future drug candidates and specific aspects of our treatment methods. We may also pursue additional patent protection for features of our TOUR006 platform, though we will rely on confidentiality and trade secret protections for certain aspects of that platform.

We have sought patent protection in the United States, Taiwan, and internationally through Patent Cooperation Treaty (PCT) related to the use of TOUR006 in targeting specific diseases. As of the date of this prospectus, our patent portfolio consists of eight US provisional applications, four pending PCT applications, and four pending Taiwan non-provisional applications. Two of the provisional applications were filed less than one year ago, and the PCT and Taiwan applications claim benefit of priority to the other provisional applications. The non-provisional applications are projected to expire in 2043 or 2044, prior to consideration of any additional patent term. We intend to pursue, when possible, further composition, method of use, dosing, formulation, and other patent protection directed to TOUR006 and any new products developed. We may also pursue patent protection with respect to manufacturing and drug development processes and technology.

Trademarks

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

Trade Secrets and Confidential Information

For certain of our technologies, we rely on unpatented trade secrets and confidential know-how to develop and maintain our competitive position. However, trade secrets are notoriously difficult to protect. Breaches of trade secret or confidentiality provisions can be challenging to detect, and even more challenging to prove. We seek to protect our proprietary information, in part, through confidentiality and non-competition agreements with employees, consultants, partners, and other advisors. These agreements may be breached and we may not be able to successfully defend our rights. Moreover, we may not be able to secure adequate remedies for harm caused by such breach. Furthermore, our trade secrets or confidential information may be independently developed by a third party, and it may not have any ability to restrain or secure any remedy from them. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. See the section titled "Risk Factors—Risks Related to Intellectual Property" for a more comprehensive description of risks related to our trade secrets and confidential information.

Government Regulation

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

FDA Drug Approval Process

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

The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

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

Preclinical and Clinical Development

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

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

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

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

- Phase 1—The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism, distribution and elimination of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2—The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.
- Phase 3—The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval and labeling.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These so-called Phase 4 studies may be made a condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate. In addition, the sponsor must develop and validate analytical methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

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

BLA Submission, Review and Approval

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

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

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

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

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

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

Expedited Development and Review Programs

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

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

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

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

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. The FDA may require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. In addition, for products being considered for accelerated approval, the FDA generally requires, unless otherwise informed by the agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period, which could adversely impact the timing of the commercial launch of the product.

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

Orphan Drug Designation

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

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

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

Post-Approval Requirements

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, requirements relating to quality control and quality assurance, record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our third-party manufacturers.

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

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, mandated modification of promotional materials or issuance of corrective information, issuance by FDA or other regulatory authorities of safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product, or complete withdrawal of the product from the market or product recalls;
- fines, warning or untitled letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products; or
- injunctions, consent decrees or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. However, manufacturers and third parties acting on their behalf are prohibited from marketing or promoting drugs in a manner inconsistent with the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Biosimilars and Reference Product Exclusivity

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

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

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

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

Other U.S. Healthcare Laws and Compliance Requirements

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

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

Additionally, the intent standard under the Anti-Kickback Statute was amended by the ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Violations of the Anti-Kickback Statute can result in significant civil and criminal fines and penalties, imprisonment, and exclusion from federal healthcare programs. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act ("FCA").

The federal false claims and civil monetary penalty laws, including the FCA, which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, including federal healthcare programs, such as Medicare and Medicaid, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. For instance, historically, pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses. Penalties for federal civil FCA violations may include up to three times the actual damages sustained by the government, plus significant mandatory civil penalties, and exclusion from participation in federal healthcare programs.

HIPAA created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

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

Additionally, the federal Physician Payments Sunshine Act (the "Sunshine Act") within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties. In addition, many states also govern the reporting of payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted, and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

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

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

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to our products in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

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

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future governmental regulations that apply to us, it may be subject to significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private "qui tam" actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and results of operations.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may obtain regulatory approval. In the United States and in foreign markets, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial payors are critical to new product acceptance.

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

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

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

Third-party payors are increasingly challenging the price, examining the medical necessity, and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develops.

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

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care, the increasing influence of health maintenance organizations, and additional legislative changes in the United States has increased, and we expect will continue to increase, the pressure on healthcare pricing. The downward pressure on the rise in healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

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

For example, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (the "IRA"), into law, which among other things, (1) directs HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. The IRA includes certain exemptions to the price negotiation program, including a limited exemption for products with orphan drug designation. This exemption applies only to products with one orphan drug designation that is (i) for a rare disease or condition and (ii) is approved for indication(s) for such rare disease or condition. By limiting price negotiation exemption to products with only one orphan drug designation, the IRA may decrease our interest in pursuing orphan drug designation for our product candidates in multiple indications. The IRA also, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025 and eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry.

The ACA has substantially changed healthcare financing and delivery by both governmental and private insurers. Among the ACA provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts, which through subsequent legislative amendments, has been increased to 70%, starting in 2019, off negotiated prices of applicable branded drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;

- expansion of the entities eligible for discounts under the 340B Drug Discount Program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- expansion of healthcare fraud and abuse laws, including the FCA and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected;
- requirements to report certain financial arrangements with physicians and teaching hospitals;
- a requirement to annually report certain information regarding drug samples that manufacturers and distributors provide to physicians;
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending; and
- a licensure framework for follow on biologic products.

Some of the provisions of the ACA have yet to be implemented, and there have been legal and political challenges to certain aspects of the ACA. In December 2017, Congress repealed the tax penalty for an individual's failure to maintain ACA-mandated health insurance as part of a tax reform bill. Moreover, the Bipartisan Budget Act of 2018 , among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the United States Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA and IRA may be subject to judicial or Congressional challenges in the future.

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

Further legislation or regulation could be passed that could harm our business, financial condition and results of operations. Other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect beginning on April 1, 2013 and, due to subsequent legislative amendments, will stay in effect through 2032 unless additional Congressional action is taken. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, in an executive order, the administration of President Biden expressed its intent to pursue certain policy initiatives to reduce drug prices and, in response, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to lower drug prices. Further, in response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS, Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control biopharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

The Foreign Corrupt Practices Act

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

Additional Regulation

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

Other Regulations

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

Employees and Human Capital Resources

As of January 22, 2024, we had 42 full-time employees, including 29 who are engaged in research and development activities. None of our employees are subject to a collective bargaining agreement or represented by a trade or labor union. We consider our relationship with our employees to be good.

Our human capital objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating new and existing employees. The principal purposes of our equity incentive plans are to attract, retain and motivate our employees, directors and selected consultants through the granting of stock-based compensation awards and cash-based performance bonus awards.

Corporate Information

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

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

Available Information

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

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TOURMALINE MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations and the unaudited interim condensed financial statements and related notes should be read in conjunction with (i) the unaudited interim financial statements of Tourmaline Sub, Inc. (formerly Tourmaline Bio, Inc.) ("Legacy Tourmaline") as of and for the periods ended September 30, 2023 and 2022, together with related notes thereto, filed as Exhibit 99.1 to the Current Report on Form 8-K, filed with the Securities and Exchange Commission (the "SEC") on November 14, 2023 and (ii) Legacy Tourmaline's audited financial statements and the related notes for the year ended December 31, 2022 and the period from September 17, 2021 (inception) to December 31, 2021 included in the proxy statement/prospectus (the "Proxy Statement/Prospectus") filed pursuant to Rule 424(b) under the Securities Act of 1933, as amended (the "Securities Act"), with the SEC on September 15, 2023. References to "we", "our" and "the Company" refers to Legacy Tourmaline for periods prior to the closing of the Merger (as defined below), and to Tourmaline Bio, Inc. (formerly Talaris Therapeutics, Inc.) for all other periods, as the context requires.

