

PROSPECTUS SUPPLEMENT
(To Prospectus dated June 24, 2022)

3,500,000 Shares of Common Stock
Pre-Funded Warrants to Purchase up to 2,632,076 Shares of Common Stock
Warrants to Purchase up to 6,132,076 Shares of Common Stock



We are offering on a “best efforts” basis 3,500,000 shares (the “Shares”) of our common stock, par value \$0.0001 per share (our “common stock”). The purchase price of each Share is \$1.06. We are also offering pre-funded warrants (the “Pre-Funded Warrants”) to purchase up to 2,632,076 shares of our common stock to a purchaser whose purchase of additional Shares in this offering would otherwise result in such purchaser, together with their affiliates and certain related parties, beneficially owning more than 9.99% of our outstanding common stock immediately following the consummation of this offering. The purchase price of each Pre-Funded Warrant is equal to \$1.0599, which is equal to the purchase price of the Shares minus \$0.0001, the exercise price of each Pre-Funded Warrant. The Pre-Funded Warrants are immediately exercisable and may be exercised at any time until all of the Pre-Funded Warrants are exercised in full.

The Shares and Pre-Funded Warrants are being sold together with warrants to purchase up to 6,132,076 shares of our common stock (the “Common Warrants”) and together with the Shares and the Pre-Funded Warrants, the “Securities”). Each Common Warrant has an exercise price per share of \$1.06, will be exercisable six months after its issuance and will expire on the fifth anniversary of the date on which the Common Warrants become exercisable.

The Shares, Pre-Funded Warrants and Common Warrants can only be purchased together in this offering but will be issued separately and will be immediately separable upon issuance. The Securities are being sold in this offering to a certain investor pursuant to the securities purchase agreement dated July 17, 2022 between us and the purchaser.

Our common stock is listed on the Nasdaq Capital Market (“Nasdaq”) under the symbol “ATNF”. On July 15, 2022, the closing sale price of our common stock was \$1.14 per share. There is no established public trading market for the Pre-Funded Warrants or the Common Warrants and we do not expect a market to develop. In addition, we do not intend to apply for a listing of the Pre-Funded Warrants or the Common Warrants on any national securities exchange or other nationally recognized trading system.

Investing in our securities involves a high degree of risk. See the “Risk Factors” section beginning on page S-3 of this prospectus supplement and page 3 of the accompanying prospectus, as well as our other filings 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.

We have engaged A.G.P./Alliance Global Partners to act as our exclusive placement agent (the “Placement Agent”) in connection with this offering. This offering is being conducted on a “best efforts” basis and the Placement Agent has no obligation to buy any of the Securities from us or to arrange for the purchase or sale of any specific number or dollar amount of Securities. We have agreed to pay the Placement Agent fees as set forth in the table below:

	Per Share and Accompanying Warrant	Per Pre- Funded Warrant and Accompanying Warrant	Total
Offering price	\$ 1.06	\$ 1.0599	\$ 6,499,737.35
Placement Agent fees ⁽¹⁾	\$ 0.07	\$ 0.07	\$ 454,981.61
Proceeds, before expenses, to us	\$ 0.99	\$ 0.9899	\$ 6,044,755.74

(1) We have agreed to pay the Placement Agent a cash placement commission equal to 7% of the gross proceeds from the sale of 3,500,000 Shares and Pre-Funded Warrants to purchase 2,632,076 shares of common stock sold in this offering. We have also agreed to reimburse the Placement Agent for certain expenses incurred in connection with this offering. See “*Plan of Distribution*” beginning on page S-12 for additional information regarding the compensation to be paid to the Placement Agent.

Delivery of the Shares, the Pre-Funded Warrants and the Common Warrants being offered pursuant to this prospectus supplement and the accompanying prospectus is expected to be made on or about July 20, 2022, subject to satisfaction of customary closing conditions.

A.G.P.

This prospectus supplement is dated July 17, 2022.

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PROSPECTUS

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus are part of a “shelf” registration statement on Form S-3 that we filed with the Securities and Exchange Commission (the “SEC”) using a “shelf” registration process.

This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the “prospectus,” we are referring to both parts, combined. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference herein or therein that we filed with the SEC before the date of this prospectus supplement, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference herein and therein. You should read this prospectus supplement and the accompanying prospectus, including the information incorporated by reference herein and therein.

You should rely only on the information that we have included or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any

free writing prospectus we may authorize to be delivered or made available to you. We have not, and the Placement Agent has not, authorized anyone to give any information or to make any representation other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus we may authorize to be delivered or made available to you. You must not rely upon any information or representation not contained or incorporated by reference in this prospectus supplement or the accompanying prospectus. This prospectus supplement and the accompanying 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 does this prospectus supplement or the accompanying 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 supplement or the accompanying 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 herein or therein is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus supplement or accompanying prospectus is delivered, or securities are sold, on a later date.

This prospectus supplement contains or incorporates by reference 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 or will be filed or have been or will be incorporated by reference as exhibits to the registration statement of which this prospectus supplement forms apart, and you may obtain copies of those documents as described in this prospectus supplement under the heading “Where You Can Find More Information.”

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 into this prospectus supplement or the accompanying prospectus 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.

Unless otherwise stated in this prospectus, or the context otherwise requires, references to the “Company,” “we,” “us” or “our” refer specifically to 180 Life Sciences Corp. and its consolidated subsidiaries. When we refer to “you,” we mean the potential holders of our securities. Capitalized terms used, but not defined, in this prospectus supplement are defined in the accompanying prospectus.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained in other parts of this prospectus supplement. Because it is only a summary, it does not contain all of the information that you should consider before investing in shares of our common stock, and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus supplement, the accompanying prospectus, and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. You should read all such documents carefully, and you should pay special attention to the information contained under the caption entitled “Risk Factors” in this prospectus supplement, the accompanying prospectus, in our most recent Annual Report on Form 10-K, in any subsequent Quarterly Reports on Form 10-Q and in our other reports filed from time to time with the SEC, which are incorporated by reference into this prospectus supplement and the accompanying prospectus, before deciding to buy our securities.

Overview

We are a clinical stage biotechnology company headquartered in Palo Alto, California, focused on the development of therapeutics for unmet medical needs in chronic pain, inflammation and fibrosis by employing innovative research, and, where appropriate, combination therapy. We were founded by Prof. Sir Marc Feldmann, Prof. Lawrence Steinman, Prof. Raphael Mechoulam, Dr. Jonathan Rothbard and Prof. Jagdeep Nanchahal, all of whom are scientists in the biotechnology and pharmaceutical sectors with significant experience, and previous success, in drug discovery. These scientists are from the University of Oxford, Stanford University and Hebrew University of Jerusalem, and our management team has extensive experience in financing and growing early-stage healthcare companies.

