Filed Pursuant to Rule 424(b)(5)
Registration No. 333-289360

PROSPECTUS SUPPLEMENT
(To Prospectus dated August 18, 2025)

aTyr Pharma, Inc.
Up to $79,994,251
Common Stock

This prospectus supplement amends and restates the information in our prospectus supplement dated December 23, 2024 and, accordingly, the information in this prospectus supplement supersedes the information contained in that prospectus supplement, or the prior prospectus supplement. We previously entered into an Open Market Sale Agreement℠, or the sales agreement, with Jefferies LLC, or Jefferies, dated April 22, 2022, as amended December 23, 2024, relating to the sale of shares of our common stock, par value $0.001 per share. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to $215.0 million (inclusive of $65.0 million of sales made prior to the amendment of the sales agreement, which sales were made pursuant to a prospectus supplement and accompanying prospectus that was amended and restated by the prior prospectus supplement) from time to time and at our option through Jefferies, acting as our sales agent. Pursuant to the prior prospectus supplement and accompanying prospectus contained in our Registration Statement on Form S-3 (File No. 333-275455), or the prior prospectus, we issued and sold 445,732 shares of our common stock under the sales agreement for gross proceeds of approximately $70.0 million. As of immediately prior to the filing date of this prospectus supplement, shares of our common stock having an aggregate offering price of up to $79,994,251 remained unsold under the sales agreement and the prior prospectus. The common stock remaining available to be sold under the prior prospectus as of the filing date of this prospectus supplement will no longer be offered and sold under the prior prospectus and will instead be offered and sold under this prospectus supplement and the accompanying prospectus. Accordingly, this prospectus supplement and accompanying prospectus covers the offer and sale of our common stock having an aggregate offering price of up to $79,994,251 to be sold under the sales agreement as of the date of this prospectus supplement.

Our common stock is traded on the Nasdaq Capital Market under the symbol "ATYR." On November 5, 2026, the last reported sale price of our common stock on the Nasdaq Capital Market was $6.03 per share.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made by any method deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Jefferies is not required to sell any specific number or dollar amount of our securities, but will act as sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Jefferies and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

We may also sell shares of our common stock to Jefferies as principal for its own account upon terms to be agreed upon between us and Jefferies.

Jefferies will be entitled to compensation under the terms of the sales agreement at a fixed commission rate of up to 3.0% of the gross sales price per share sold under the sales agreement. In connection with the sale of common stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities. See "Plan of Distribution" beginning on page S-16 of this prospectus supplement for additional information regarding the compensation to be paid to Jefferies.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-8 of this prospectus supplement and under similar headings in the accompanying prospectus and other documents that are incorporated by reference into this prospectus supplement and the accompanying prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR PASSED UPON THE ADEQUACY OR ACCURACY OF THIS PROSPECTUS SUPPLEMENT OR THE ACCOMPANYING PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

Jefferies

The date of this prospectus supplement is November 6, 2026.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of a "shelf" registration statement on Form S-3 (File No. 333-289360) that we filed with the Securities and Exchange Commission, or the SEC, and is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates the information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information, some of which may not be applicable to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We have not, and Jefferies has not, authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus we have authorized for use in connection with this offering. We and Jefferies take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in, or incorporated by reference into, this prospectus supplement, the accompanying prospectus and any free writing prospectus we have authorized for use in connection with this offering is accurate only as of the respective dates thereof, regardless of the time of delivery of each such document. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, and any free writing prospectus we have authorized for use in connection with this offering in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections titled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference" in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and soliciting offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless the context indicates otherwise, as used in this prospectus supplement and the accompanying prospectus, references to "we," "us," "our," the "Company" and "aTyr" refer to aTyr Pharma, Inc. and our subsidiary. We own various U.S. federal trademark applications and unregistered trademarks, including our company name. All other trademarks or trade names referred to in this prospectus supplement and the accompanying prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement and the accompanying prospectus are referred to without the symbols ® and ™, but such references should not be construed as any indication that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

INDUSTRY, MARKET AND OTHER DATA

Certain industry, market and competitive position data contained in this prospectus supplement and the information incorporated by reference herein relate to or are based on industry studies, research, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, research, publications, surveys and other data to be reliable as of the date of this prospectus supplement and based on reasonable assumptions, we have not independently verified, and make no representations as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources, and all such data involve risks and uncertainties and are subject to change based on various factors. Internal estimates are derived from publicly available information released by industry analysts and third-party sources, our internal research and our industry experience, and are based on assumptions made by us based on such data and our knowledge of the industry and market, which we believe to be reasonable.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement or the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement, including the information under the heading "Risk Factors" in this prospectus supplement beginning on page S-8 and in the documents incorporated by reference into this prospectus supplement.

Company Overview

We are a clinical stage biotechnology company leveraging evolutionary intelligence to translate tRNA synthetase biology into new therapies for fibrosis and inflammation. tRNA synthetases are ancient, essential proteins that have evolved novel domains that regulate diverse pathways extracellularly in humans. Our discovery platform is focused on unlocking hidden therapeutic intervention points by uncovering signaling pathways driven by our proprietary library of domains derived from all 20 tRNA synthetases.

Efzofitimod

Our lead therapeutic candidate is efzofitimod, a novel biologic immunomodulator in clinical development for the treatment of interstitial lung disease, or ILD, a group of immune-mediated disorders that can cause inflammation and fibrosis, or scarring, of the lungs. Efzofitimod is a tRNA synthetase derived therapy that selectively modulates activated myeloid cells through neuropilin-2, or NRP2, to resolve aberrant inflammation without immune suppression and potentially prevent the progression of fibrosis. ILDs are predominantly immune-mediated disorders that are characterized by chronic inflammation, which can lead to progressive fibrosis of the lung. There are limited treatment options for ILD and there remains a high unmet medical need. Pulmonary sarcoidosis and systemic sclerosis, or SSc, also known as scleroderma-associated ILD, or SSc-ILD, are two major forms of ILD.

Pulmonary Sarcoidosis

In September 2025, we announced top-line data from a global Phase 3 randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis, or the EFZO-FIT study. The EFZO-FIT study was a 52-week study in 268 patients with pulmonary sarcoidosis consisting of three parallel cohorts randomized equally to either 3.0 mg/kg or 5.0 mg/kg of efzofitimod or placebo dosed intravenously once every four weeks for a total of 12 doses, with a 4-week safety follow-up. The study design incorporated a protocol guided steroid taper in the first 12 weeks of the study, followed by continued taper or rescue until week 48. The study did not meet its primary endpoint of change from baseline in mean daily oral corticosteroid, or OCS, dose at week 48. The change from baseline in mean daily OCS dose reduced to an average of 2.79 mg for 5.0 mg/kg efzofitimod vs. 3.52 mg for placebo (p=0.3313). The study's statistical analysis plan was designed on a hierarchical assessment basis, as such, since the primary endpoint was not met, all subsequent statistical testing is reported as nominal findings. The study demonstrated a clinically meaningful improvement in the King's Sarcoidosis Questionnaire, or KSQ,-Lung score at week 48 for 5.0 mg/kg efzofitimod compared to placebo (p=0.0479), with a responder analysis of patients who achieved complete steroid withdrawal at week 48 with an improved KSQ-Lung score also showing improvement in patients treated with 5.0 mg/kg efzofitimod compared to placebo (p=0.0196). Lung function as measured by forced vital capacity, or FVC, at week 48 was maintained in all groups. Efzofitimod was generally well-tolerated at both the 3.0 mg/kg and 5.0 mg/kg doses, consistent with previously observed safety profile in all trials conducted to date. At the European Respiratory Society Congress in late September 2025, we announced additional findings from the EFZO-FIT study, including analyses of additional pre-specified outcomes that demonstrated clinical improvements in mean change from baseline in the Fatigue Assessment Total Score (p=0.0226) and KSQ-General Health score (p=0.0197) in patients treated with 5.0 mg/kg efzofitimod versus placebo. Treatment with efzofitimod was also associated with a trend toward a greater proportion of patients achieving steroid-free status for at least six months. Based on the trial findings, which we believe indicate drug activity for efzofitimod as evidenced by improvements across multiple clinically relevant efficacy endpoints, we held a Type C meeting with the FDA in mid-April 2026 to review the results of the EFZO-FIT study and determine the path forward for efzofitimod in pulmonary sarcoidosis. In May 2026, we received the official meeting minutes from the FDA.