This discussion and analysis contain forward-looking statements based upon current beliefs, plans and expectations related to future events and our future financial performance that involve risks, uncertainties and assumptions, such as statements regarding our intentions, plans, objectives and expectations for our business. Our actual results and the timing of selected events could differ materially from those described in or implied by these forward-looking statements as a result of several factors, including those set forth under "Risk Factors" in Part II, Item 1A of the Quarterly Report on Form 10-Q for the period ended September 30, 2023, filed with the SEC on November 14, 2023. Defined terms included below have the same meaning as terms defined and included elsewhere in the Current Report of which this exhibits forms a part, including Exhibit 99.1 thereto, unless defined below.

Overview

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

Our initial product candidate is TOUR006, a fully human monoclonal antibody that selectively binds to interleukin-6 ("IL-6"), a key proinflammatory cytokine involved in the pathogenesis of many autoimmune and inflammatory disorders. The anti-IL-6 and anti-IL-6 receptor ("IL-6R") antibody class ("IL-6 class") has over two decades of clinical and commercial experience treating over a million patients with a variety of autoimmune and inflammatory diseases. To date, four anti-IL-6 or anti-IL-6R antibodies have been approved in the United States. These four anti-IL-6 or anti-IL-6R antibodies together generated more than $3.5 billion in global sales in 2022.

TOUR006 is a long-acting anti-IL-6 antibody which we believe has best-in-class properties including a high binding affinity to IL-6, long half-life, and low observed immunogenicity. These characteristics may allow TOUR006 to achieve substantial IL-6 pathway suppression with relatively low amounts of drug exposure, potentially enabling delivery in a convenient, low volume, infrequently administered, subcutaneous injection.

We are pursuing two strategic paths for TOUR006. First is our "FcRn+" strategy. Neonatal Fc receptor ("FcRn") inhibitors have emerged as a novel therapeutic class to treat autoantibody-driven diseases. However, FcRn inhibitors have significant limitations including suboptimal efficacy, lack of durable efficacy, high burden dosing profile, and an unknown long-term safety profile. We believe TOUR006 has the potential to be a superior therapy for a wide range of autoantibody-driven diseases compared to FcRn inhibitors. We have identified thyroid eye disease ("TED") as our beachhead indication for our FcRn+ strategy. TED is an autoimmune disease characterized by autoantibody-mediated activation of the tissues surrounding the eye, causing inflammation and disfigurement which can be sight-threatening in severe cases. We have identified a substantial body of published clinical observations characterizing the beneficial off-label use of IL-6 pathway inhibitors, namely Actemra® (tocilizumab), an anti-IL-6R monoclonal antibody, in reducing inflammation, eye-bulging, and levels of autoantibodies in patients with TED. However, there has not previously been a formal, industry-sponsored development effort to study the IL-6 class for the treatment of TED. We are currently evaluating TOUR006 in our pivotal Phase 2b spiriTED trial in first-line TED. We initiated the spiriTED trial in September 2023 and expect to have topline data in the first half of 2025. Further, we expect to commence a pivotal Phase 3 trial of TOUR006 in first-line TED in 2024 with topline data expected in 2026.

Our second strategic path is cardiovascular inflammation. We believe TOUR006 has the potential to transform the care of high-risk patients by targeting key inflammatory pathways driving cardiovascular disease. Atherosclerotic cardiovascular disease ("ASCVD") is a leading cause of death globally. Preventing major adverse cardiovascular events ("MACE"), such as death, nonfatal myocardial infarction or nonfatal stroke, has the potential to significantly reduce global disease burden. IL-6 has been identified as a promising drug target for addressing the risk of MACE in ASCVD and multiple external Phase 3 cardiovascular outcome trials investigating IL-6 blockade are ongoing. We believe that TOUR006 potentially offers a meaningfully enhanced product profile to these competitor programs with a potential for subcutaneous dosing once every three months. As previously announced in January 2024, we have reached alignment with the FDA on the ASCVD clinical development program, including a Phase 2 trial evaluating the reduction of C-reactive protein ((("CRP),"), a validated biomarker for inflammation, with quarterly dosing of TOUR006 in patients with elevated cardiovascular risk. This trial is targeted to commence in the first half of 2024, with topline data expected in the first half of 2025. Pending success, the results from the Phase 2 trial are expected to position us to be ready in 2025 to commence a pivotal Phase 3 trial in cardiovascular disease.

We also plan to identify additional indication opportunities for TOUR006. In addition, we continue to evaluate new in-licensing and acquisition opportunities for assets that we believe have standard-of-care changing potential for patients with immune and inflammatory diseases.

Since our inception, we have funded our operations primarily with outside capital, including proceeds from the sale of Series A convertible preferred stock and a pre-closing financing, as discussed below, having raised aggregate gross proceeds of approximately $187.2 million as of the date hereof. However, we have incurred significant recurring losses, including net losses of $29.2 million, $19.7 million and $0.2 million for the nine months ended September 30, 2023, the year ended December 31, 2022 and the period from September 17, 2021 (inception) through December 31, 2021, respectively. In addition, we had an accumulated deficit of $49.1 million as of September 30, 2023.

Recent Developments

Merger with Talaris and Pre-Merger Financing Transaction

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

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

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

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

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

Series A Convertible Preferred Stock Financing Extension

On May 2, 2023, we entered into a Series A Preferred Stock Purchase Agreement (the "Series A Extension") with various entities and individuals for the purchase of additional shares of Series A convertible preferred stock. On May 2, 2023, we authorized the issuance and sale of 92,200,000 shares of our Series A convertible preferred stock, for total proceeds of $92.2 million. In addition, we issued 8,823,529 additional shares of our Series A convertible preferred stock to Pfizer Inc. ("Pfizer") pursuant to the anti-dilution provisions of the Pfizer License Agreement. See "*—Recent Developments—Pfizer License Agreement*" included below for further details on this arrangement.

License Agreements

Pfizer License Agreement

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

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

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

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

As of September 30, 2023, we do not owe any amounts under the Pfizer License Agreement and no royalties or milestone payments have been paid to date under the Pfizer License Agreement.

Lonza License Agreement

In May 2022, we entered into the Lonza License Agreement with Lonza Sales AG ("Lonza"), pursuant to which we obtained a worldwide, non-exclusive, sublicensable (subject to certain conditions) license under certain know-how to market, sell, offer for sale, distribute, import and export products containing TOUR006 ("Product"). We also obtained a non-exclusive, sublicensable (subject to certain conditions) license under certain licensed know-how to use, develop, and manufacture (including have manufactured in accordance with the terms of the Lonza License Agreement) the Product at premises approved by Lonza.

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

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

As of September 30, 2023, no royalty payments or other fees have been paid under the Lonza License Agreement.

Macroeconomic Considerations

Worldwide economic conditions remain uncertain and we continue to monitor the impact of macroeconomic conditions, including those related to COVID-19, global geopolitical conflicts such as the war in Ukraine and hostilities in the Middle East and rising inflation rates. The effect of macroeconomic conditions may not be fully reflected in our results of operations until future periods. If, however, economic uncertainty increases or the global economy worsens, our business, financial condition and results of operations may be harmed.

Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may experience increases in the near future on our operating costs, including our labor costs and research and development costs, due to supply chain constraints, consequences associated with COVID-19, global geopolitical conflicts, and employee availability and wage increases, which may result in additional stress on our working capital resources.

Components of Results of Operations

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the near future, if at all. If our development efforts are successful and result in commercialization of TOUR006 or any future product candidates or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from product sales, payments from such collaboration or license agreements or a combination thereof.

Operating Expenses

Research and Development Expenses

Research and development expenses consist primarily of consulting fees for medical and manufacturing advisory services related to our clinical trials, costs related to manufacturing material for preclinical studies and other costs incurred for the development of our product candidates. Research and development expenses include:

- personnel-related costs, including salaries, bonuses, related benefits and stock-based compensation expenses for employees engaged in research and development functions;
- payments to third parties in connection with the research and development of TOUR006 and any future product candidates, including agreements with third parties such as contract research organizations ("CROs"), clinical trial sites and consultants;
- the cost of manufacturing products for use in our clinical and preclinical studies, including payments to contract development and manufacturing organizations ("CDMOs") and consultants; and
- payments to third parties in connection with the preclinical development of TOUR006 and any future product candidates, including for outsourced professional scientific development services, consulting research and collaborative research.