We have three different product development platforms that are focused on different diseases or medical conditions, and that target different factors, molecules or proteins, as follows:

- Anti-TNF platform: focusing on fibrosis and anti-tumor necrosis factor (“anti-TNF”);
- SCAs platform: focusing on drugs which are synthetic cannabidiol (“CBD”) or cannabigerol analogs (“SCAs”); and
- $\alpha 7nAChR$ platform: focusing on alpha 7 nicotinic acetylcholine receptor (“ $\alpha 7nAChR$ ”).

Our lead product candidate recently completed a Phase 2b clinical trial in the United Kingdom and the Netherlands for early-stage Dupuytren’s Contracture, a condition that affects the development of fibrous connective tissue in the palm of the hand. Currently, we are conducting clinical trials only for certain indications under the anti-TNF platform. Of our three product development platforms, only one, the SCAs platform, involves products that are related to CBD (and not to cannabis or THC), and no clinical trials for any indications or products under the SCAs platform are currently being conducted in the United States or abroad. We are currently undertaking preclinical research and development activities for the SCA and the $\alpha 7nAChR$ platforms.

Corporate Information

We were originally formed as KBL Merger Corp. IV, a blank check company organized under the laws of the State of Delaware on September 7, 2016, which consummated its initial public offering on June 7, 2017. On July 25, 2019, we entered into a business combination agreement and, on November 6, 2020, we consummated the transactions contemplated by the business combination agreement (the “Business Combination”) and changed our name to 180 Life Sciences Corp.

Our principal executive offices are located at 3000 El Camino Real, Bldg. 4, Suite 200, Palo Alto, California 94306, and our telephone number is (650) 507-0669. We maintain a website at www.180lifesciences.com. We have not incorporated by reference into this prospectus the information in, or that can be accessed through, our website, and you should not consider it to be a part of this prospectus.

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Common stock offered by us	3,500,000 shares of common stock
Common stock to be outstanding immediately after this offering	37,643,823 shares of common stock
Pre-Funded Warrants	We are also offering Pre-Funded Warrants to purchase up to 2,632,076 shares of our common stock to a purchaser whose purchase of additional Shares in this offering would otherwise result in such purchaser, together with their affiliates and certain related parties, beneficially owning more than 9.99% of our outstanding common stock immediately following the consummation of this offering. The purchase price of each Pre-Funded Warrant is equal to \$1.0599, which is equal to the purchase price of the Shares minus \$0.0001, the exercise price of each Pre-Funded Warrant. The Pre-Funded Warrants are immediately exercisable and may be exercised at any time until all of the Pre-Funded Warrants are exercised in full. This offering also relates to the shares of common stock issuable upon exercise of any Pre-Funded Warrants sold in this offering.
Common Warrants	We are also offering Common Warrants to purchase an aggregate of 6,132,076 shares of our common stock. The Shares and Pre-Funded Warrants are being sold together with the Common Warrants. Each Common Warrant has an exercise price per share of \$1.06, will be exercisable six months after its issuance and will expire on the fifth anniversary of the date on which the Common Warrants become exercisable. This offering also relates to the offering of the shares of common stock issuable upon exercise of the Common Warrants.
Best Efforts	We have agreed to issue and sell the Securities offered hereby to the investor through the Placement Agent, and the Placement Agent has agreed to offer and sell such Securities on a “best efforts” basis. The Placement Agent is not required to sell any specific number or dollar amount of the Securities offered hereby, but will use its best efforts to sell such Securities. See the section entitled “ <i>Plan of Distribution</i> ” on page S-12 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds from the sale of our securities under this prospectus for research and development expenses and general corporate purposes. See the section entitled “ <i>Use of Proceeds</i> ” on page S-7 of this prospectus supplement.
Risk Factors	Investing in our common stock involves a high degree of risk. See the “ <i>Risk Factors</i> ” section on page S-3 of this prospectus supplement and other information included or incorporated by reference into this prospectus supplement for a discussion of factors you should carefully consider before deciding to invest in our common stock.
Nasdaq symbol	Our common stock is listed on Nasdaq under the symbol “ATNF.”

The number of shares of our common stock to be outstanding after this offering is based on 34,143,823 shares of our common stock outstanding as of July 17, 2022, and excludes, as of such date:

- 5,275 shares of common stock issuable upon the conversion of the exchangeable shares issued concurrently with the reorganization that occurred in connection with the Business Combination;
- 3,259,000 shares of common stock issuable upon the exercise of outstanding stock options;
- 159,487 additional shares of our common stock reserved for future issuance under our 2020 Omnibus Incentive Plan;
- 2,400,000 additional shares of our common stock reserved for future issuance under our 2022 Omnibus Incentive Plan;
- 5,750,000 shares of common stock issuable upon the exercise of outstanding Public Warrants exercisable at an exercise price of \$11.50 per share, 251,250 shares of common stock issuable upon the exercise of outstanding Private Placement Warrants exercisable at an exercise price of \$11.50 per share, 2,564,000 shares of common stock issuable upon the exercise of February PIPE Warrants at an exercise price of \$5.00 per share, 25,000 shares of common stock issuable upon the exercise of the Alpha Settlement Warrants at an exercise price of \$7.07 per share, 63,658 shares of common stock issuable upon the exercise of the AGP Warrant at an exercise price of \$5.28 per share, and 2,500,000 shares of common stock issuable upon the exercise of the August PIPE Warrants at an exercise price of \$7.50 per share; and
- the shares of common stock issuable upon exercise of the Pre-Funded Warrants and Common Warrants.

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RISK FACTORS

An investment in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should carefully consider the risks and uncertainties described below, in the accompanying prospectus, and any documents incorporated by reference herein and therein. You should also consider the risks, uncertainties and assumptions discussed under the heading “Risk Factors” included in our most recent Annual Report on Form 10-K, as revised or supplemented by our most recent Quarterly Report on Form 10-Q, each of which are on file with the SEC and are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Our business, business prospects, financial condition or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to This Offering

You will experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase. You may also experience future dilution as a result of future equity offerings.