Based on feedback from the FDA, we planned to continue the development of efzofitimod in pulmonary sarcoidosis in a proposed Phase 3 study in patients with chronic, symptomatic pulmonary sarcoidosis with restrictive lung disease utilizing FVC as the primary endpoint of the study and the KSQ-Lung score as the key secondary endpoint, or the Proposed Phase 3 Study. We chose these endpoints based on the FDA's indication that FVC and KSQ-Lung are direct measures of how patients suffering from pulmonary sarcoidosis

function and feel, and we concluded FVC to be a more appropriate primary endpoint at this time pending further content validation work for KSQ-Lung as recommended by the FDA. We determined the patient population for the Proposed Phase 3 Study, those with restrictive lung disease, based on data from the EFZO-FIT study which included 44 patients with restrictive lung disease (defined as FVC percent predicted ≤ 80%) and showed a difference of 124 ml in change from baseline in FVC between restrictive patients treated with 5.0 mg/kg efzofitimod and placebo.

In September 2026, we announced that we had reached alignment with the FDA on the Proposed Phase 3 Study protocol, and that we expected to initiate study-related activities in the fourth quarter of 2026. We are prioritizing strategic partnerships to further advance the Proposed Phase 3 Study beyond the completion of these study-related activities.

The Proposed Phase 3 Study would be a global, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of efzofitimod in patients with moderate to severe pulmonary sarcoidosis. The Proposed Phase 3 Study would be a 54-week study and would consist of two parallel cohorts randomized equally to either 5.0 mg/kg efzofitimod or placebo dosed intravenously once every 3 weeks for a total of 17 doses. The Proposed Phase 3 Study would be intended to enroll up to approximately 372 patients with symptomatic pulmonary sarcoidosis with restrictive lung disease receiving a stable dose of ≤ 5.0 mg daily oral corticosteroid and/or a background immunosuppressant. All background treatment would remain stable throughout the duration of the Proposed Phase 3 Study. The primary endpoint of the Proposed Phase 3 Study would be changed from baseline in FVC at week 48 and the key secondary endpoint would be changed from baseline in the KSQ-Lung score at week 48. We expect the Proposed Phase 3 Study will include additional risk mitigation strategies, enhanced safety surveillance for potential development of anti-synthetase syndrome and a data safety monitoring committee based on the FDA's acknowledgement of the reasonableness of the increased dosing regimen from a clinical pharmacology perspective, subject to inclusion of adequate safety monitoring and risk mitigation procedures.

SSc-ILD

Our Phase 2 proof-of-concept clinical trial of efzofitimod, or the EFZO-CONNECT study, is a randomized, double-blind placebo-controlled proof-of-concept study to evaluate the efficacy, safety and tolerability of efzofitimod in patients with SSc-ILD. This is a 28-week study with three parallel cohorts randomized 2:2:1 to either 270 mg or 450 mg of efzofitimod or placebo dosed intravenously monthly for a total of six doses. The study intended to enroll up to 25 patients at multiple centers in the United States. The objective of the study is to evaluate the efficacy of multiple doses of IV efzofitimod on pulmonary, cutaneous (limited or diffuse) and systemic manifestations in patients with SSc-ILD. The primary endpoint is reduction in FVC. Secondary endpoints include certain measures regarding safety and tolerability. In July 2024, we amended the study to add an open-label extension, or OLE, to patients. Patients who complete the study and wish to receive ongoing treatment with efzofitimod are eligible to participate in the 24-week OLE. In June 2025, we announced interim data from the study showing three out of four efzofitimod-treated diffuse SSc-ILD patients showed clinically important improvement based on the modified Rodnan Skin Score, or mRSS, assessment at 12 weeks and that efzofitimod was generally well-tolerated at all doses. We have completed enrollment of the study with 23 patients. Full study results are anticipated in the second quarter of 2027.

Discovery Platform

In parallel with our clinical development of efzofitimod, we have been advancing our discovery pipeline of tRNA synthetases and NRP2 antibodies.

tRNA Synthetase Candidates

Using efzofitimod as a model, we have developed a process to advance novel tRNA synthetase domains from a concept to therapeutic candidate. This process leverages our early discovery work as well as current scientific understanding of tRNA synthetase evolution, protein structure, gene splicing and tissue-specific regulation to identify potentially active protein domains. Screening approaches are employed to identify target cells and extracellular receptors for these tRNA synthetase-derived proteins. These cellular systems can then be used in mechanism-of-action studies to elucidate the role these proteins play in cellular responses and their potential therapeutic utility. We are working to identify new tRNA synthetase based drug candidates through our internal discovery efforts and external collaboration efforts. Utilizing our novel approach, we have identified target receptors for domains of certain additional tRNA synthetases, gaining insights into their potential biological activity in immunology and fibrosis. These fragments form the basis of our additional pipeline candidates. We plan to further elucidate the therapeutic potential of these candidates through mechanistic investigations, including nonclinical studies.

ATYR0101

ATYR0101 is a fusion protein derived from a domain of aspartyl-tRNA synthetase, or DARS, that is engineered with a human Fc region to extend its serum half-life. The molecule possesses a unique mechanism of action focused on the selective elimination of activated myofibroblasts, which are the primary cellular drivers of pathological extracellular matrix, or ECM, deposition in fibrotic diseases. ATYR0101 specifically targets Latent TGF-β Binding Protein-1, or LTBP-1, within the ECM, binding to a region that encompasses the fibrillin-1 binding domain at the C-terminus. LTBP-1 serves a dual role in matrix architecture by organizing structural proteins and modulating the signaling of Transforming Growth Factor-beta, or TGF-β, through a complex mechanosensory apparatus. Early data suggest ATYR0101 exerts its antifibrotic effects by inducing apoptosis of myofibroblasts in a TGFβ dependent manner. We believe ATYR0101 may have broad therapeutic applications in multiple fibrotic diseases, such as pulmonary fibrosis, SSc, liver fibrosis and kidney fibrosis. In October 2026, we announced a publication demonstrating the anti-fibrotic effects of ATYR0101 in the Journal of Biological Chemistry. We have initiated IND-enabling activities for ATYR0101 and expect to advance ATYR0101 into a clinical trial in 2027.