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

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

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

The successful development of TOUR006 and any future product candidates is highly uncertain, and management does not believe it is possible at this time to accurately project the nature, timing and estimated costs of the efforts necessary to complete the development of, and obtain regulatory approval for, TOUR006 and any future product candidates. To the extent TOUR006 and any future product candidates continue to advance into larger and later-stage clinical trials, our expenses will increase substantially and may become more variable. The duration, costs and timing of development of TOUR006 and any future product candidates are subject to numerous uncertainties and will depend on a variety of factors, including:

- per patient trial costs;

- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to activate clinical sites and recruit, screen, and enroll eligible patients;
- the number of patients that participate in the trials;
- the length of hospitalization of patients in clinical trials
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the cost and timing of manufacturing TOUR006 and any future product candidates;
- the phase of development of TOUR006 and any future product candidates;
- the efficacy and safety profile of TOUR006 and any future product candidates;
- the timing and progress of nonclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- raising necessary additional funds;
- the progress of the development efforts of parties with whom we may enter into collaboration arrangements;
- our ability to maintain our current development program and to establish new ones;
- our ability to establish new licensing or collaboration arrangements;
- the successful initiation and completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority;
- the receipt and related terms of regulatory approvals from applicable regulatory authorities;
- the availability of drug substance and drug product for use in production of TOUR006 and any future product candidates;
- the development of commercial scale manufacturing and distribution processes for TOUR006 and any future product candidates;
- establishing and maintaining agreements with third-party manufacturers for commercial manufacturing, if we pursue a third party manufacturing strategy outside of the United States, and if TOUR006 and any future product candidates are approved;
- our ability to obtain and maintain patents, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- our ability to protect our rights in our intellectual property portfolio;
- the commercialization of TOUR006 and any future product candidates, if and when approved;
- obtaining and maintaining third-party insurance coverage and adequate reimbursement;
- the acceptance of TOUR006 and any future product candidates, if approved, by patients, the medical community and third-party payors;

- evolving standards of care in target indications;
- competition with other marketed or development-stage products; and
- a continued acceptable safety profile of our therapies following approval, if and when approved.

A change in the outcome of any of these variables with respect to the development of TOUR006 or any future product candidates could significantly change the costs and timing associated with the development of that product candidate. We may never succeed in obtaining regulatory approval for our product candidate or any future product candidates.

General and Administrative Expenses

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

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

Other Income, Net

Other income, net is primarily comprised of dividend income earned on investments in money market funds.

Income Tax

Since inception, we have not recorded any U.S. federal or state income tax benefits for the net losses hawse have incurred in each year, due to uncertainty of realizing a benefit from those items. We maintain a full valuation allowance on our federal and state deferred tax assets as our management has concluded that it is more likely than not that the deferred assets will not be utilized.

Results of Operations

Comparison of Nine Months Ended September 30, 2023 and 2022

The following table summarizes our results of operations for the periods presented:

	Nine months ended September 30,		
	2023	2022	Change
	(in thousands)		
Operating expenses:			
Research and development	$ 24,353	$ 13,733	$ 10,620
General and administrative	6,166	1,048	5,118
Total operating expenses	30,519	14,781	15,738
Loss from operations	(30,519)	(14,781)	(15,738)
Other income, net	1,297	—	1,297
Net loss	$(29,222)	$ (14,781)	$(14,441)

Research and Development Expense

Research and development expenses were $24.4 million for the nine months ended September 30, 2023, compared to $13.7 million for the nine months ended September 30, 2022. The increase of $10.6 million was primarily due to a $7.8 million increase in costs to manufacture products for use in clinical and preclinical studies, a $3.6 million increase in employee related expenses due to an increase in headcount, a $1.4 million increase in clinical and regulatory consulting services, and a $1.1 million increase in clinical trial costs as the TED 2b clinical trial commenced in the third quarter of 2023. The increase was partially offset by a decrease of $3.3 million in costs incurred related to the Pfizer License Agreement, as we recognized $8.8 million of expense related to the issuance of additional shares to Pfizer under the anti-dilution provision of the Pfizer License Agreement during the nine months ended September 30, 2023 and $12.1 million of expense related to the acquisition of IPR&D under the Pfizer License Agreement during the nine months ended September 30, 2022.

General and Administrative Expenses

General and administrative expenses were $6.2 million for the nine months ended September 30, 2023, compared to $1.0 million for the nine months ended September 30, 2022. The increase of $5.1 million was due to a $2.6 million increase in employee-related expenses due to an increase in headcount, a $0.3 million increase in legal fees related to commercial, employment and intellectual property matters, a $0.6 million increase in accounting, audit and tax fees, a $1.3 million increase in consulting fees, and a $0.3 million increase in other costs.

Other Income, Net

Other income, net for the nine months ended September 30, 2023 was $1.3 million. This consisted primarily of $1.3 million of dividends received from investments in money market funds.

Comparison of Year Ended December 31, 2022 and Period from September 17, 2021 (Inception) to December 31, 2021

The following table summarizes Tourmaline's results of operations for the periods presented:

	Year Ended December 31, 2022	Period from September 17, 2021 (Inception) to December 31, 2021	Change
		(in thousands)	
Operating expenses:			
Research and development	$ 17,526	$ 53	$ 17,473
General and administrative	2,175	173	2,002
Total operating expenses	19,701	226	19,475
Net loss	$ (19,701)	$ (226)	$(19,475)

Research and Development Expenses

Research and development expenses were $17.5 million for the year ended December 31, 2022, compared to $0.1 million for the period from September 17, 2021 (inception) to December 31, 2021. The increase of $17.4 million was primarily due to a $12.1 million increase in fees related to the acquisition of IPR&D under the Pfizer License Agreement, a $3.4 million increase in costs to manufacture products for use in clinical and preclinical studies, a $1.5 million increase in employee related expenses due to an increase in headcount and recruitment efforts, and a $0.4 million increase in clinical consulting fees.

General and Administrative Expenses

General and administrative expenses were $2.2 million for the year ended December 31, 2022, compared to $0.2 million for the period from September 17, 2021 (inception) to December 31, 2021. The increase of $2.0 million was primarily due to a $1.0 million increase in employee related expenses due to an increase in headcount, a $0.5 million increase in legal fees related to Tourmaline's legal entity conversion, intellectual property, and other corporate matters, a $0.3 million increase in accounting, audit and tax fees, a $0.1 million increase in other consulting fees and a $0.1 million increase in other costs.

Liquidity and Capital Resources

Sources of Liquidity

Since inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. We expect to continue to incur significant expenses and operating losses for the foreseeable future as we advance the clinical development of our product candidate and any future product candidates. We expect that our research and development and general and administrative costs will continue to increase significantly, including in connection with conducting clinical trials and potentially manufacturing for our product candidate and any future product candidates to support commercialization and providing general and administrative support for our operations, including the cost associated with operating as a public company. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements or other sources.

Since our inception, we have funded our operations primarily with outside capital, including proceeds from the sale of Series A convertible preferred stock and the Pre-Merger Financing Transaction, having raised aggregate gross proceeds of approximately $187.2 million as of the date hereof. However, we have incurred significant recurring losses, including net losses of $29.2 million, $19.7 million and $0.2 million for the nine months ended September 30, 2023, the year ended December 31, 2022 and the period from September 17, 2021 (inception) through December 31, 2021, respectively. In addition, we have an accumulated deficit of $49.1 million as of September 30, 2023.

As of September 30, 2023, we had $78.0 million in cash and cash equivalents. Based upon our current operating plan, we believe that our working capital will be sufficient to fund our operating expenses and capital expenditure requirements for the next twelve months from the date of our most recent financial statements and through 2026. We have based this estimate on assumptions that may prove to be incorrect, and we may use all of our available capital resources sooner than we expect.