The price per share, together with the number of shares of our common stock we propose to issue and ultimately will issue if this offering is completed, may result in an immediate decrease in the market price of our common stock. Our historical net tangible book value as of March 31, 2022 was \$(9,816,289), or approximately \$(0.29) per share of our common stock. After giving effect to the 3,500,000 shares of our common stock to be sold in this offering at a public offering price of \$1.06 per share and assuming exercise of the Pre-Funded Warrants in this offering for 2,632,076 shares of common stock, our as adjusted net tangible book value as of March 31, 2022 would have been \$(3,771,289), or approximately \$(0.09) per share of our common stock. This represents an immediate increase in the net tangible book value of \$0.19 per share of our

common stock to our existing stockholders and an immediate dilution in net tangible book value of approximately \$1.15 per share of our common stock to new investors, representing the difference between the public offering price and our as adjusted net tangible book value as of March 31, 2022, after giving effect to this offering, and the public offering price per share. Furthermore, if outstanding options or warrants are exercised, you could experience further dilution.

In addition, we have a significant number of stock options and warrants outstanding, and, 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 in this offering. In the event that the outstanding options or warrants are exercised or settled, or that we make additional issuances of common stock or other convertible or exchangeable securities, you could experience additional dilution. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater 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, including investors who purchase shares of common stock in this offering. The price per share at which we sell additional shares of our common stock or securities convertible into common stock in future transactions, may be higher or lower than the price per share in this offering. As a result, purchasers of the shares we sell, as well as our existing stockholders, will experience significant dilution if we sell at prices significantly below the price at which they invested. See the section entitled “*Dilution*” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

Resales of our common stock in the public market during this offering by our stockholders may cause the market price of our common stock to fall.

Sales of a substantial number of shares of our common stock could occur at any time. The issuance of new shares of our common stock could result in resales of our common stock by our current stockholders concerned about the potential ownership dilution of their holdings. In turn, these resales could have the effect of depressing the market price for our common stock.

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We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We currently intend to use the net proceeds from the offering of securities under this prospectus for research and development expenses, and general corporate purposes, as described in the section of this prospectus supplement entitled “*Use of Proceeds*.” We will have broad discretion in the application of the net proceeds in the category of other working capital and general corporate purposes and investors will be relying on the judgment of our management regarding the application of the proceeds of this offering.

The precise amount and timing of the application of these proceeds, if any, will depend upon a number of factors, such as the timing and progress of our research and development efforts, our funding requirements and the availability and costs of other funds. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Depending on the outcome of our efforts and other unforeseen events, our plans and priorities may change and we may apply the net proceeds of this offering in different manners than we currently anticipate.

The failure by our management to apply these funds effectively could harm our business, financial condition and results of operations. Pending their use, we may invest the net proceeds from this offering in short-term, interest-bearing instruments. These investments may not yield a favorable return to our stockholders.

This offering may cause the trading price of our common stock to decrease.

The price per share, together with the number of shares of common stock we propose to issue and ultimately will issue if this offering is completed, may result in an immediate decrease in the market price of our common stock. This decrease may continue after the completion of this offering.

There is no public market for the Pre-Funded Warrants or the Common Warrants being offered in this offering.

There is no established public trading market for the Pre-Funded Warrants or the Common Warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the Pre-Funded Warrants or the Common Warrants on any securities exchange or nationally recognized trading system. Without an active market, the liquidity of the Pre-Funded Warrants or the Common Warrants will be limited.

Holders of our Pre-Funded Warrants or the Common Warrants will have no rights as a common stockholder until they acquire our common stock.

Until you acquire shares of our common stock upon exercise of your Pre-Funded Warrants or the Common Warrants, you will have no rights with respect to shares of our common stock issuable upon exercise of your Pre-Funded Warrants or the Common Warrants. Upon exercise of your Pre-Funded Warrants or the Common Warrants, you will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

If we do not maintain a current and effective prospectus relating to the common stock issuable upon exercise of the Pre-Funded Warrants or the Common Warrants, holders will only be able to exercise such Pre-Funded Warrants or the Common Warrants on a “cashless basis.”

If we do not maintain a current and effective prospectus relating to the shares of common stock issuable upon exercise of the Pre-Funded Warrants or the Common Warrants at the time that holders wish to exercise such warrants, they will only be able to exercise them on a “cashless basis,” and under no circumstances would we be required to make any cash payments or net cash settle such warrants to the holders. As a result, the number of shares of common stock that holders will receive upon exercise of the Pre-Funded Warrants or the Common Warrants will be fewer than it would have been had such holders exercised their Pre-Funded Warrants or the Common Warrants for cash. Under the terms of the Pre-Funded Warrants or the Common Warrants, we have agreed to use our best efforts to maintain a current and effective prospectus relating to the shares of common stock issuable upon exercise of such warrants until the expiration of such warrants. However, we cannot assure you that we will be able to do so. If we are unable to do so, the potential “upside” of the holder’s investment in our company may be reduced.

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The Pre-Funded Warrants and the Common Warrants are speculative in nature.

The Pre-Funded Warrants and Common Warrants offered hereby do not confer any rights of common stock ownership on their holders, such as voting rights or the right to receive dividends, but rather merely represent the right to acquire shares of common stock at a fixed price. Specifically, commencing on the date of issuance, holders of the Pre-Funded Warrants may acquire the common stock issuable upon exercise of such warrants at an exercise price of \$0.0001 per share and holders of the Common Warrants may acquire the common stock issuable upon exercise of such warrants at an exercise price of \$1.06 per share. Moreover, following this offering, the market value of the Pre-Funded Warrants and the Common Warrants is uncertain and there can be no assurance that the market value of the Pre-Funded Warrants or the Common Warrants will equal or exceed their public offering price.

The Common Warrants may not have any value.

The Common Warrants have an exercise price of \$1.06 per share, are exercisable six months after their issuance and will expire on the fifth anniversary of the date on which the Common Warrants become exercisable. In the event our common stock price does not exceed the exercise price of the Common Warrants during the period when the warrants are exercisable, the Common Warrants may not have any value.

This offering is being conducted on a “best efforts” basis.

The Placement Agent is offering the shares on a “best efforts” basis, and the Placement Agent is under no obligation to purchase any shares for its own account. The Placement Agent is not required to sell any specific number or dollar amount of shares of common stock in this offering but will use its best efforts to sell the securities offered in this prospectus supplement. As a “best efforts” offering, there can be no assurance that the offering contemplated hereby will ultimately be consummated.