NRP2 antibodies

ATYR2810

ATYR2810 is a fully humanized monoclonal antibody that is designed to specifically and functionally block the interaction between NRP2 and one of its primary ligands, vascular endothelial growth factor, or VEGF. NRP2 is a pleiotropic cell surface receptor that is highly expressed on certain tumors and increased NRP2 expression is associated with worse outcomes in many cancers, such as overall survival, metastasis and resistance to targeted therapies. The role of NRP2 and VEGF signaling in the tumor microenvironment and its importance in the progression of certain aggressive cancers is becoming increasingly validated. In October 2026, we announced that we entered into a research collaboration with Albert Einstein College of Medicine to further the development and testing of ATYR2810. The collaboration will be led by Bang H. Hoang, M.D., Arnold and Madaleine Penner, Professor and Co-Director of Orthopaedic Oncology in the Department of Orthopaedic Surgery at Montefiore Einstein. Dr. Hoang's research focuses on the pathophysiology and molecular mechanisms of bone and soft tissue cancer, including evaluating the role of NRP2 in pediatric bone cancers such as osteosarcoma. ATYR2810 has demonstrated anti-tumor effects in multiple nonclinical models, including non-small cell lung cancer, triple-negative breast cancer, renal cell carcinoma and glioblastoma. These findings have been presented at scientific conferences, including the American Academy of Cancer Research, and published in a landmark publication in Science Translational Medicine.

Corporate Restructuring and Program Prioritization

In August 2026, our board of directors approved the implementation of a corporate restructuring and program prioritization plan, or the Restructuring Plan, to streamline our operations and conserve capital. In connection with the Restructuring Plan, we reduced our total workforce by approximately 60% to 20 full-time employees. We recorded charges of approximately $4.6 million for employee severance, employee health benefit obligations and other related termination benefits. As of September 30, 2026, approximately $2.9 million of these amounts remain to be paid through September 2027. In addition, we recorded approximately $1.8 million in non-cash stock-based compensation charges related to the acceleration of vesting of outstanding equity awards in accordance with our Executive Severance and Change in Control Policy as well as for modifications to certain stock option awards to extend the post-termination exercise periods, and we recorded approximately $1.5 million in non-cash impairment charges of certain of our long-lived assets, including approximately $0.9 million in non-cash impairment of our operating lease ROU and approximately $0.6 million related to our property and equipment.

Recent Developments

On October 16, 2026, at a special meeting of stockholders, our stockholders approved a series of alternate amendments to our Restated Certificate of Incorporation, as amended, to effect, at the option of our board of directors, a reverse stock split of all issued and outstanding shares of our common stock, at a ratio between 1-for-10 to 1-for-50, inclusive, with the final ratio to be determined by our board of directors in its sole discretion. On October 16, 2026, our board of directors approved effecting a reverse stock split of all issued and outstanding shares of our common stock at a ratio of 1-for-40. On October 27, 2026, we filed a Certificate of Amendment to the Restated Certificate of Incorporation with the Secretary of State of the State of Delaware to effect such a reverse stock split. The reverse stock split became effective at 5:00 p.m. Eastern Time on October 28, 2026.

Our common stock began trading on the Nasdaq Capital Market on a split-adjusted basis on October 29, 2026.

Corporate Information

We were incorporated under the laws of the State of Delaware in September 2005. Our principal executive office is located at 10240 Sorrento Valley Road, Suite #300, San Diego, California 92121 and our telephone number is (858) 731-8389. Our website address is www.atyrpharma.com. The information on, or that can be accessed through, our website does not constitute part of this prospectus supplement, and you should not rely on any such information in making the decision whether to purchase our common stock.

The Offering

Common Stock Offered by Us	Shares of our common stock having an aggregate offering price of up to $79,994,251.
Common Stock to be Outstanding after this Offering[(1)]	Up to 15,777,709 shares (as more fully described in the notes following this table), assuming sales of 13,266,044 shares of our common stock in this offering at an assumed offering price of $6.03 per share, which was the last reported sale price of our common stock on the Nasdaq Capital Market on November 5, 2026. The actual number of shares issued will vary depending on how many shares of our common stock we choose to sell and the prices at which such sales occur.
Plan of Distribution	"At the market offering" that may be made from time to time, if at all, through or to Jefferies, as sales agent or principal. See "Plan of Distribution" on page S-16 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds from this offering for general corporate purposes. See "Use of Proceeds" on page S-12 of this prospectus supplement for more information about the intended use of net proceeds from this offering.
Risk Factors	See the section titled "Risk Factors" on page S-8 in this prospectus supplement, and other information included in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus for a discussion of certain factors you should carefully consider before deciding to invest in shares of our common stock.
Nasdaq Capital Market Symbol	"ATYR"

(1) The number of shares of our common stock to be outstanding after this offering is based on 2,511,665 shares of common stock outstanding as of September 30, 2026 and excludes:

- 301,111 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2026 at a weighted average exercise price of $113.01 per share;
- 5,203 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2026;
- 194,622 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, as amended, as of September 30, 2026;
- 6,826 shares of common stock reserved for future issuance under our 2022 Inducement Plan as of September 30, 2026; and
- 13,519 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan as of September 30, 2026.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of the outstanding stock options described above and no vesting and settlement of outstanding restricted stock units described above and gives effect to a 1-for-40 reverse stock split of all issued and outstanding shares of our common stock that became effective at 5:00 p.m. Eastern Time on October 28, 2026.

The number of shares of our common stock to be outstanding immediately after this offering as shown above does not include 37,565 shares of our common stock sold between September 30, 2026 and the date of this prospectus supplement under the sales agreement.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described in the documents incorporated by reference in this prospectus supplement, the accompanying prospectus and any applicable prospectus supplement, as well as other information we include or incorporate by reference into this prospectus supplement, the accompanying prospectus and any applicable prospectus supplement, and in any free writing prospectus that we have authorized for use in connection with this offering before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our common stock could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus supplement, the accompanying prospectus, the documents incorporated herein by reference, and any free writing prospectus that we have authorized for use in connection with this offering also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in the documents incorporated herein by reference, including our most recent Annual Report on Form 10-K, as updated by our subsequent Quarterly Reports on Form 10-Q, each of which is incorporated by reference into this prospectus supplement, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future, and other documents we file with the SEC that are incorporated by reference into this prospectus supplement.

Risks Related to this Offering

Our management may invest or spend the net proceeds from this offering in ways with which you may not agree or in ways which may not yield a significant return.

We currently anticipate that we will use the net proceeds from this offering as described in "Use of Proceeds". However, our management will have considerable discretion in the application of the net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not improve our operating results or enhance the value of our common stock.

You may experience dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 13,266,044 shares of our common stock are sold at an assumed offering price of $6.03 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on November 5, 2026, for aggregate gross proceeds of approximately $80.0 million, and after deducting commissions and estimated offering expenses payable by us, you may experience immediate dilution. The exercise of outstanding stock options and the vesting and settlement of outstanding restricted stock units may result in further dilution of your investment. See the section entitled "Dilution" beginning on page S-14 for a more detailed illustration of the dilution you may incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share paid by investors in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

The common stock offered hereby will be sold in "at the market offerings," and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and accordingly may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and number of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of sales made at prices lower than the prices they paid.

The actual number of shares we will issue under the sales agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver sales notices to Jefferies at any time throughout the term of the sales agreement. The number of shares that are sold by Jefferies after delivering a sales notice will fluctuate based on the market price of our common stock during the sales period and limits we set with Jefferies.

Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares that will be ultimately issued.

It is not possible to predict the actual number of shares we will sell under the sales agreement, or the gross proceeds resulting from those sales.

Subject to certain limitations in the sales agreement and compliance with applicable law, we have the discretion to deliver instruction to Jefferies to sell shares of our common stock at any time throughout the term of the sales agreement. The number of shares that are sold through Jefferies after our instruction will fluctuate based on a number of factors, including the market price of our common stock during the sales period, the limits we set with Jefferies in any instruction to sell shares, and the demand for our common stock during the sales period. Because the price per share of each share sold will fluctuate during this offering, it is not currently possible to predict the number of shares that will be sold or the gross proceeds to be raised in connection with those sales.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

If securities or industry analysts do not continue to publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price will likely decline. In addition, if one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Future sales of our common stock in the public market, or the perception that such sales could occur, could cause our stock price to fall.