Future Capital Requirements

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

In order to complete the development of TOUR006 and any future product candidates and to build the sales, marketing and distribution infrastructure that management believes will be necessary to commercialize product candidates, if approved, we will require substantial additional capital. Accordingly, until such time that we can generate a sufficient amount of revenue from product sales or other sources, if ever, management expects to seek to raise any necessary additional capital through private or public equity or debt financings, loans or other capital sources, which could include income from collaborations, partnerships or other marketing, distribution, licensing or other strategic arrangements with third parties, or from grants. To the extent that we raise additional capital through equity financings or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, including restricting our operations and limiting our ability to incur liens, issue additional debt, pay dividends, repurchase our own common stock, make certain investments or engage in merger, consolidation, licensing, or asset sale transactions. If we raise capital through collaborations, partnerships, and other similar arrangements with third parties, we may be required to grant rights to develop and market product candidates that we would otherwise prefer to develop and market themselves. We may be unable to raise additional capital from these sources on favorable terms, or at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from recent bank failures, other general macroeconomic conditions (including the ongoing impacts of COVID-19) and otherwise. The failure to obtain sufficient capital on acceptable terms when needed could have a material adverse effect on our business, results of operations or financial condition, including requiring us to delay, reduce or curtail our research, product development or future commercialization efforts. We may also be required to license rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose. Management cannot provide assurance that we will ever generate positive cash flow from operating activities.

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

- the scope, timing, progress, results, and costs of researching and developing TOUR006, and conducting larger and later-stage clinical trials;
- the scope, timing, progress, results, and costs of researching and developing other product candidates that we may pursue;
- the costs, timing, and outcome of regulatory review of TOUR006 and any future product candidates;
- the costs of future activities, including product sales, medical affairs, marketing, manufacturing, and distribution, for TOUR006 and any future product candidates for which we receive marketing approval;
- the costs of manufacturing commercial-grade products and sufficient inventory to support commercial launch;
- the revenue, if any, received from commercial sale of our products, should any of our product candidate and any future product candidates receive marketing approval;
- the cost and timing of attracting, hiring, and retaining skilled personnel to support our operations and continued growth;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish, maintain, and derive value from collaborations, partnerships or other marketing, distribution, licensing, or other strategic arrangements with third parties on favorable terms, if at all;
- the extent to which the profile of marketed or development stage competing products affects the clinical and commercial potential of our products;
- the extent to which we acquire or in-licenses other product candidates and technologies, if any; and
- the costs associated with operating as a public company.

A change in the outcome of any of these or other factors with respect to the development of TOUR006 and any of our future product candidates could significantly change the costs and timing associated with the development of that product candidate. Furthermore, our operating plans may change in the future, and we may need additional capital to meet the capital requirements associated with such operating plans.

As described above, if we progress TOUR006 through clinical development and, if approved, commercialize it, we may be required to pay Pfizer up to $128.0 million upon the achievement of specific development and regulatory milestones and up to $525.0 million upon the first achievement of specific sales milestones. We are also obligated to pay Pfizer a marginal royalty rate in the low double digits (less than 15%), subject to specified royalty reductions and pay Lonza a royalty in the low-single digits on the Net Sales (as defined in the Lonza License Agreement) of Product. In addition, we may owe Lonza a low six figure annual fee following the occurrence of a specified event depending on which entity manufactures the drug substance, all as specified in the Lonza License Agreement.

Cash Flows

Comparison of Nine Months Ended September 30, 2023 and 2022

The following table summarizes our sources and uses of cash for each of the periods presented:

	Nine months ended September 30,		
	2023	2022	Change
		(in thousands)	
Net cash used in operating activities	$(18,728)	$ (1,961)	$(16,767)
Net cash used in investing activities	(54)	(5,013)	4,959
Net cash provided by financing activities	88,578	19,850	68,728
Net increase in cash, cash equivalents and restricted cash	$ 69,796	$ 12,876	$ 56,920

Cash Flows from Operating Activities

For the nine months ended September 30, 2023, net cash used in operating activities was $18.7 million. This consisted primarily of a net loss of $29.2 million, offset by non-cash expenses of $10.5 million. Non-cash operating expenses consisted primarily of $8.8 million of research and development expense arising from the issuance of Series A convertible preferred stock pursuant to the Pfizer License Agreement's anti-dilution provision and stock-based compensation expense of $1.5 million.

For the nine months ended September 30, 2022, net cash used in operating activities was $2.0 million. This consisted primarily of a net loss of $14.8 million, offset by $12.1 million of non-cash expense recognized for IPR&D acquired under the Pfizer License Agreement and a decrease in operating assets and liabilities of $0.7 million. The decrease in net operating assets and liabilities was primarily attributable to an increase in accounts payable and accrued expenses of $0.8 million, offset by an increase in prepaid expenses of $0.1 million.

Cash Flows from Investing Activities

For the nine months ended September 30, 2023, net cash used in investing activities consisted of immaterial purchases of property and equipment.

For the nine months ended September 30, 2022, net cash used in investing activities consisted of $5.0 million related to the acquisition of IPR&D under the Pfizer License Agreement.

Cash Flows from Financing Activities

For the nine months ended September 30, 2023, net cash provided by financing activities was $88.6 million. This consisted of $91.8 million in net proceeds from the issuance of Series A convertible preferred stock and $0.1 million received from stock option exercises, partially offset by $3.4 million in payments of deferred offering costs.

For the nine months ended September 30, 2022, net cash provided by financing activities was $19.9 million. This consisted of $20.0 million in net proceeds from the issuance of Series A convertible preferred stock and $0.3 million from the issuance of a related party note payable, partially offset by the repayment of related party notes payable of $0.4 million.

Comparison of Year Ended December 31, 2022 and Period from September 17, 2021 (Inception) to December 31, 2021

The following table summarizes Tourmaline's sources and uses of cash for each of the periods presented:

	Year Ended December 31, 2022	Period from September 17, 2021 (Inception) to December 31, 2021	Change
		(in thousands)	
Net cash used in operating activities	$ (6,458)	$ —	$ (6,458)
Net cash used in investing activities	(5,068)	—	(5,068)
Net cash provided by financing activities	19,850	150	19,700
Net increase in cash and restricted cash	$ 8,324	$ 150	$ 8,174

Cash Flows from Operating Activities

For the year ended December 31, 2022, net cash used in operating activities was $6.5 million. This consisted primarily of a net loss of $19.7 million, partially offset by a decrease in net operating assets and liabilities of $0.9 million and net non-cash operating expenses of $12.3 million. The decrease in net operating assets and liabilities was primarily attributable to increases in accounts payable and accrued expenses of $1.0 million, offset by an increase in prepaid expenses of $0.1 million. The non-cash operating expenses consisted mainly of the write-off of the acquisition of IPR&D with no alternative future use in connection with the Pfizer License Agreement of $12.1 million and stock-based compensation expense of $0.2 million.

For the period from September 17, 2021 (Inception) to December 31, 2021, there were no cash flows used in or provided by operating activities.

Cash Flows from Investing Activities

For the year ended December 31, 2022, net cash used in investing activities was $5.1 million. This consisted primarily of $5.0 million for the acquisition of in-process research and development and $0.1 million for purchases of property and equipment.

For the period from September 17, 2021 (Inception) to December 31, 2021, there were no cash flows used in or provided by investing activities.

Cash Flows from Financing Activities

For the year ended December 31, 2022, net cash provided by financing activities was $19.9 million. This consisted primarily of $20.0 million in proceeds from the issuance of Series A convertible preferred stock and $0.3 million from the issuance of a related party note payable, partially offset by the repayment of related party notes payable of $0.4 million.

For the period from September 17, 2021 (Inception) to December 31, 2021, net cash provided by financing activities consisted of $0.2 million from the issuance of a related party note payable.

Contractual Obligations and Commitments

Research and Development and Manufacturing Agreements

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

Pfizer License Agreement

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

Critical Accounting Policies and Critical Accounting Estimates

Our financial statements are prepared in accordance with U.S. generally accepted accounting principles. The preparation of the financial statements and related disclosures requires management to make estimates and judgments that affect the reported amounts of assets, liabilities, costs and expenses, and the disclosure of contingent assets and liabilities in our financial statements. We base our estimates on historical experience, known trends and events and various other factors that management believes are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Management evaluates estimates and assumptions on a periodic basis. Our actual results may differ from these estimates.