Provisions of the Pre-Funded Warrants and Common Warrants could discourage an acquisition of us by a third party.

Certain provisions of the Pre-Funded Warrants and Common Warrants offered by this prospectus could make it more difficult or expensive for a third party to acquire us. The Pre-Funded Warrants and Common Warrants prohibit us from engaging in certain transactions constituting “fundamental transactions” unless, among other things, the surviving entity assumes our obligations under the Pre-Funded Warrants and Common Warrants. Further, the Common Warrants provide that, in the event of certain transactions constituting “fundamental transactions,” with some exception, holders of such warrants will have the right, at their option, to require us to repurchase such Common Stock Warrants at a price described in such warrants. These and other provisions of the Pre-Funded Warrants and Common Warrants offered by this prospectus could prevent or deter a third party from acquiring us even where the acquisition could be beneficial to you.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement and the accompanying prospectus (including documents incorporated by reference herein and therein) contains forward-looking statements under federal securities laws, including within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by the following words: “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “ongoing,” “plan,” “potential,” “predict,” “project,” “should,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. Forward-looking statements are not a guarantee of future performance or results, and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved. Forward-looking statements are based on information available at the time the statements are made and involve known and unknown risks, uncertainties and other factors that may cause our results, levels of activity, performance or achievements to be materially different from the information expressed or implied by the forward-looking statements in this prospectus supplement and the accompanying prospectus (including documents incorporated by reference herein and therein). Forward-looking statements include, but are not limited to, any statements that are not statements of current or historical facts. These statements are based on management’s current expectations, but actual results may differ materially due to various factors, including, but not limited to:

- our ability to execute our plans to develop, manufacture, distribute and market new drug products and the timing and costs of these development, manufacturing, distribution and marketing programs, including approval by the applicable regulatory authorities;
- regulatory developments in the United States and foreign countries;
- our success in retaining or recruiting, or changes required in, our officers, key employees or directors;
- our ability to obtain additional financing to advance our business and the terms of any further financing, which may be highly dilutive and may include onerous terms;
- the continued impact of the COVID-19 pandemic on our business operations and our research and development initiatives;
- the sufficiency of our existing capital resources combined with future anticipated cash flows to finance our operating requirements;
- the use of proceeds from this offering, if any; and
- our ability to maintain our listing on Nasdaq.

Any forward-looking statements in this prospectus supplement and the accompanying prospectus (including documents incorporated by reference herein and therein) reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

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USE OF PROCEEDS

We intend to use the net proceeds from the offering of securities under this prospectus for research and development expenses, and general corporate purposes.

These expected uses represent our intentions based upon our current plans and business conditions, 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 development, the status of and results from clinical trials, and any unforeseen cash needs. As a result, our management will have broad discretion in the application 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.

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DILUTION

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. We calculate net tangible book value per share by dividing our net tangible assets (tangible assets less total liabilities) by the number of shares of our common stock issued and outstanding as of March 31, 2022.

Our net tangible book value as of March 31, 2022 was \$(9,816,289), or approximately \$(0.29) per share. After giving effect to the sale of our common stock in this offering at a public offering price of \$1.06 per share and assuming exercise of the Pre-Funded Warrants in this offering for 2,632,076 shares of common stock, our as adjusted net tangible book value as of March 31, 2022 would have been \$(3,771,289), or approximately \$(0.09) per share of our common stock. This represents an immediate increase in the net tangible book value of \$0.19 per share of our common stock to our existing stockholders and an immediate dilution in net tangible book value of approximately \$1.15 per share of our common stock to new investors. The following table illustrates this per share dilution:

Public offering price per share of our common stock		\$ 1.06
Net tangible book value per share as of March 31, 2022	\$ (0.29)	
Increase in net tangible book value per share of our common stock attributable to this offering	\$ 0.19	
As adjusted net tangible book value per share of our common stock as of March 31, 2022, after giving effect to this offering		\$ (0.09)
Dilution per share to new investors purchasing shares of our common stock in this offering		\$ 1.15

The above discussion and table are based on 34,087,244 shares of our common stock outstanding as of March 31, 2022 and assumes the exercise of the Pre-Funded Warrants. The number of shares outstanding as of March 31, 2022 excludes, as of such date:

- 5,275 shares of common stock issuable upon the conversion of the exchangeable shares issued concurrently with the reorganization that occurred in connection with the Business Combination;
- 2,741,000 shares of common stock issuable upon the exercise of outstanding stock options;
- 159,487 additional shares of our common stock reserved for future issuance under our 2020 Omnibus Incentive Plan;
- 2,400,000 additional shares of our common stock reserved for future issuance under our 2022 Omnibus Incentive Plan; and
- 5,750,000 shares of common stock issuable upon the exercise of outstanding Public Warrants exercisable at an exercise price of \$11.50 per share, 251,250 shares of common stock issuable upon the exercise of outstanding Private Placement Warrants exercisable at an exercise price of \$11.50 per share, 2,564,000 shares of common stock issuable upon the exercise of February PIPE Warrants at an exercise price of \$5.00 per share, 25,000 shares of common stock issuable upon the exercise of the Alpha Settlement Warrants at an exercise price of \$7.07 per share, 63,658 shares of common stock issuable upon the exercise of the AGP Warrant at an exercise price of \$5.28 per share, and 2,500,000 shares of common stock issuable upon the exercise of the August PIPE Warrants at an exercise price of \$7.50 per share.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise or forfeiture of the outstanding options or warrants after March 31, 2022, including, for the avoidance of doubt, any Common Warrants but not the Pre-Funded Warrants, which are assumed will be exercised for purposes of the above dilution calculation.

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DESCRIPTION OF SECURITIES WE ARE OFFERING

We are offering (i) 3,500,000 shares of our common stock, (ii) Pre-Funded Warrants to purchase up to 2,632,076 shares of our common stock and (iii) Common Warrants to purchase up to 6,132,076 shares of our common stock. Each share of common stock and Pre-Funded Warrant is being sold together with a Common Warrant to purchase one (1) share of common stock. The Shares, Pre-Funded Warrants and accompanying Common Warrants will be issued separately. We are also registering the shares of our common stock issuable from time to time upon exercise of the Pre-Funded Warrants and Common Warrants offered hereby.

Common Stock

The material terms and provisions of our common stock and each other class of our securities that qualifies or limits our common stock are described in the section entitled “*Description of Capital Stock*” beginning on page 5 of the accompanying prospectus.