The sale of a substantial number of shares of our common stock or other equity-related securities in the public markets, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We may sell large quantities of our common stock at any time pursuant to this prospectus supplement or in one or more separate offerings. We cannot predict the effect that future sales of common stock or other equity-related securities would have on the market price of our common stock.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus, including the documents that we incorporate by reference herein, contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as "may," "will," "could," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "potential," "continue," and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus supplement, including the documents incorporated herein by reference, and in particular those factors referenced in the section "Risk Factors" of this prospectus supplement and in the documents incorporated herein by reference.

These forward-looking statements are based on our management's belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our clinical trials of our product candidates and whether the results of our trials will be sufficient to support U.S. or foreign regulatory approvals;
- whether our existing capital resources will be sufficient to enable us to complete any particular portion of our planned clinical development of our product candidates or support our operations through particular time periods;
- our ability to enter new collaborations and licensing arrangements and the timing of any payments we may receive under such arrangements;
- the cost increases as a result of global geopolitical tension, armed conflicts, potential future health pandemics, liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets, tariffs and trade tensions, higher interest rates and financial and credit market fluctuations, volatility in the capital markets, labor shortages, economic slowdowns, recessions or market corrections, inflation and monetary supply shifts and tightening of credit markets;
- the likelihood and timing of regulatory approvals for our product candidates;
- our ability to identify and discover additional product candidates;
- our ability to obtain, maintain, defend and enforce intellectual property rights protecting our product candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- the performance of third-party service providers and independent contractors upon whom we rely to conduct our clinical trials and to manufacture our product candidates or certain components of our product candidates;
- our ability to develop sales and marketing capabilities or to enter into strategic partnerships to develop and commercialize our product candidates;
- the timing and success of the commercialization of our product candidates;
- the rate and degree of market acceptance of our product candidates;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific, medical or management personnel;
- our expected use of net proceeds from this offering; and
- other risks and uncertainties, including those described under the heading "Risk Factors" in our filings with the SEC.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, the risks discussed in the "Risk Factors" section, and the risk factors and cautionary statements

described in other documents that we file from time to time with the SEC, specifically under "Item 1A. Risk Factors" and elsewhere in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q, and our Current Reports on Form 8-K.

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

Given these uncertainties, you should not place undue reliance on our forward-looking statements. These forward-looking statements speak only as of the date on which the statements were made. Except as may be required by applicable law, we do not undertake to update any forward-looking statements after the date of this prospectus supplement or the respective dates of documents incorporated by reference herein that include forward-looking statements.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to $79,994,251 from time to time in this offering. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. There can be no assurance that we will sell any shares under or fully utilize the sales agreement with Jefferies as a source of financing.

We currently intend to use the net proceeds from this offering primarily for general corporate purposes. General corporate purposes may include research and development, manufacturing and clinical development costs to support the advancement of our product candidates, and the expansion of our product candidate pipeline, working capital and capital expenditures. In addition, we may use a portion of the net proceeds for acquisitions of, or investments in, businesses, products and technologies that complement our business, although we have no current plans, commitments or agreements to do so as of the date of this prospectus supplement.

This expected use of our net proceeds from this offering represents our intentions based upon our current plans and business conditions as of the date of this prospectus supplement, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our product candidate development, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. Given the nature of this offering, we cannot specify with certainty all of our anticipated uses of the net proceeds from this offering as of the date of this prospectus supplement.

As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the application of the net proceeds from this offering. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. In addition, any future debt instruments may materially restrict our ability to pay dividends on our common stock. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, tax considerations, legal or contractual restrictions, business prospects, the requirements of current or then-existing debt instruments, general economic conditions and other factors our board of directors may deem relevant.

DILUTION

Our net tangible book value as of September 30, 2026 was approximately $33.8 million, or $13.45 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2026. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the assumed sale of 13,266,044 shares of our common stock in this offering at an assumed offering price of $6.03 per share, the last reported sale price of our common stock on the Nasdaq Capital Market on November 5, 2026, and, after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2026 would have been approximately $111.2 million, or $7.05 per share. This represents an immediate increase (decrease) in net tangible book value of $(6.40) per share to existing stockholders and immediate dilution (accretion) of $(1.02) in the as adjusted net tangible book value per share to new investors in this offering. Dilution (accretion) per share to new investors is determined by subtracting as adjusted net tangible book value per share after giving effect to this offering from the assumed offering price per share paid by new investors. The following table illustrates this per share dilution to new investors purchasing shares of our common stock in this offering:

Assumed offering price per share			$	6.03
Net tangible book value per share as of September 30, 2026	$	13.45		
Increase (decrease) per share attributable to new investors in this offering	$	(6.40)		
As adjusted net tangible book value per share after giving effect to this offering			$	7.05
Dilution (accretion) in net tangible book value per share to investors purchasing shares in this offering at the assumed offering price			$	(1.02)

The table above assumes for illustrative purposes only an aggregate of 13,266,044 shares of our common stock are sold at a price of $6.03 per share during the term of the sales agreement with Jefferies. The shares, if any, sold in this offering will be sold from time to time at various prices. An increase of $1.00 per share in the price at which the shares are sold to an assumed offering price of $7.03 per share shown in the table above, assuming all of our common stock in the aggregate amount of approximately $80.0 million is sold at that price, would increase our adjusted net tangible book value per share after the offering to $8.01 per share and would result in immediate dilution (accretion) in net tangible book value per share to new investors in this offering to $(0.98) per share, after deducting commissions and estimated offering expenses payable by us. A decrease of $1.00 per share in the price at which the shares are sold to an assumed offering price of $5.03 per share, assuming all of our common stock in the aggregate amount of approximately $80.0 million is sold at that price, would decrease our adjusted net tangible book value per share after the offering to $6.04 per share and would result in immediate dilution (accretion) in net tangible book value per share to new investors in this offering to $(1.01) per share, after deducting commissions and estimated offering expenses payable by us. This information is supplied for illustrative purposes only.

The above discussion and table are based on 2,511,665 shares of common stock outstanding as of September 30, 2026, and excludes:

- 301,111 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2026 at a weighted average exercise price of $113.01 per share;
- 5,203 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2026;
- 194,622 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, as amended, as of September 30, 2026;
- 6,826 shares of common stock reserved for future issuance under our 2022 Inducement Plan as of September 30, 2026; and
- 13,519 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan as of September 30, 2026.

Unless otherwise indicated, the discussion and table above gives effect to a 1-for-40 reverse stock split of all issued and outstanding shares of our common stock that became effective at 5:00 p.m. Eastern Time on October 28, 2026.

To the extent that any outstanding stock options are exercised, any restricted stock units vest and settle, warrants are issued, new options or restricted stock units are issued under our stock-based compensation plans, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

The number of shares of our common stock outstanding as shown above does not include 37,565 shares of our common stock sold under the sales agreement between September 30, 2026 and the date of this prospectus supplement.