While our significant accounting policies are described in more detail in the audited financial statements and related notes thereto of Legacy Tourmaline as of and for the year ended December 31, 2022, included in the proxy statement/prospectus filed with the SEC on September 15, 2023, management believes that the following accounting policies are critical to understanding our historical and future performance, as the policies relate to the more significant areas involving management's judgments and estimates used in the preparation of the financial statements.

Research and Development Expenses

Research and development expenses include all direct and indirect operating expenses supporting the products and processes in development, including payroll and benefits, which includes stock-based compensation, for research and development employees, consulting expenses, licensing fees, manufacturing costs, clinical research costs, and data and study acquisition costs.

Substantial portions of our clinical trials are performed by third-party laboratories, medical centers, CROs and other vendors. These vendors generally bill monthly for services performed, or bill based upon milestone achievement. For clinical trials, we accrue expenses based upon the estimated percentage of work completed and the remaining contract milestones. At times, we are obligated to make upfront payments upon execution of research and development agreements. Upfront payments, including nonrefundable amounts, for goods or services that will be used or rendered for future research and development activities are capitalized as prepaid expenses until such goods are delivered or the related services are performed. We estimate the period over which such services will be performed based on the terms of the agreements as well as the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, management adjusts the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, management's understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Costs incurred in obtaining licenses through asset acquisitions are charged to research and development expense if the licensed product is in the process of being researched and developed and the licensed product has no alternative future use.

Contingent Milestone Payments

As described above, we will be responsible for significant future contingent payments to Pfizer under the Pfizer License Agreement upon the achievement of certain development, regulatory and sales milestones. The size and timing of these milestone payments will vary greatly depending on numerous factors outlined above.

The transaction provided for under the Pfizer License Agreement was accounted for as an asset acquisition. Contingent consideration in an asset acquisition is generally recognized when it is probable that a liability has been incurred, and the amount can be reasonably estimated. None of the milestone payments are probable and no liability has been incurred as of the date hereof.

Stock-Based Compensation Expense

We record stock-based compensation issued to employees, advisors and non-employee directors based on our estimate of the fair value of stock-based awards at the grant date. We estimate the fair value of our stock-based awards using the Black-Scholes option-pricing model which requires inputs, including (a) the quoted market price of our common stock, (b) the expected stock price volatility, (c) the calculation of expected term of the award, (d) the risk-free interest rate and (e) expected dividends. The grant date fair value of the award is then recognized over the requisite service period, which is the vesting period of the award and is generally four years. Forfeitures are recognized as they are incurred.

Due to the lack of significant trading history of our common stock on the public market and a lack of company-specific historical and implied volatility data, management based its estimate of expected volatility on the historical volatility of a representative group of companies with similar characteristics to ours, including industry and therapeutic focus, stage of development, size, and market capitalization. Management believes the group selected has sufficient similar economic and industry characteristics and includes companies that are most representative of us.

The expected term is calculated as the midpoint between the vesting term and original contractual term. The risk-free interest rate is based on observed interest rates appropriate for the term of the stock-based awards. The dividend yield assumption is based on history and expectation of paying no dividends.

Recently Issued and Adopted Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842), and subsequently has issued additional guidance (collectively, "ASC 842"), which requires companies to generally recognize operating and financing lease liabilities and corresponding right-of-use assets on the balance sheet. The Company adopted ASC 842 on January 1, 2022 using the modified retrospective approach, with no restatement of prior periods. The Company's adoption of ASU No. 2016-02 is described in detail in the audited financial statements and related notes thereto of Legacy Tourmaline as of and for the year ended December 31, 2022, included in the proxy statement/prospectus filed with the SEC on September 15, 2023.

UNAUDITED PRO FORMA CONDENSED COMBINED FINANCIAL INFORMATION

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

Immediately prior to the effective time of the Merger, Talaris effected a 1-for-10 reverse stock split of its common stock (the "Reverse Stock Split"). The historical per share information of Talaris and the exchange ratio included within the unaudited pro forma condensed combined financial information reflect the impact of the Reverse Stock Split.

Subject to the terms and conditions of the Merger Agreement, at the closing of the Merger and related transactions (the "effective time"): (i) each then-outstanding share of Legacy Tourmaline common stock (including shares of Legacy Tourmaline common stock issued upon conversion of Legacy Tourmaline Series A convertible preferred stock and shares of Legacy Tourmaline common stock issued in the Pre-Merger Financing Transaction (as defined below)) was converted into the right to receive 0.07977 shares of Talaris common stock in accordance with the exchange ratio set forth in the Merger Agreement and (ii) each then-outstanding option to purchase Legacy Tourmaline common stock was converted into and became an option to purchase Talaris common stock, subject to adjustment as set forth in the Merger Agreement. Under the terms of the Merger Agreement, immediately prior to the effective time, the board of directors of Talaris took action to accelerate the vesting of certain equity awards of Talaris. Prior to the effective time, all Talaris equity awards were settled or cancelled.

The equity holders of Talaris immediately prior to the effective time owned approximately 21.1% of the aggregate number of outstanding shares of the Combined Company's common stock immediately after the effective time, and the equity holders of Legacy Tourmaline immediately prior to the effective time owned approximately 78.9% of the aggregate number of outstanding shares of the Combined Company's common stock immediately after the effective time on a fully-diluted basis using the treasury stock method.

On June 22, 2023, Legacy Tourmaline entered into a securities purchase agreement with certain investors, pursuant to which Legacy Tourmaline sold 51,297,919 shares of Legacy Tourmaline common stock for an aggregate purchase price of approximately $75.0 million immediately prior to the Closing (the "Pre-Merger Financing Transaction"). Shares of Legacy Tourmaline common stock issued pursuant to the Pre-Merger Financing Transaction were converted into shares of Combined Company common stock in accordance with the exchange ratio set forth in the Merger Agreement.

In addition, in connection with the closing of the Merger, Talaris declared a cash dividend to the pre-Merger Talaris stockholders of approximately $64.7 million in the aggregate (which, together with certain cash payments to Talaris equity award holders was approximately $67.5 million in the aggregate).

The following unaudited pro forma condensed combined financial information gives effect to the Merger, which has been accounted for as a reverse recapitalization under U.S. generally accepted accounting principles ("GAAP"), and gives effect to the Pre-Merger Financing Transaction. The transaction was accounted for as a reverse recapitalization of Talaris by Legacy Tourmaline because on the effective date of the Merger, the pre-combination assets of Talaris were primarily cash, marketable securities and other non-operating assets. Also, under GAAP, Legacy Tourmaline is considered the accounting acquirer for financial reporting purposes. This determination is based on the facts that, immediately following the Merger: (i) Legacy Tourmaline's equity holders own a substantial majority of the voting rights in the Combined Company (ii) Legacy Tourmaline's largest stockholder retained the largest interest in the combined company; (iii) Legacy Tourmaline designated a majority (five of seven) of the initial members of the board of directors of the Combined Company and (iv) Legacy Tourmaline's executive management team became the management of the Combined Company.

As a result of Legacy Tourmaline being treated as the accounting acquirer, Legacy Tourmaline's assets and liabilities were recorded at their pre-combination carrying amounts. Talaris' assets and liabilities were measured and recognized at their fair values as of the effective date of the Merger, and combined with the assets, liabilities, and results of operations of Legacy Tourmaline after the consummation of the Merger. As a result, upon consummation of the Merger, the historical financial statements of Legacy Tourmaline became the historical consolidated financial statements of the Combined Company.