Pre-Funded Warrants

The following summary of certain terms and provisions of Pre-Funded Warrants that are being offered hereby is not complete and is subject to, and qualified in its entirety by, the provisions of the Pre-Funded Warrant, the form of which is filed as an exhibit to the registration statement of which this prospectus forms a part. Prospective investors should carefully review the terms and provisions of the form of Pre-Funded Warrant for a complete description of the terms and conditions of the Pre-Funded Warrants.

Duration and Exercise Price

Each Pre-Funded Warrant offered hereby will have an initial exercise price of \$0.0001 per share. The Pre-Funded Warrants will be immediately exercisable and may be exercised at any time until the Pre-Funded Warrants are exercised in full. The exercise price and number of shares of common stock issuable upon exercise is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock and the exercise price.

Exercisability

The Pre-Funded Warrants will be exercisable, at the option of each holder, in whole or in part, by delivering to us a duly executed exercise notice accompanied by payment in full for the number of shares purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of the Pre-Funded Warrant to the extent that the holder would own more than 9.99% of the outstanding common stock immediately after exercise, except that upon at least 61 days’ prior notice from the holder to us, the holder may decrease the amount of ownership of outstanding stock after exercising the holder’s Pre-Funded Warrants. No fractional shares of common stock will be issued in connection with the exercise of a Pre-Funded Warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the exercise price.

Cashless Exercise

In lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect

instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the Pre-Funded Warrants.

Fundamental Transaction

In the event of a fundamental transaction, as described in the Pre-Funded Warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding voting securities, the holders of the Pre-Funded Warrants will be entitled to receive upon exercise of the Pre-Funded Warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the Pre-Funded Warrants immediately prior to such fundamental transaction. In addition, the holders of the Pre-Funded Warrants have the right to require us or a successor entity to redeem the Pre-Funded Warrant for the cash paid in the fundamental transaction in the amount of the Black Scholes value of the unexercised portion of the Pre-Funded Warrant on the date of the consummation of the fundamental transaction.

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Transferability

Subject to applicable laws, a Pre-Funded Warrant may be transferred at the option of the holder upon surrender of the Pre-Funded Warrant to us together with the appropriate instruments of transfer.

Exchange Listing

We do not intend to list the Pre-Funded Warrants on any securities exchange or nationally recognized trading system.

Rights as a Stockholder

Except as otherwise provided in the Pre-Funded Warrants or by virtue of such holder's ownership of, the holders of the Pre-Funded Warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise their Pre-Funded Warrants.

Common Warrants

The following summary of certain terms and provisions of the Common Warrants that are being offered hereby is not complete and is subject to, and qualified in its entirety by, the provisions of the Common Warrants, the form of which is filed as an exhibit to the registration statement of which this prospectus forms a part. Prospective investors should carefully review the terms and provisions of the form of Common Warrant for a complete description of the terms and conditions of the Common Warrants.

Duration and Exercise Price

Each Common Warrant offered will have an initial exercise price of \$1.06 per share. The Common Warrants will be exercisable six months after their issuance and will expire on the fifth anniversary of the date on which the Common Warrants become exercisable. The exercise price and number of shares of common stock issuable upon exercise is subject to appropriate adjustment in the event of stock dividends, stock splits, reorganizations or similar events affecting our common stock and the exercise price. Common Warrants will be issued separately from the common stock and Pre-Funded Warrants and may be transferred separately immediately thereafter. A Common Warrant to purchase one share of our common stock will be issued for each share of common stock (or Pre-Funded Warrant, as applicable) purchased in this offering.

Exercisability

The Common Warrants will be exercisable, at the option of each holder, in whole or in part, by delivering a duly executed exercise notice accompanied by payment in full for the number of shares purchased upon such exercise (except in the case of a cashless exercise as discussed below). A holder (together with its affiliates) may not exercise any portion of the Common Warrant to the extent that the holder would own more than 4.99% of the outstanding common stock immediately after exercise, except that upon at least 61 days' prior notice from the holder to us, the holder may decrease the amount of ownership of outstanding stock after exercising the holder's warrants. No fractional shares of common stock will be issued in connection with the exercise of a Common Warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the exercise price.

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Cashless Exercise

If, at the time a holder exercises its Common Warrants, a registration statement registering the issuance of the shares of common stock underlying the Common Warrants under the Securities Act is not then effective or available, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the Common Warrants.

Fundamental Transaction

In the event of a fundamental transaction, as described in the Common Warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding voting securities, the holders of the Common Warrants will be entitled to receive upon exercise of the Common Warrants the kind and amount of securities, cash or other property that the holders would have received had they exercised the Common Warrants immediately prior to such fundamental transaction. In addition, the holders of the Common Warrants have the right to require us or a successor entity to redeem the Common Warrant for the cash paid in the fundamental transaction in the amount of the Black Scholes value of the unexercised portion of the Common Warrant on the date of the consummation of the fundamental transaction.

Transferability

Subject to applicable laws, a Common Warrant may be transferred at the option of the holder upon surrender of the Common Warrant together with the appropriate instruments of transfer.

Exchange Listing

We do not intend to list the Common Warrants on any securities exchange or nationally recognized trading system.

Right as a Stockholder

Except as otherwise provided in the Common Warrants or by virtue of such holder's ownership of, the holders of the Common Warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise their Common Warrants.

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PLAN OF DISTRIBUTION

A.G.P./Alliance Global Partners has agreed to act as our exclusive placement agent in connection with this offering subject to the terms and conditions of the placement agent agreement dated July 17, 2022. The Placement Agent is not purchasing or selling any of the Securities offered by this prospectus supplement, nor is it required to arrange the purchase or sale of any specific number or dollar amount of Securities, but has agreed to use its reasonable best efforts to arrange for the sale of all of the Securities offered hereby. Therefore, we will enter into a securities purchase agreement directly with a certain investor in connection with this offering and we may not sell the entire amount of Securities offered pursuant to this prospectus supplement.

We will deliver the Securities being issued to the investor upon receipt of investor funds for the purchase of the Securities offered pursuant to this prospectus supplement. We expect to deliver the Shares, Pre-Funded Warrants and Common Warrants being offered pursuant to this prospectus supplement on or about July 20, 2022.

We have agreed to indemnify the Placement Agent against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the Placement Agent may be required to make in respect thereof.