In addition, we may choose to raise additional capital due to market conditions or strategic conditions, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our shareholders.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies, under which we may offer and sell up to $215,000,000 of our shares of common stock from time to time through Jefferies acting as agent (inclusive of $65.0 million of sales made prior to the amendment of the sales agreement, which sales were made pursuant to a prospectus supplement and accompanying prospectus that was amended and restated by the prior prospectus supplement). Sales of our shares of common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell our shares of common stock under the sales agreement, we will notify Jefferies of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the sales agreement to sell our shares of common stock are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Jefferies is generally anticipated to occur on the first trading day following the date on which the sale was made. Sales of our shares of common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission rate equal to 3.0% of the aggregate gross proceeds we receive from each sale of our shares of common stock. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. In addition, we agreed to reimburse Jefferies for the fees and disbursements of its counsel, which became payable upon execution of the amendment to the sales agreement, in an amount not to exceed $50,000, in addition to certain ongoing disbursements of its legal counsel. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the sales agreement, as amended, will be approximately $100,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on the Nasdaq Capital Market on the day following each day on which our shares of common stock are sold under the sales agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of our shares of common stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of our shares of common stock pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all shares of common stock subject to the sales agreement and (ii) the termination of the sales agreement as permitted therein. We and Jefferies may each terminate the sales agreement at any time upon ten trading days' prior notice.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement, as amended, is filed as an exhibit to our reports filed with the SEC under the Exchange Act and incorporated by reference into this prospectus supplement. See the sections titled "Where You Can Find More Information" and "Incorporation of Certain Information by Reference" below for more information.

Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Jefferies may at any time hold long or short positions in such securities.

A prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute the prospectus supplement and the accompanying prospectus electronically.

LEGAL MATTERS

The validity of the issuance of the common stock offered hereby will be passed upon for us by Cooley LLP, San Diego, California. Jefferies is being represented in this offering by Duane Morris, LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2025, as set forth in their report, which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the information requirements of the Exchange Act and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents may be accessed through the SEC's electronic data gathering, analysis and retrieval system via electronic means, including the SEC's home page on the Internet (http://www.sec.gov).

Copies of certain information filed by us with the SEC are also available on our website at www.atyrpharma.com. Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus.

This prospectus supplement and the accompanying prospectus are part of a registration statement on Form S-3 that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus supplement in accordance with the rules of the SEC. Documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus supplement or the accompanying prospectus about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website, as provided above.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement and the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. Any statement contained in this prospectus supplement, the accompanying prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement and accompanying prospectus to the extent that a statement contained in this prospectus supplement and accompanying prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be "filed" with the SEC) until this offering is completed:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2025, filed with the SEC on March 5, 2026;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2025 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), filed with the SEC on March 26, 2026;
- our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2026, June 30, 2026 and September 30, 2026, filed with the SEC on May 15, 2026, August 7, 2026 and November 5, 2026, respectively;

- our Current Reports on Form 8-K filed with the SEC on May 11, 2026, June 8, 2026, July 31, 2026, September 24, 2026, October 16, 2026, and October 27, 2026.
- The description of our common stock contained in our registration statement on Form 8-A (Registration No. 001-37378) filed with the SEC on May 6, 2015 under Section 12(b) of the Exchange Act, including any amendment or report filed for the purpose of updating such description, including Exhibit 4.6 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, as filed with the Commission on March 14, 2024.

Upon written or oral request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, a copy of the documents incorporated by reference into this prospectus supplement but not delivered with the prospectus supplement. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus supplement, at no cost by writing or telephoning us at the following address:

aTyr Pharma, Inc., 10240 Sorrento Valley Road, Suite #300, San Diego, California 92121, Attention: Secretary, or by telephone request to (858) 731-8389.

You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.atyrpharma.com. Information contained on our website is not incorporated by reference into this prospectus supplement, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus supplement.

This prospectus supplement and the accompanying prospectus are part of a registration statement we filed with the SEC. We have incorporated exhibits into this prospectus supplement and the accompanying prospectus. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus supplement or the accompanying prospectus. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement, the accompanying prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus supplement or those documents.

PROSPECTUS

$300,000,000



Common Stock
Preferred Stock
Debt Securities
Warrants

From time to time, we may offer and sell up to $300,000,000 of any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

Our common stock is listed on The Nasdaq Capital Market under the symbol "ATYR." On August 6, 2025, the closing price for our common stock, as reported on The Nasdaq Capital Market, was $5.34 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on The Nasdaq Capital Market or any securities market or other exchange of the securities, if any, covered by the applicable prospectus supplement.

We may sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or options to purchase additional securities will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading "Risk Factors" contained in this prospectus beginning on page 7 as well as those contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is , 2025.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission (SEC), using a "shelf" registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings for up to a total aggregate offering price of $300,000,000. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading "Incorporation of Certain Information by Reference," before investing in any of the securities offered.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

Neither we, nor any agent, underwriter or dealer has authorized any person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus prepared by or on behalf of us or to which we have referred you. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

This prospectus and the information incorporated herein by reference contain summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading "Where You Can Find More Information."

PROSPECTUS SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements and related notes, and the exhibits to the registration statement of which this prospectus is a part, before making an investment decision.

Unless the context otherwise indicates, references in this prospectus to "aTyr Pharma," "we," "our," "us" and "Company" refer, collectively, to aTyr Pharma, Inc., together with our subsidiary, Pangu BioPharma Limited.

Company Overview

We are a clinical stage biotechnology company leveraging evolutionary intelligence to translate tRNA synthetase biology into new therapies for fibrosis and inflammation. tRNA synthetases are ancient, essential proteins that have evolved novel domains that regulate diverse pathways extracellularly in humans. Our discovery platform is focused on unlocking hidden therapeutic intervention points by uncovering signaling pathways driven by our proprietary library of domains derived from all 20 tRNA synthetases.

Efzofitimod

Our lead therapeutic candidate is efzofitimod, a first-in-class biologic immunomodulator in clinical development for the treatment of interstitial lung disease (ILD), a group of immune-mediated disorders that can cause inflammation and fibrosis, or scarring, of the lungs. Efzofitimod is a tRNA synthetase derived therapy that selectively modulates activated myeloid cells through neuropilin-2 (NRP2) to resolve aberrant inflammation without immune suppression and potentially prevent the progression of fibrosis. ILDs are predominantly immune-mediated disorders that are characterized by chronic inflammation, which can lead to progressive fibrosis of the lung. There are limited treatment options for ILD and there remains a high unmet medical need. Sarcoidosis and systemic sclerosis (SSc, also known as scleroderma)-associated ILD (SSc-ILD) are two major forms of ILD. The U.S. Food and Drug Administration (FDA) has granted efzofitimod orphan drug designations for the treatment of sarcoidosis and for the treatment of SSc, and Fast Track designations for the treatment of pulmonary sarcoidosis and for the treatment of SSc-ILD. The European Commission has granted efzofitimod orphan drug designations for the treatment of sarcoidosis and for the treatment of SSc, based on the opinion of the European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP). The Pharmaceutical and Medical Devices Agency (PMDA) has granted efzofitimod orphan drug designation for the treatment of sarcoidosis to Kyorin Pharmaceutical Co., Ltd. (Kyorin), our partner in Japan.

In September 2021, we announced positive results and clinical proof-of-concept from a double-blind, placebo-controlled Phase 1b/2a clinical trial in 37 patients with pulmonary sarcoidosis. The study was designed to evaluate the safety, tolerability, immunogenicity and preliminary efficacy of three doses of intravenous (IV) efzofitimod, 1.0, 3.0 and 5.0 mg/kg, in the context of a forced steroid taper. Efzofitimod was safe and well-tolerated at all doses administered with no serious drug-related adverse events or signal of immunogenicity. Additionally, the study demonstrated consistent dose response for efzofitimod on key efficacy endpoints and improvements compared to placebo, including measures of steroid reduction, lung function, pulmonary sarcoidosis symptom measures and inflammatory biomarkers. These data were subsequently presented at the American Thoracic Society (ATS) International Conference and published in the peer-reviewed journal CHEST during 2022. In October 2024, the same published data for efzofitimod was featured in the Best of CHEST Journals session at the CHEST 2024 Annual Meeting.