The unaudited pro forma condensed combined balance sheet combines the historical balance sheets of Talaris and Legacy Tourmaline as of September 30, 2023 and depicts the accounting of the Merger under GAAP ("pro forma balance sheet transaction accounting adjustments"). The unaudited pro forma condensed combined statements of operations for the nine-month period ended September 30, 2023 and for the year ended December 31, 2022 combines the historical results of Talaris and Legacy Tourmaline for those periods and depicts the pro forma balance sheet transaction accounting adjustments assuming that those adjustments were made as of January 1, 2022 ("pro forma statements of operations transaction accounting adjustments"). Collectively, the pro forma balance sheet transaction accounting adjustments and the pro forma statements of operations transaction accounting adjustments are "transaction accounting adjustments."

The unaudited pro forma condensed combined financial information is provided for illustrative purposes only, does not necessarily reflect what the actual consolidated results of operations would have been had the Merger occurred on the dates indicated and may not be useful in predicting the future consolidated results of operations or financial position. The unaudited pro forma condensed combined financial information is based on the assumptions and adjustments that are described in the accompanying notes.

The unaudited pro forma condensed combined financial information does not give effect to the potential impact of current financial conditions, regulatory matters, operating efficiencies or other savings or expenses that may be associated with the integration of the two companies. The actual results reported in periods following the Merger may differ significantly from those reflected in the unaudited pro forma condensed combined financial information presented herein for a number of reasons, including, but not limited to, differences in the assumptions used to prepare this unaudited pro forma condensed combined financial information.

The unaudited pro forma condensed combined financial information, including the notes thereto, should be read in conjunction with the separate historical financial statements of Talaris and Legacy Tourmaline, and their respective management's discussion and analysis of financial condition and results of operations included in Talaris' Quarterly Report on Form 10-Q for the quarter ended September 30, 2023 filed with the U.S. Securities and Exchange Commission (the "SEC") on November 14, 2023, the Combined Company's Current Report on Form 8-K filed with the SEC on November 14, 2023 (including Exhibit 99.2 therein) and Exhibit 99.2 to the Current Report on Form 8-K of which this exhibit forms a part.

GAAP requires the evaluation of certain assumptions, estimates, or determination of financial statement classifications. During the preparation of the unaudited pro forma condensed combined financial information, management conducted a final review of the Combined Company's accounting policies in order to determine if differences in accounting policies require adjustment or reclassification of Talaris' results of operations or reclassification of assets or liabilities to conform to Legacy Tourmaline's accounting policies and classifications. As a result of this review, management did not identify any material differences that impact these unaudited pro forma condensed combined financial statements.

UNAUDITED PRO FORMA CONDENSED COMBINED BALANCE SHEET
AS OF SEPTEMBER 30, 2023
(in thousands)

	Historical		Transaction Accounting Adjustments	Notes	Pro Forma Combined Total
	Talaris	Legacy Tourmaline			
Assets					
Current assets:					
Cash and cash equivalents	$ 67,083	$ 78,043	$ (5,634)	A, B, C, E, G	$139,492
Marketable securities	79,941	—	—		79,941
Prepaid expenses and other current assets	4,023	1,619	—		5,642
Total current assets	151,047	79,662	(5,634)		225,075
Property and equipment, net	—	94	—		94
Assets held for sale	14	—	—		14
Right-of-use assets	—	396	—		396
Restricted cash	—	227	—		227
Other assets	—	4,756	(4,756)	A	—
Total assets	$ 151,061	$ 85,135	$ (10,390)		$225,806
Liabilities, convertible preferred stock, and stockholders' equity (deficit)					
Current liabilities:					
Accounts payable	$ 136	$ 1,014	$ (66)	A	$ 1,084
Accrued expenses and other current liabilities	7,335	3,238	(1,300)	A	9,273
Lease liability, current	634	220	—		854
Total current liabilities	8,105	4,472	(1,366)		11,211
Share repurchase liability	82	—	(82)	F	—
Other liabilities	—	65	—		65
Lease liability, net of current	—	233	—		233
Total liabilities	8,187	4,770	(1,448)		11,509
Series A convertible preferred stock	—	127,772	(127,772)	D	—
Stockholders' equity (deficit):					
Common stock	—	1	1	K	2
Additional paid-in capital	351,980	1,741	(80,522)	K	273,199
Accumulated deficit	(208,991)	(49,149)	199,236	K	(58,904)
Accumulated other comprehensive loss	(115)	—	115	K	—
Total stockholders' equity (deficit)	142,874	(47,407)	118,830	K	214,297
Total liabilities, convertible preferred stock, and stockholders' equity (deficit)	$ 151,061	$ 85,135	$ (10,390)		$225,806

UNAUDITED PRO FORMA CONDENSED COMBINED STATEMENT OF OPERATIONS FOR THE NINE MONTHS ENDED SEPTEMBER 30, 2023
(in thousands, except share and per share data)

	Historical		Transaction Accounting Adjustments	Notes	Pro Forma Combined Total
	Talaris	Legacy Tourmaline			
Operating expenses					
Research and development	$ 17,770	$ 24,353	$ —		$ 42,123
General and administrative	21,322	6,166	—		27,488
Restructuring costs	10,958	—	—		10,958
Total operating expenses	50,050	30,519	—		80,569
Gain on asset sales	538	—	—		538
Loss from operations	(49,512)	(30,519)	—		(80,031)
Interest and other income, net	5,262	1,297	—		6,559
Net loss	$ (44,250)	$ (29,222)	$ —		$ (73,472)
Net loss per common share, basic and diluted	$ (10.48)	$ (2.35)			$ (3.73)
Weighted average number of shares of common stock outstanding, basic and diluted	4,221,205	12,456,670		J	19,706,120

UNAUDITED PRO FORMA CONDENSED COMBINED STATEMENT OF OPERATIONS
FOR THE YEAR ENDED DECEMBER 31, 2022
(in thousands, except share and per share data)

	Historical		Transaction Accounting Adjustments	Notes	Pro Forma Combined Total
	Talaris	Legacy Tourmaline			
Operating expenses					
Research and development	$ 57,005	$ 17,526	$ 3,292	B, E	$ 77,823
General and administrative	19,472	2,175	5,545	B, E	27,192
Total operating expenses	76,477	19,701	8,837		105,015
Loss from operations	(76,477)	(19,701)	(8,837)		(105,015)
Interest and other income, net	2,583	—	—		2,583
Net loss	$ (73,894)	$ (19,701)	$ (8,837)		$ (102,432)
Net loss per common share, basic and diluted	$ (17.91)	$ (1.79)			$ (5.25)
Weighted average number of shares of common stock outstanding, basic and diluted	4,124,839	10,996,529		J	19,493,278

NOTES TO THE UNAUDITED PRO FORMA CONDENSED COMBINED FINANCIAL INFORMATION

1. Description of the Transaction

On June 22, 2023, Legacy Tourmaline, Talaris, and Merger Sub entered into the Merger Agreement, pursuant to which Merger Sub, a wholly owned subsidiary of Talaris, merged with and into Legacy Tourmaline at the closing, with Legacy Tourmaline surviving as a wholly owned subsidiary of Talaris.

Immediately prior to the effective time, Talaris effected the Reverse Stock Split. The historical per share information of Talaris and the exchange ratio set forth in the Merger Agreement included within the unaudited pro forma condensed combined financial information reflect the impact of the Reverse Stock Split.

On October 19, 2023, Legacy Tourmaline, Talaris, and Merger Sub consummated the transactions contemplated by the Merger Agreement. Upon the completion of the Merger, Legacy Tourmaline changed its name from "Tourmaline Bio, Inc." to "Tourmaline Sub, Inc.," and Talaris changed its name from "Talaris Therapeutics, Inc." to "Tourmaline Bio, Inc."

Upon the effective time, all shares of Legacy Tourmaline common stock and Legacy Tourmaline Series A convertible preferred stock outstanding immediately prior to the effective time were converted into the right to receive 15,877,090 shares of Talaris common stock in the aggregate, based on the exchange ratio of 0.07977 Talaris shares per Legacy Tourmaline shares. Talaris assumed outstanding and unexercised stock options to purchase shares of Legacy Tourmaline common stock (the "Legacy Tourmaline options"), and in connection with the Merger the Legacy Tourmaline options were converted into stock options to purchase shares of the Combined Company's common stock based on the exchange ratio set forth in the Merger Agreement.