Fees and Expenses

We have engaged A.G.P./Alliance Global Partners as our exclusive placement agent in connection with this offering. This offering is being conducted on a "best efforts" basis and the Placement Agent has no obligation to buy any of the Securities from us or to arrange for the purchase or sale of any specific number or dollar amount of Securities. We have agreed to pay the placement agent fees set forth in the table below.

	Per Share and Accompanying Warrant	Per Pre-Funded Warrant and Accompanying Warrant	Total
Public offering price	\$ 1.06	\$ 1.0599	\$ 6,499,737.35
Placement agent fees ⁽¹⁾	\$ 0.07	\$ 0.07	\$ 454,981.61
Proceeds, before expenses, to us ⁽²⁾	\$ 0.99	\$ 0.9899	\$ 6,044,755.74

(1) We have agreed to pay the Placement Agent a cash placement commission equal to 7% of the gross proceeds from the sale of 3,500,000 Shares and Pre-Funded Warrants to purchase 2,632,076 shares of common stock sold in this offering. We have also agreed to reimburse the Placement Agent for certain expenses incurred in connection with this offering. See "Plan of Distribution" beginning on page S-12 for additional information regarding the compensation to be paid to the Placement Agent.

We have also agreed to reimburse the Placement Agent at closing for legal and other expenses incurred by them in connection with the offering in an aggregate amount not to exceed \$75,000. We estimate the total expenses payable by us for this offering, excluding the placement agent fees and expenses, will be approximately \$200,000.

The Placement Agent may be deemed to be an underwriter within the meaning of Section 2(a)(11) of the Securities Act, and any commissions received by it and any profit realized on the resale of the shares sold by it while acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. As an underwriter, the Placement Agent would be required to comply with the requirements of the Securities Act and the Exchange Act, including, without limitation, Rule 415(a)(4) under the Securities Act and Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of shares by the Placement Agent acting as principal. Under these rules and regulations, the Placement Agent:

- may not engage in any stabilization activity in connection with our securities; and
- may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities, other than as permitted under the Exchange Act, until it has completed its participation in the distribution.

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Listing

Our common stock is listed on the Nasdaq Capital Market under the trading symbol "ATNF."

Lock-Up Agreements

Our directors and executive officers have entered into lock-up agreements. Under these agreements, these individuals have agreed, subject to specified exceptions, not to sell or transfer any shares of common stock or securities convertible into, or exchangeable or exercisable for, our shares of common stock during a period ending 90 days after the date of this prospectus supplement, without first obtaining the written consent of the investor. Specifically, these individuals have agreed, in part, not to:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended;
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of our securities, whether any such transaction is to be settled by delivery of our shares of common stock, in cash or otherwise;
- make any demand for or exercise any right with respect to the registration of any of our securities;
- publicly disclose the intention to make any offer, sale, pledge or disposition, or to enter into any transaction, swap, hedge;

- or other arrangement relating to any of our securities.

Notwithstanding these limitations, these shares of common stock may be transferred under limited circumstances, including, without limitation, by gift, will or intestate succession.

In addition, we have agreed that, subject to certain exceptions, (i) we will not conduct any issuances of our common stock for a period of 90 days following closing of this offering and that (ii) we will not enter into a variable rate transaction for a period of 12 months following the closing of this offering, provided, however that this restriction shall only apply from the date hereof until six (6) months following the closing date of the offering with respect to an at-the-market offering.

Discretionary Accounts

The Placement Agent does not intend to confirm sales of the securities offered hereby to any accounts over which it has discretionary authority.

Other Activities and Relationships

The Placement Agent and certain of its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The Placement Agent and certain of its affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the Placement Agent and certain of its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the Placement Agent or its affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The Placement Agent and its affiliates may hedge such exposure by entering into transactions that consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The Placement Agent and certain of its affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

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LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by DLA Piper LLP (US), Philadelphia, Pennsylvania. A.G.P./Alliance Global Partners LLC is being represented in connection with this offering by Sullivan & Worcester LLP, New York, New York.

EXPERTS

The consolidated financial statements of 180 Life Sciences Corp. and Subsidiaries as of December 31, 2021 and 2020 and for each of the two years in the period ended December 31, 2021, incorporated in this prospectus supplement and the accompanying prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021, have been so incorporated in reliance on the report, which includes an explanatory paragraph as to the 180 Life Sciences Corp.'s ability to continue as a going concern, of Marcum LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus form part of the registration statement on Form S-3 we filed with the SEC under the Securities Act. Whenever a reference is made in this prospectus supplement and the accompanying prospectus to a contract or other document that is an exhibit to the registration statement, the reference is only a summary and you should refer to the exhibits that are a part of the registration statement for a copy of the contract or other documents incorporated by reference. You may review a copy of the registration statement and the documents incorporated by reference herein through the SEC's website listed above.

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 filed electronically with the SEC, which is available at <http://www.sec.gov>. We also make these documents available on our website at www.180lifesciences.com. Our website and the information contained, or connected to, our website is not incorporated by reference in this prospectus supplement or the accompanying prospectus, and you should not consider it part of this prospectus supplement or the accompanying prospectus.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows the Company to "incorporate by reference" information into this prospectus supplement, which means important information may be disclosed to you by referring you to another document filed separately with the SEC. Any information incorporated by reference is deemed to be part of this prospectus supplement.

The Company incorporates by reference in this prospectus supplement the documents set forth below that have been previously filed with the SEC as well as any filings the Company makes with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, on or after the date of this prospectus supplement and before the termination of the applicable offering; provided, however, that, except as specifically provided below, we are not incorporating any documents or information deemed to have been furnished rather than filed in accordance with SEC rules:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 31, 2022 (as amended by Amendment No. 1 to our Annual Report on [Form 10-K](#) filed with the SEC on April 28, 2022);
- our Definitive Proxy Statement on [Schedule 14A](#) filed on April 28, 2022 (to the extent incorporated by reference into our Annual Report on Form 10-K);
- our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2022, filed with the SEC on May 16, 2022;
- our Current Reports on Form 8-K filed with the SEC on [March 28, 2022](#), [April 14, 2022](#), [April 28, 2022](#), [May 27, 2022](#) and [June 14, 2022](#); and

- the description of our common stock contained in the registration statement on [Form 8-A](#) (File No. 001-38105) filed with the SEC on May 31, 2017, including any amendments or reports filed for the purpose of updating such description.

Any statement contained in a document incorporated by reference in this prospectus supplement shall be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained herein or in any other subsequently filed document that also is incorporated by reference in this prospectus supplement modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus supplement or the accompanying prospectus.