In February 2022, we met with the FDA in an end-of-Phase 2 meeting to discuss our plans for subsequent clinical development and path to registration for efzofitimod for pulmonary sarcoidosis. Subsequently, we initiated a global pivotal Phase 3 randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis (the EFZO-FIT study). The EFZO-FIT study is a 52-week study consisting of three parallel cohorts randomized equally to either 3.0 mg/kg or 5.0 mg/kg of efzofitimod or placebo dosed intravenously once a month for a total of 12 doses. The study design incorporates a forced steroid taper. The objective of the study is to evaluate the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis. The primary endpoint of the study is steroid reduction. Secondary endpoints include measures of lung function assessed by health-related quality of life assessments and questionnaires (KSQ lung score) and forced vital capacity (FVC). In September 2022, we dosed the first patient in the study. During 2023, 2024 and 2025, we have had data and safety monitoring board (DSMB) reviews of our EFZO-FIT study. The DSMB reviews concluded that the study could continue unmodified. In July 2024, we completed enrollment of 268 subjects with pulmonary sarcoidosis at multiple centers in the United States, Europe, Brazil

and Japan, exceeding target enrollment. In July 2025, we completed the last patient visit in the EFZO-FIT study. Topline data from the study are expected in mid-September 2025.

In February 2024, we announced an Individual Patient Expanded Access Program (Individual Patient EAP). The Individual Patient EAP has been initiated based on blinded EFZO-FIT study investigator and patient participant feedback. The program is designed to allow access for patients who complete the Phase 3 EFZO-FIT study and wish to receive treatment with efzofitimod outside of the clinical trial. The administration of efzofitimod as part of the Individual Patient EAP will occur independent of the EFZO-FIT study protocol, and we, principal investigators and patients will remain blinded to the treatment that occurred as part of the EFZO-FIT study. As this Individual Patient EAP will occur independent of the EFZO-FIT study, this program is not an open-label extension (OLE) and no long-term data will be collected by us.

Based on the results of the Phase 1b/2a clinical trial, we believe efzofitimod has potential applications in the treatment of other ILDs, such as chronic hypersensitivity pneumonitis (CHP) and connective tissue disease related ILD (CTD-ILD), including SSc-ILD and rheumatoid arthritis-associated ILD. As such, we designed a focused Phase 2 proof-of-concept clinical trial of efzofitimod (the EFZO-CONNECT study) in patients with SSc-ILD. The EFZO-CONNECT study is a randomized, double-blind placebo-controlled proof-of-concept study to evaluate the efficacy, safety and tolerability of efzofitimod in patients with SSc-ILD. This is a 28-week study with three parallel cohorts randomized 2:2:1 to either 270 mg or 450 mg of efzofitimod or placebo dosed intravenously monthly for a total of six doses. The study intends to enroll up to 25 patients at multiple centers in the United States. The objective of the study is to evaluate the efficacy of multiple doses of IV efzofitimod on pulmonary, cutaneous (limited or diffuse) and systemic manifestations in patients with SSc-ILD. The primary endpoint is reduction in FVC. Secondary endpoints include certain measures regarding safety and tolerability. In July 2024, we amended the study to add an OLE to patients. Patients who complete the study and wish to receive ongoing treatment with efzofitimod are eligible to participate in the 24-week OLE. In June 2025 we announced interim data from the study showing three out of four efzoftimod-treated diffuse SSc-ILD patients showed clinically important improvement based on the modified Rodnan Skin Score (mRSS) assessment at 12 weeks and that efzofitimod was generally safe and well tolerated at all doses. We are continuing enrollment and moving toward the 24-week endpoints, including the evaluation of the lung function endpoints to evaluate the ILD component of the disease.

In January 2020, we entered into a collaboration and license agreement (Kyorin Agreement) with Kyorin for the development and commercialization of efzofitimod for the treatment of ILD in Japan. Under the terms of the Kyorin Agreement, Kyorin received exclusive rights to develop and commercialize efzofitimod in Japan for all forms of ILD, and is obligated to fund all research, development, regulatory, marketing and commercialization activities in Japan. We are responsible for supplying all drug product for Japan, as well as supporting development activities for efzofitimod. In 2020, Kyorin conducted and funded a Phase 1 clinical trial of efzofitimod (known as KRP-R120 in Japan). The Phase 1 clinical trial was a placebo-controlled clinical trial to evaluate the safety, pharmacokinetics (PK) and immunogenicity of efzofitimod in 32 healthy Japanese male volunteers. Efzofitimod was observed to be generally well-tolerated with no drug-related serious adverse events, and PK findings were consistent with previous studies of efzofitimod. Kyorin is also participating in the EFZO-FIT study as the local sponsor in Japan. In February 2023, Kyorin dosed the first patient in Japan in the EFZO-FIT study which triggered a $10.0 million milestone payment to us. To date, the Kyorin Agreement has generated $20.0 million in upfront and milestone payments to us and we are eligible to receive up to an additional $155.0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well as tiered royalties on any net sales in Japan.

Discovery Platform

Using efzofitimod as a model, we have developed a process to advance novel tRNA synthetase domains from a concept to therapeutic candidate. This process leverages our early discovery work as well as current scientific understanding of tRNA synthetase evolution, protein structure, gene splicing and tissue-specific regulation to identify potentially active protein domains. Screening approaches are employed to identify target cells and extracellular receptors for these tRNA synthetase-derived proteins. These cellular systems can then be used in mechanism-of-action studies to elucidate the role these proteins play in cellular responses and their potential therapeutic utility. We are working to identify new tRNA synthetase based drug candidates through our internal discovery efforts and external collaboration efforts.

tRNA Synthetase Candidates

Utilizing our novel approach, we have identified target receptors for domains of two additional tRNA synthetases, gaining insights into their potential biological activity in immunology and fibrosis. These fragments form the basis of our additional pipeline candidates. We plan to further elucidate the therapeutic potential of these candidates through mechanistic investigations, including *in vitro* and *in vivo* preclinical studies.

ATYR0101

ATYR0101 is a fusion protein derived from a domain of aspartyl-tRNA synthetase (DARS). ATYR0101 binds directly to latent-transforming growth factor beta-binding protein 1 (LTBP1), which regulates transforming growth factor beta (TGFβ), which is at the apex of fibrotic signaling. Derived from a naturally occurring tRNA synthetase, ATYR0101 interacts with LTBP1 in a unique way that presents a differentiated approach to targeting fibrosis. Early data suggest ATYR0101 exerts its antifibrotic effects by inducing apoptosis of myofibroblasts in a TGFβ dependent manner. We believe ATYR0101 may have broad therapeutic applications in multiple fibrotic diseases, such as lung and kidney fibrosis.

ATYR0750

ATYR0750 is a fusion protein derived from a domain of alanyl-tRNA synthetase (AARS). ATYR0750 is a novel ligand to fibroblast growth factor receptor 4 (FGFR4), which is involved in many cellular processes, including cell proliferation, differentiation, and tissue repair. FGFR4 is known to play a role in diseases related to inflammation and fibrosis, particularly in the liver. As a novel ligand, ATYR0750 interacts with FGFR4 in a differentiated way to other approaches targeting the receptor, which may lead to improved therapeutic benefit.