As a result of the Merger, holders of Legacy Tourmaline capital stock and stock options to purchase Legacy Tourmaline common stock own, or hold rights to acquire, in the aggregate approximately 78.9% of the fully-diluted common stock of the Combined Company and Talaris stockholders and option holders own, or hold rights to acquire, in the aggregate approximately 21.1% of the fully-diluted common stock of the Combined Company following the effective time.

The aggregate value of the consideration paid by Legacy Tourmaline in the Merger was approximately $53.2 million. The fair value of consideration transferred is based on the number of shares of common stock Talaris stockholders owned upon consummation of the Merger, multiplied by the closing price of Talaris common stock on the effective date of October 19, 2023. The fair value of consideration transferred is not indicative of the combined entities enterprise value upon consummation of the Merger. As the Merger was accounted for as a reverse recapitalization, any difference between the consideration transferred in the Merger and the fair value of the net assets acquired was recorded as an adjustment to additional paid-in capital.

Concurrently with the execution and delivery of the Merger Agreement, certain parties entered into subscription agreements with Legacy Tourmaline and purchased, prior to the consummation of the Merger, 51,297,919 shares of Legacy Tourmaline common stock in the Pre-Merger Financing Transaction for an aggregate purchase price of approximately $75.0 million. In connection with the Pre-Merger Financing Transaction, Legacy Tourmaline amended its certificate of incorporation to increase the authorized number of shares of common stock. Shares of Legacy Tourmaline common stock issued pursuant to the Pre-Merger Financing Transaction were converted into shares of the Combined Company's common stock in accordance with the exchange ratio set forth in the Merger Agreement at the effective time.

In addition, in connection with the closing of the Merger, Talaris declared a cash dividend to the pre-Merger Talaris stockholders of approximately $64.7 million in the aggregate (which, together with certain cash payments to Talaris equity award holders was approximately $67.5 million in the aggregate).

2. Basis of Pro Forma Presentation

The unaudited pro forma condensed combined financial information has been prepared pursuant to the rules and regulations of Article 11 of SEC Regulation S-X. The unaudited pro forma condensed combined statements of operations for the nine month period ended September 30, 2023 and for the year ended December 31, 2022, give effect to the Merger as if it had been consummated on January 1, 2022.

The unaudited pro forma condensed combined balance sheet as of September 30, 2023 gives effect to the Merger and combines the historical balance sheets of Talaris and Legacy Tourmaline as of such date. Based on Legacy Tourmaline's review of Legacy Tourmaline's and Talaris' summary of significant accounting policies and discussions between management teams of Legacy Tourmaline and Talaris, the nature and amount of any adjustments to the historical financial statements of Talaris to conform its accounting policies to those of Legacy Tourmaline were not material.

For accounting purposes, Legacy Tourmaline is considered to be the acquiring company and the Merger was accounted for as a reverse recapitalization of Talaris by Legacy Tourmaline.

For purposes of these pro forma financial statements, the purchase price consideration consists of the following (in thousands, except share and per share amounts):

	Amount
Number of shares of common stock of the Combined Company to be owned by Talaris stockholders (i)	4,331,860
Multiplied by the fair value per share of Talaris common stock (ii)	$ 12.08
Total	$ 52,329
Fair value of accelerated Talaris equity awards based on pre-combination service (iii)	$ 918
Total purchase price	$ 53,247

(i) Reflects the number of shares of common stock of the Combined Company that Talaris equity holders owned as of the closing of the Merger pursuant to the Merger Agreement. For purposes of this unaudited pro forma condensed combined financial information, this amount is calculated based on shares of Talaris common stock outstanding as of October 19, 2023 and excludes accelerated Talaris equity awards, which are included in item (iii) below.

(ii) Reflects the price per share of Talaris common stock, which is the closing trading price of Talaris common stock on October 19, 2023.

(iii) Reflects the acquisition-date fair value of the accelerated Talaris equity awards attributable to pre-combination service.

Under reverse recapitalization accounting, the assets and liabilities of Talaris were recorded, as of the completion of the Merger, at their fair value. Any difference between the consideration transferred and the fair value of the net assets of Talaris following determination of the actual purchase consideration for Talaris was reflected as an adjustment to additional paid-in capital. Consequently, under reverse recapitalization accounting, the subsequent financial statements of Legacy Tourmaline reflect the operations of the acquirer for accounting purposes together with a deemed issuance of shares, equivalent to the shares held by Talaris stockholders and a recapitalization of the equity of Legacy Tourmaline. The accompanying unaudited proforma condensed combined financial information is derived from the historical financial statements of Talaris and Legacy Tourmaline and include adjustments to give pro forma effect to reflect the accounting for the transaction in accordance with GAAP. The historical financial statements of Legacy Tourmaline shall become the historical financial statements of the Combined Company.

Legacy Tourmaline and Talaris may incur significant costs associated with integrating the operations of Legacy Tourmaline and Talaris after the Merger is completed. The unaudited pro forma condensed combined financial information does not reflect the costs of any integration activities or benefits that may result from realization of future cost savings from operating efficiencies expected to result from the Merger.

3. Shares of Talaris Common Stock Issued to Legacy Tourmaline Stockholders upon Closing of the Merger

Prior to the completion of the Merger, all outstanding shares of Legacy Tourmaline Series A convertible preferred stock were converted into shares of Legacy Tourmaline common stock, which was exchanged for shares of Talaris common stock based on the exchange ratio determined in accordance with the Merger Agreement. The exchange ratio for purposes of the unaudited pro forma condensed combined financial information was derived on a fully-diluted basis as of October 19, 2023 using a valuation for Legacy Tourmaline of approximately $305.0 million, inclusive of the Pre-Merger Financing Transaction, and a valuation for Talaris of approximately $81.7 million (including Talaris legacy proceeds of ($0.8) million). The number of shares of common stock that Talaris issued to Legacy Tourmaline stockholders (ignoring rounding of fractional shares) was determined as follows:

	Amount
Shares of Legacy Tourmaline common stock outstanding as of September 30, 2023	19,589,325
Shares of Legacy Tourmaline common stock issued upon conversion of Legacy Tourmaline Series A convertible preferred stock	128,148,529
Shares of Legacy Tourmaline common stock issuable upon exercise of outstanding options to purchase common stock (1)	9,575,883
Shares of Legacy Tourmaline common stock issued upon consummation of the Pre-Merger Financing Transaction (See Note 4.C)	51,297,919
Total Legacy Tourmaline common equivalent shares	208,611,656
Exchange Ratio	0.07977
Shares of Talaris common stock issued to Legacy Tourmaline stockholders upon closing of the Merger	16,640,952

(1) Calculated on a fully-diluted basis using the treasury stock method.

4. Adjustments to Unaudited Pro Forma Condensed Combined Financial Statements

The impact of transactions that will not recur in the statement of operations of the registrant beyond twelve months following the consummation of the Merger are shown as adjustments to the unaudited pro forma condensed combined financial statements. These adjustments include expenses, gains or losses, and the related tax effects incurred in connection with the Merger and the Pre-Merger Financing Transaction.

Adjustments included in the column under the heading "Transaction Accounting Adjustments" are primarily based on information contained within the Merger Agreement and the Pre-Merger Financing Transaction.

Given Legacy Tourmaline's history of net losses and valuation allowance, management assumed a statutory tax rate of 0%. Therefore, the pro forma adjustments to the condensed combined statements of operations resulted in no additional income tax adjustment to the unaudited pro forma condensed combined financial information.