Information furnished under Items 2.02 and 7.01 of any Current Report on Form 8-K of the Company, including any related exhibits under Item 9.01, will not be incorporated by reference in this prospectus supplement.

To obtain copies of these filings, see “*Where You Can Find More Information.*” We will provide to each person, including any beneficial owner, to whom this prospectus supplement is delivered, without charge upon written or oral request, a copy of any or all of the information that has been incorporated by reference into this prospectus supplement but not delivered with the prospectus supplement, including exhibits that are specifically incorporated by reference into such documents. You should direct any requests for such information to:

180 Life Sciences Corp.
3000 El Camino Real, Bldg. 4, Suite 200
Palo Alto, California 94306
(650) 507-0669

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PROSPECTUS



\$125,000,000

**Common Stock
Preferred Stock
Debt Securities
Warrants
Units**

We may issue securities from time to time in one or more offerings, in amounts, at prices and on terms determined at the time of offering. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus, which will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this prospectus. You should read this prospectus and any applicable prospectus supplement before you invest. The aggregate offering price of the securities we sell pursuant to this prospectus will not exceed \$125,000,000.

The securities may be sold directly to you, through agents or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement. The price to the public of those securities and the net proceeds we expect to receive from that sale will also be set forth in a prospectus supplement.

Investing in these securities involves risks that are described in the “*Risk Factors*” section beginning on page 3 of this prospectus.

Our common stock and warrants are listed on the Nasdaq Capital Market (“[Nasdaq](#)”) under the symbols “ATNF” and “ATNFW,” respectively. On June 2, 2022, the closing sale price of our common stock was \$2.01 per share, and the closing sale price of our warrants was \$0.30 per warrant. Each prospectus supplement will indicate whether the securities offered thereby will be listed on any securities exchange.

We are an “[emerging growth company](#)” as defined in Section 2(a) of the Securities Act of 1933, as amended (the “[Securities Act](#)”).

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. Any representation to the contrary is a criminal offense.

The date of this prospectus is June 24, 2022.

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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 (the “SEC”) using a “shelf” registration process. By using a shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings.

This prospectus provides you with a general description of the securities that may be offered. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering and the securities being offered. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the additional information described under the headings “Where You Can Find More Information” and “Incorporation of Certain Information by Reference,” and any free writing prospectus that we may prepare and distribute.

You should rely only on the information contained or incorporated by reference in this prospectus, any prospectus supplement or in any free writing prospectus we may authorize to be delivered or made available to you. We have not authorized anyone to provide you with any information or to make any representations other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, nor provide any assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted.

This prospectus is dated as of the date set forth on the cover hereof. You should not assume that the information contained in this prospectus, any prospectus supplement or in any free writing prospectus we may authorize to be delivered or made available to you is accurate as of any date other than the date of such document. You should not assume that the information incorporated by reference in this prospectus, any prospectus supplement or in any free writing prospectus we may authorize to be delivered or made available to you is accurate as of any date other than the date of such incorporated document.

Any statement made in this prospectus or in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained or incorporated by reference in a prospectus supplement or in any other subsequently filed document that is also incorporated or deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

Unless otherwise stated in this prospectus, or the context otherwise requires, references to the “Company,” “we,” “us” or “our” refer specifically to 180 Life Sciences Corp. and its consolidated subsidiaries. When we refer to “you,” we mean the potential holders of our securities.

In this prospectus, we refer to our common stock, preferred stock, debt securities, warrants and units, collectively, as “securities.”

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus (including documents incorporated by reference herein) contains forward-looking statements under federal securities laws, including within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by the following words: “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “ongoing,” “plan,” “potential,” “predict,” “project,” “should,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. Forward-looking statements are not a guarantee of future performance or results, and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved. Forward-looking statements are based on information available at the time the statements are made and involve known and unknown risks, uncertainties and other factors that may cause our results, levels of activity, performance or achievements to be materially different from the information expressed or implied by the forward-looking statements in this prospectus (including documents incorporated by reference herein). Forward-looking statements include, but are not limited to, any statements that are not statements of current or historical facts. These statements are based on management’s current expectations, but actual results may differ materially due to various factors, including, but not limited to:

- our ability to execute our plans to develop, manufacture, distribute and market new drug products and the timing and costs of these development, manufacturing, distribution and marketing programs, including approval by the applicable regulatory authorities;
- regulatory developments in the United States and foreign countries;
- our success in retaining or recruiting, or changes required in, our officers, key employees or directors;

- our ability to obtain additional financing to advance our business and the terms of any further financing, which may be highly dilutive and may include onerous terms;
- the continued impact of the COVID-19 pandemic on our business operations and our research and development initiatives;
- the sufficiency of our existing capital resources combined with future anticipated cash flows to finance our operating requirements; and
- our ability to maintain our listing on Nasdaq.

Any forward-looking statements in this prospectus (including documents incorporated by reference herein) reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in, or incorporated by reference into, this prospectus. Because it is only a summary, it does not contain all of the information that you should consider before investing in our securities, and it is qualified in its entirety by, and should be read in conjunction with, the more detailed information appearing elsewhere in this prospectus, any applicable prospectus supplement and the documents incorporated by reference in this prospectus and any applicable prospectus supplement. You should read all such documents carefully, and you should pay special attention to the information contained under the caption entitled "Risk Factors" in this prospectus, any applicable prospectus supplement, in our most recent Annual Report on Form 10-K, in any subsequent Quarterly Reports on Form 10-Q and in our other reports filed from time to time with the SEC, which are incorporated by reference into this prospectus, before deciding to buy our securities.

Unless otherwise specified, share calculations do not include any shares of common stock issuable upon the exercise of outstanding warrants to purchase common stock.

Overview

We are a clinical stage biotechnology company headquartered in Palo Alto, California, focused on the development of therapeutics for unmet medical needs in chronic pain, inflammation and fibrosis by employing innovative research, and, where appropriate, combination therapy. We were founded by Prof. Sir Marc Feldmann, Prof. Lawrence Steinman, Prof. Raphael Mechoulam, Dr. Jonathan Rothbard and Prof. Jagdeep Nanchahal, all of whom are scientists in the biotechnology and pharmaceutical sectors with significant experience, and previous success, in drug discovery. These scientists are from the University of Oxford, Stanford University and Hebrew University of Jerusalem, and our management team has extensive experience in financing and growing early-stage healthcare companies.