Corporate Information

We were incorporated under the laws of the State of Delaware in September 2005. Our principal executive offices are located at 10240 Sorrento Valley Road, Suite 300, San Diego, California 92121 and our telephone number is (858) 731-8389. Our website address is www.atyrpharma.com. The information on, or that can be accessed through, our website will not be deemed to be incorporated by reference in, and is not considered part of, this prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock.

Risks Associated with our Business

Our business is subject to numerous risks, as described under the heading "Risk Factors" contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

Implications of Being a Smaller Reporting Company

We are a "smaller reporting company" as defined in Item 10(f)(1) of Regulation S-K. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things, providing only two years of audited financial statements and reduced disclosure obligations regarding executive compensation. We will be a smaller reporting company and may continue to take advantage of the scaled-back disclosures available to smaller reporting companies for so long as (i) the market value of our common stock held by non-affiliates is less than $250.0 million measured on the last business day of our most recently completed second fiscal quarter or (ii) at the time of determination at the end of the fiscal year, (a) our annual revenue is less than $100.0 million during the most recently completed fiscal year for which audited financial statements are then-available and (b) the market value of our common stock held by non-affiliates is less than $700.0 million measured on the last business day of our most recently completed second fiscal quarter. To the extent we take advantage of any reduced disclosure obligations, it may make the comparison of our financial statements with other public companies difficult or impossible.

The Securities We May Offer

We may offer shares of our common stock, shares of our preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination, up to a total aggregate offering price of $300,000,000 from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;

- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking, if applicable;
- restrictive covenants, if any;
- voting or other rights, if any; and
- a discussion of material U.S. federal income tax considerations, if any.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding options to purchase additional securities, if any; and
- the estimated net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. Holders of our common stock are entitled to one vote per share for the election of directors and on all other matters that require stockholder approval. Subject to any preferential rights of any then outstanding preferred stock, in the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the assets remaining after payment of liabilities and the liquidation preferences of any then outstanding preferred stock. Our common stock does not carry any preemptive rights enabling a holder to subscribe for, or receive shares of, our common stock or any other securities convertible into shares of common stock, or any conversion or redemption rights and no sinking fund provisions are applicable. The rights, preferences and privileges of our common stock are subject to, and may be adversely affected by, the rights of shares of any series of preferred stock that we may designate in the future.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our amended and restated certificate of incorporation, our board of directors (Board) has the authority, without further action by the stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible or exchangeable debt securities will be convertible into or exchangeable for our common stock or other securities. Conversion or exchange may be mandatory or at the holder's option and would be at prescribed conversion rates or exchange prices.

The debt securities issued under this prospectus will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. A form of indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental warrant agreements and forms of warrant certificates will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

Use of Proceeds

Except as described in any prospectus supplement or any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds from the sale of the securities offered hereby for general corporate purposes, including working capital, operating expenses and capital expenditures. See "Use of Proceeds" in this prospectus.

Nasdaq Capital Market Listing

Our common stock is listed on The Nasdaq Capital Market under the symbol "ATYR."

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks referenced below and described in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks referenced below and described in the documents incorporated herein by reference, including (i) our most recent Annual Report on Form 10-K, as updated by our subsequent Quarterly Reports on Form 10-Q and other filings under the Securities Exchange Act of 1934, as amended (Exchange Act), and (ii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act), and Section 21E of the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as "may," "will," "could," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "potential," "continue," and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors referenced under the heading "Risk Factors."

This prospectus contains forward-looking statements that are based on our management's beliefs and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our clinical trials and whether the results of our trials will be sufficient to support U.S. or foreign regulatory approvals;
- the results and timing of our clinical trials of efzofitimod, our lead therapeutic product candidate;
- whether our existing capital resources will be sufficient to enable us to complete any particular portion of our planned clinical development of our product candidates or support our operations through particular time periods;
- the success of our existing collaboration with Kyorin, our ability to enter new collaborations and licensing arrangements and the timing of any payments we may receive under such arrangements;
- the effect of international trade policies, including tariffs, sanctions and trade barriers;
- the likelihood and timing of regulatory approvals for our product candidates;
- our ability to identify and discover additional product candidates;
- our ability to obtain, maintain, defend and enforce intellectual property rights protecting our product candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- the performance of third-party service providers and independent contractors upon whom we rely to conduct our clinical trial and to manufacture our product candidates or certain components of our product candidates;
- our ability to develop sales and marketing capabilities or to enter into strategic partnerships to develop and commercialize our product candidates;
- the timing and success of the commercialization of our product candidates;
- the rate and degree of market acceptance of our product candidates;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific, medical or management personnel;
- our expected use of net proceeds from this offering; and
- other risks and uncertainties, including those described under the heading "Risk Factors" in any accompanying prospectus supplement and in our filings with the SEC.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation: the possibility that we may experience slower than expected clinical site initiation or slower than expected identification and enrollment of evaluable patients; the potential for delays or problems in analyzing data or the need for additional analysis, data or patients; the potential that future pre-clinical and clinical results may not support further development of our product candidates; the potential for unexpected adverse events in the conduct of one of our clinical trials to impact our ability to continue the clinical trial or further development of a product candidate; the risk that we may encounter other unexpected hurdles or issues in the development and manufacture of our product candidates that may impact our cost, timing or progress, as well as those risks more fully discussed under the heading "Risk Factors" and the documents incorporated by reference herein.

Given these uncertainties, you should not place undue reliance on our forward-looking statements. You should read this prospectus, the documents incorporated by reference herein and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect or express in any forward-looking statements. We qualify all of the forward-looking statements in this prospectus and the documents incorporated by reference herein by these cautionary statements. Except as required by law, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development, clinical development and commercial preparation costs to support the advancement of our product candidates and the expansion of our product candidate pipeline, working capital, and capital expenditures. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including investment grade instruments, commercial paper, corporate debt securities, municipal bonds, certificates of deposit or direct or guaranteed obligations of the U.S. government, or may hold such proceeds as cash, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of the net proceeds from the sale of the securities offered hereby.

DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. The following description of our capital stock does not purport to be complete and is subject to, and qualified in its entirety by, our amended and restated certificate of incorporation and amended and restated bylaws, which are included as exhibits to the registration statement of which this prospectus forms a part, and by the applicable provisions of the General Corporation Law of the State of Delaware (DGCL). The terms of our common stock and preferred stock may also be affected by the DGCL.

Authorized Capital Stock

As of June 30, 2025, our authorized capital stock consisted of 170,000,000 shares of common stock, par value $0.001 per share, and 7,285,456 shares of preferred stock, par value $0.001 per share, of which 72,000 shares were designated Series B redeemable convertible preferred stock, 15,957 shares were designated Series C redeemable convertible preferred stock, 2,197,499 shares were designated Series D redeemable convertible preferred stock and 5,000,000 shares were undesignated preferred stock. The designated preferred stock is not available for future issuance.

Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our Board out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

Preferred Stock

The rights of holders of our common stock described above, are and will be subject to, and may be adversely affected by, the rights of currently authorized and outstanding preferred stock and any preferred stock that we may designate and issue in the future. Our Board is authorized to issue up to 5,000,000 shares of undesignated preferred stock in one or more series without stockholder approval. Our Board may determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock, any or all of which may be more favorable than the rights of our common stock. The issuance of shares of our undesignated preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

The purpose of authorizing our Board to issue preferred stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. Examples of rights and preferences that the Board may fix are:

- dividend rights;
- conversion rights;
- voting rights;
- terms of redemption;
- liquidation preferences;
- sinking fund terms; and

- the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock.