The transaction accounting adjustments included in the unaudited pro forma condensed combined financial information are as follows:

A. To reflect transaction costs that were incurred by Legacy Tourmaline of $10.6 million in connection with the Merger, including the Pre-Merger Financing Transaction (See Note 4.C for further details), such as legal fees, accounting expenses and consulting fees. As all Legacy Tourmaline transaction costs have been paid by the date hereof, of which $3.4 million of these costs have been paid as of September 30, 2023 and $1.4 million of these costs have been accrued in the historical balance sheet as of September 30, 2023, the adjustment was recorded as a decrease to cash and cash equivalents of $7.2 million, a decrease to other assets of $4.8 million, a decrease to accounts payable of $0.1 million, a decrease in accrued liabilities of $1.3 million, and a reduction to additional paid-in capital of $10.6 million in the unaudited pro forma condensed combined balance sheet. As the Merger was accounted for as a reverse recapitalization equivalent to the issuance of equity for the net assets, primarily cash and marketable securities, of Talaris, these direct and incremental costs are treated as a reduction of the net proceeds received within additional paid-in capital. The transaction costs incurred in connection with the Pre-Merger Financing Transaction are recorded as a reduction of the net proceeds received within additional paid-in capital.

B. To reflect compensation expense of $5.9 million related to severance and retention bonuses resulting from pre-existing employment agreements or from approval by Talaris' board of directors that was paid in cash in connection with the Merger that were not incurred as of September 30, 2023. As all severance and retention bonuses have been paid by the date hereof, the adjustment was recorded as a decrease in cash and cash equivalents of $5.9 million and an increase to accumulated deficit of $5.9 million in the unaudited pro forma condensed combined balance sheet. In the unaudited pro forma condensed combined statement of operations for the year ended December 31, 2022, $1.9 million and $4.0 million are reflected as research and development and general and administrative expense, respectively.

C. To reflect the Pre-Merger Financing Transaction, in which 51,297,919 shares of Legacy Tourmaline common stock were issued at approximately $1.46 per share for total cash proceeds of approximately $75.0 million, as an increase in cash and cash equivalents, common stock, and additional paid-in capital for in the unaudited pro forma condensed combined balance sheet. See Note 4.A for transaction costs incurred in connection with the Merger, which includes transaction costs related to the Pre-Merger Financing Transaction.

D. To reflect (1) the conversion of 128,148,529 shares of Legacy Tourmaline Series A convertible preferred stock into 128,148,529 shares of Legacy Tourmaline common stock immediately prior to the Merger and (2) the exchange of outstanding Legacy Tourmaline common stock, which includes the aforementioned conversion of Legacy Tourmaline Series A convertible preferred stock and the shares of Legacy Tourmaline common stock issued upon consummation of the Pre-Merger Financing Transaction (See Note 4.C), into shares of Talaris common stock based on the exchange ratio set forth in the Merger Agreement. The number of shares of common stock that Talaris issued to Legacy Tourmaline stockholders was determined as follows:

	Amount
Shares of Legacy Tourmaline common stock outstanding as of September 30, 2023	19,589,325
Shares of Legacy Tourmaline common stock issued upon conversion of Legacy Tourmaline Series A convertible preferred stock	128,148,529
Shares of Legacy Tourmaline common stock issued upon consummation of the Pre-Merger Financing Transaction (See Note 4.C)	51,297,919
Total Legacy Tourmaline shares of common stock outstanding at the effective time	199,035,773
Exchange Ratio	0.07977
Shares of Talaris common stock issued to Legacy Tourmaline stockholders upon closing of the Merger	15,877,090

E. To reflect $0.9 million related to pre-combination stock-based compensation expense and $1.9 million related to post-combination stock-based compensation expense as an increase in additional paid-in capital and accumulated deficit in the unaudited pro forma condensed combined balance sheet related to the modification of Talaris equity awards to accelerate vesting. In addition, to reflect $1.0 million of post-combination stock-based compensation expense related to the payment of cash in excess of fair value to settle Talaris equity awards as a decrease in cash and cash equivalents and accumulated deficit in the unaudited pro forma condensed combined balance sheet. In the unaudited pro forma condensed combined statement of operations for the year ended December 31, 2022, $1.4 million and $1.5 million is reflected as research and development and general and administrative expense, respectively.

F. To reflect the reclassification of the share repurchase liability to additional paid-in capital as a result of the accelerated vesting of Talaris equity awards. In the unaudited pro forma condensed combined balance sheet, $0.1 million is reflected as a decrease to share repurchase liability and an increase in additional paid-in capital.

G. To reflect the payment of the $66.5 million dividend (including certain cash payments to Talaris equity award holders) to Talaris stockholders as a decrease in cash and cash equivalents and additional paid-in capital in the unaudited pro forma condensed combined balance sheet. This adjustment excludes the $1.0 million of cash payments to Talaris equity award holders reflected in Note 4.E.

H. To reflect the elimination of Talaris historical equity.

I. To reflect the effect of the reverse recapitalization of Talaris for a total of $142.9 million, which is the net assets of Talaris as of September 30, 2023.

J. The pro forma combined basic and diluted earnings per share have been adjusted to reflect the pro forma net income for the nine months ended September 30, 2023 and the year ended December 31, 2022. In addition, the number of shares used in calculating the pro forma combined basic and diluted net loss per share has been adjusted to reflect the total number of shares of common stock of the Combined Company for the respective periods. For the nine months ended September 30, 2023 and the year ended December 31, 2022 , the pro forma weighted average shares have been calculated as follows:

	September 30, 2023	December 31, 2022
Historical weighted-average number of Legacy Tourmaline shares of common stock outstanding–basic and diluted	12,456,670	10,996,529
Impact of the Pre-Merger Financing Transaction assuming consummation as of January 1, 2022	51,297,919	51,297,919
Impact of Legacy Tourmaline Series A convertible preferred stock assuming conversion as of January 1, 2022	128,148,529	128,148,529
Total	191,903,118	190,442,977
Application of exchange ratio to historical weighted-average number of Legacy Tourmaline shares of common stock outstanding	0.07977	0.07977
Adjusted Legacy Tourmaline weighted-average number of shares of common stock outstanding–basic and diluted	15,308,112	15,191,636
Historical weighted-average number of Talaris common shares outstanding–basic and diluted	4,221,205	4,124,839
Impact of Talaris shares of common stock related to stock awards assuming accelerated vesting as of January 1, 2022	176,803	176,803
Pro forma combined weighted average number of shares of common stock outstanding–basic and diluted	19,706,120	19,493,278

K. The total impact to equity for the above adjustments as reflected in the table below:

(in thousands, except share data)	Notes	Common Stock – Talaris Shares	Common Stock – Talaris Amount	Common Stock – Legacy Tourmaline Shares	Common Stock – Legacy Tourmaline Amount	Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive loss	Stockholders' equity (deficit)
Conversion of outstanding Legacy Tourmaline Series A convertible preferred stock into common stock	D	—	$ —	128,148,529	$ 13	$ 127,759	$ —	$ —	$ 127,772
Pre-Merger Financing Transaction	C	—	—	51,297,919	5	74,995	—	—	75,000
Pre-combination stock-based compensation for accelerated Talaris equity awards	E	—	—	—	—	918	(918)	—	—
Elimination of Talaris' historical equity carrying value	H	(4,282,848)	—	—	—	(351,980)	208,991	115	(142,874)
Exchange of outstanding Legacy Tourmaline common stock into Talaris common stock based on the Exchange Ratio	D	15,877,090	2	(199,035,773)	(19)	17	—	—	—
Reverse recapitalization of Talaris	I	4,459,651	—	—	—	142,874	—	—	142,874
Transaction costs associated with the Merger and Pre-Merger Financing Transaction	A	—	—	—	—	(10,644)	—	—	(10,644)
Reclass of share repurchase liability	F	—	—	—	—	82	—	—	82
Pre-closing dividend (including certain cash payments to Talaris equity award holders)	G	—	—	—	—	(66,495)	—	—	(66,495)
Retention and severance payments to Talaris employees	B	—	—	—	—	—	(5,880)	—	(5,880)
Recognition of post-combination stock compensation for accelerated Talaris equity awards	E	—	—	—	—	1,952	(2,957)	—	(1,005)
Total adjustment		16,053,893	$ 2	(19,589,325)	$ (1)	$ (80,522)	$ 199,236	$ 115	$ 118,830