The existence of authorized but unissued shares of undesignated preferred stock may enable our Board to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our Board were to determine that a takeover proposal is not in the best interests of us or our stockholders, our Board could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer, stockholder or stockholder group.

We will incorporate by reference as an exhibit to the registration statement, which includes this prospectus, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. This description and the applicable prospectus supplement will include:

- the title and stated value;
- the number of shares authorized;
- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date, and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material United States federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

When we issue shares of preferred stock under this prospectus, the shares will be fully paid and nonassessable and will not be subject to any preemptive or similar rights.

Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws and Delaware Anti-Takeover Law

Certain provisions of the DGCL, and of our amended and restated certificate of incorporation and amended and restated bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our Board. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Board Composition and Filling Vacancies. Our amended and restated certificate of incorporation provides for the division of our Board into three classes serving staggered three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our Board, however occurring, including a vacancy resulting from an increase in the size of our Board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No Written Consent of Stockholders. Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of Stockholders. Our amended and restated certificate of incorporation and amended and restated bylaws provide that only a majority of the members of our Board then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements. Our amended and restated bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken.

Amendment to Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws. As required by the DGCL, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our Board, and if required by law or our amended and restated certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our amended and restated certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the amended and restated bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if our Board recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Undesignated Preferred Stock. Our amended and restated certificate of incorporation provides for 5,000,000 authorized shares of undesignated preferred stock. Our other classes of designated preferred stock may not be issued. The existence of authorized but unissued shares of undesignated preferred stock may enable our Board to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our Board were to determine that a takeover proposal is not in the best interests of our stockholders, our Board could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our amended and restated certificate of

incorporation grants our Board broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of undesignated preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Delaware Anti-Takeover Law. We are subject to the provisions of Section 203 of the DGCL. In general, Section 203 of the DGCL prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203 of the DGCL, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 of the DGCL defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 of the DGCL defines an interested stockholder as any entity or person beneficially owning or having owned in the past three years 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Exclusive Jurisdiction of Certain Actions. Our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws, or (iv) any action asserting a claim against us governed by the internal affairs doctrine. Although we believe this provision benefits us by providing increased consistency in the application of the DGCL in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers. This choice of forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Act or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

This choice of forum provision may limit a stockholder's ability to bring certain claims in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. If a court were to find this choice of forum provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Listing

Our common stock is listed on The Nasdaq Capital Market under the symbol "ATYR."

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Equiniti Trust Company, LLC. The transfer agent and registrar's address is 55 Challenger Road 2nd Floor, Ridgefield Park, New Jersey 07660.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended (Trust Indenture Act). We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as “discount securities,” which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with original issue discount (OID), for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;
- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;

- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions

pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request;
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under "Description of Debt Securities—Consolidation, Merger or Sale;"
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;
- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under "Description of Debt Securities—General" to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or

- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company (DTC), or another depositary named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and in any related free writing prospectuses, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be offered and issued independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms relating to a series of warrants being offered, including, to the extent applicable:

- the title of such securities;
- the offering price or prices and aggregate number of warrants offered;
- the currency or currencies for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- in the case of warrants to purchase common stock, the number of shares of common stock purchasable upon the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased upon such exercise;
- in the case of warrants to purchase preferred stock, the number of shares of preferred stock purchasable upon the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased upon such exercise;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at which, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;
- the terms of any rights to force the exercise of the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;

- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special U.S. federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase common stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any;
- in the case of warrants to purchase preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any; or
- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent in connection with the exercise of the warrant.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements, and any claim, controversy or dispute arising under or related to the warrants or warrant agreements, will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depositary or warrant agent maintain for this purpose as the "holders" of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as "indirect holders" of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depositary or its participants. Consequently, for global securities, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in "street name." Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depositary will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depositary will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not legal holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under "—Special Situations When a Global Security Will Be Terminated." As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depositary, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depositary that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;
- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

- an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in the global security, nor will we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, a global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the prospectus supplement. When a global security terminates, the depositary, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities covered hereby from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. A distribution of these securities offered by this prospectus may also be effected through the issuance of derivative securities, including without limitation, warrants. We may sell the securities to or through one or more underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

We may also sell equity securities covered by this registration statement in an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

- on or through the facilities of The Nasdaq Capital Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker other than on The Nasdaq Capital Market or such other securities exchanges or quotation or trading services.

Such at-the-market offerings, if any, may be conducted by underwriters acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents, if any;
- the purchase price of the securities and the proceeds we will receive from the sale;
- any options to purchase additional securities granted to the underwriters;
- any agency fees or underwriting discounts and other items constituting agents' or underwriters' compensation;
- any public offering price;
- any discounts or concessions allowed or reallowed or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any overallotment or other option. Any public offering price and any discounts or concessions allowed or reallowed or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions and other compensation we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

Unless otherwise specified in the related prospectus supplement, all securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any agents or underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities. There is currently no market for any of the offered securities, other than our common stock which is listed on The Nasdaq Capital Market. We have no current plans for listing of the preferred stock, debt securities or warrants on any securities exchange or quotation system; any such listing with respect to any particular preferred stock, debt securities or warrants will be described in the applicable prospectus supplement or other offering materials, as the case may be.

Any underwriter may engage in overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Rule 103 of Regulation M under the Exchange Act. Overallotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any agents or underwriters who are qualified market makers on The Nasdaq Capital Market may engage in passive market making transactions in the securities on The Nasdaq Capital Market in accordance with Rule 103 of Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker’s bid, however, the passive market maker’s bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon by Cooley LLP, San Diego, California. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

Ernst & Young LLP, an independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024, as set forth in their report, which is incorporated by reference into this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including aTyr Pharma, Inc. The address of the SEC website is www.sec.gov.

Copies of certain information filed by us with the SEC are also available on our website at www.atyrpharma.com. Information contained in or accessible through our website does not constitute a part of this prospectus and is not incorporated by reference into this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including all filings made (i) after the date of the filing of this registration statement and prior to the effectiveness of this registration statement and (ii) after the date of this prospectus and prior to the termination of this offering, except as to any portion of any future report or document that is not deemed filed under such provisions:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2024, filed with the SEC on March 13, 2025;
- the information specifically incorporated by reference in our Annual Report on Form 10-K for the year ended December 31, 2024 from our definitive proxy statement on Schedule 14A (other than information furnished and not filed), filed with the SEC on March 19, 2025;
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2025 and June 30, 2025, filed with the SEC on May 7, 2025 and August 7, 2025, respectively;
- our Current Reports on Form 8-K, filed with the SEC on May 6, 2025; and
- the description of our common stock, which is contained in our registration statement on Form 8-A, filed on May 6, 2015 under the Exchange Act, as updated by the description of our common stock contained in Exhibit 4.6 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, filed with the SEC on March 14, 2024, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items, and other information that is furnished and not filed or is otherwise not incorporated into registration statements pursuant to SEC rules) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus but prior to the termination of all offerings covered by this prospectus. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of the documents incorporated by reference into this prospectus but not delivered with the prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following address: aTyr Pharma, Inc., 10240 Sorrento Valley Road, Suite 300, San Diego, California 92121, Attention: Secretary, or by telephone request to (858) 731-8389.

You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.atyrpharma.com. Information contained on our website is not incorporated by reference into this prospectus, and you should not consider any information on, or that can be accessed from, our website as part of this prospectus or any accompanying prospectus supplement.

This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

You should rely only on the information incorporated by reference or provided in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.



Up to $79,994,251

Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

November 6, 2026