We have three different product development platforms that are focused on different diseases or medical conditions, and that target different factors, molecules or proteins, as follows:

- Anti-TNF platform: focusing on fibrosis and anti-tumor necrosis factor ("anti-TNF");
- SCAs platform: focusing on drugs which are synthetic cannabidiol ("CBD") or cannabigerol analogs ("SCAs"); and
- $\alpha 7nAChR$ platform: focusing on alpha 7 nicotinic acetylcholine receptor (" $\alpha 7nAChR$ ").

Our lead product candidate recently completed a successful Phase 2b clinical trial in the United Kingdom and the Netherlands for early-stage Dupuytren's Contracture, a condition that affects the development of fibrous connective tissue in the palm of the hand. On April 29, 2022, final results from the trial were published in *The Lancet Rheumatology*. The study demonstrated that the primary end point of nodule hardness and the secondary end point of nodule size on ultrasound scan were met with statistically significant differences. There were no treatment-related serious adverse events in the trial. Currently, we are conducting clinical trials only for certain indications under the anti-TNF platform. Of our three product development platforms, only one, the SCAs platform, involves products that are related to CBD (and not to cannabis or THC), and no clinical trials for any indications or products under the SCAs platform are currently being conducted in the United States or abroad. We are currently undertaking preclinical research and development activities for the SCA and the $\alpha 7nAChR$ platforms.

Emerging Growth Company

We are an "emerging growth company," as defined in Section 2(a) of the Securities Act, as modified by the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"), and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

Further, Section 102(b)(1) of the JOBS Act exempts emerging growth companies from being required to comply with new or revised financial accounting standards until private companies (that is, those that have not had a registration statement under the Securities Act declared effective or do not have a class of securities registered under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) are required to comply with the new or revised financial accounting standards. The JOBS Act provides that a company can elect to opt out of the extended transition period and comply with the requirements that apply to non-emerging growth companies but any such an election to opt out is irrevocable. We have elected not to opt out of such extended transition period which means that when a standard is issued or revised and it has different application dates for public or private companies, we, as an emerging growth company, can adopt the new or revised standard at the time private companies adopt the new or revised standard. This may make comparison of our financial statements with another public company which is neither an emerging growth company nor an emerging growth company which has opted out of using the extended transition period difficult or impossible because of the potential differences in accounting standards used.

We will remain an emerging growth company until the earlier of: (1) the last day of the fiscal year (a) following the fifth anniversary of the closing of our initial public

offering, (b) in which we have total annual revenue of at least \$1.07 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common equity that is held by non-affiliates exceeds \$700 million as of the end of the prior fiscal year's second fiscal quarter; and (2) the date on which we have issued more than \$1.00 billion in non-convertible debt securities during the prior three-year period.

Corporate Information

We were originally formed as KBL Merger Corp. IV, a blank check company organized under the laws of the State of Delaware on September 7, 2016, which consummated its initial public offering on June 7, 2017. On July 25, 2019, we entered into a business combination agreement and, on November 6, 2020, we consummated the transactions contemplated by the business combination agreement and changed our name to 180 Life Sciences Corp.

Our principal executive offices are located at 3000 El Camino Real, Bldg. 4, Suite 200, Palo Alto, California 94306, and our telephone number is (650) 507-0669. We maintain a website at www.180lifesciences.com. We have not incorporated by reference into this prospectus the information in, or that can be accessed through, our website, and you should not consider it to be a part of this prospectus.

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RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the risk factors and all of the other information included in or incorporated by reference into this prospectus, including those in our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and other documents we file with the SEC, before making an investment decision. Our business, prospects, financial condition, or operating results could be harmed by any of these risks, as well as other risks not currently known to us or that we currently consider immaterial.

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USE OF PROCEEDS

Unless we inform you otherwise in a prospectus supplement or free writing prospectus, we currently intend to use the net proceeds from the offering of securities under this prospectus for research and development expenses, and general corporate purposes. Any specific allocation of the net proceeds of an offering of securities to a specific purpose will be determined at the time of the offering and will be described in an accompanying prospectus supplement or free writing prospectus.

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DESCRIPTION OF CAPITAL STOCK

The following summary of the material terms of our capital stock is not intended to be a complete summary of the rights and preferences of such securities. We urge you to read our second amended and restated certificate of incorporation in its entirety for a complete description of the rights and preferences of our securities.

Authorized Capital Stock

We are authorized to issue 100,000,000 shares of our common stock and 5,000,000 shares of our preferred stock, par value \$0.0001. As of June 1, 2022, 34,143,823 shares of our common stock were outstanding. As of June 1, 2022, 1,000,000 shares of preferred stock have been designated as Series A Convertible Preferred Stock (of which none are outstanding, and of which 1,000,000 shares were previously issued and subsequently converted into an aggregate of 1,619,144 shares of common stock in 2020), one share of preferred stock has been designated as a Class C Special Voting Share, of which one is outstanding, and one share of preferred stock has been designated as a Class K Special Voting Share, of which one is outstanding. As of June 1, 2022, there were 72 holders of record of our common stock. The following description summarizes the material terms of our securities. Because it is only a summary, it may not contain all the information that is important to you.

Common Stock

Except as otherwise required by law or as otherwise provided in any certificate of designation for any series of preferred stock, the holders of common stock possess all voting power for the election of our directors and all other matters requiring stockholder action and will at all times vote together as one class on all matters submitted to a vote of the stockholders of the Company. Holders of common stock are entitled to one vote per share on matters to be voted on by stockholders and do not have the right to cumulate votes in the election of directors.

Holders of common stock will be entitled to receive dividends and other distributions, if any, in amounts declared from time to time by our board of directors (the "Board") in its discretion out of funds legally available therefor and shall share equally on a per share basis in these dividends and distributions.

In the event of our voluntary or involuntary liquidation, dissolution, distribution of assets or winding-up, the holders of the common stock will be entitled to receive an equal amount per share of all of our assets of whatever kind available for distribution to stockholders, after the rights of the holders of the preferred stock, if any, have been satisfied.

Our stockholders have no preemptive or other subscription rights and there are no sinking fund or redemption provisions applicable to our common stock.

Our Board is divided into two classes, with only one class of directors being elected in each year and each class generally serving a two-year term.

Preferred Stock

Our second amended and restated certificate of incorporation provides that shares of preferred stock may be issued from time to time in one or more series. Our Board will be authorized to fix the voting rights, if any, designations, powers, preferences, the relative, participating, optional or other special rights and any qualifications, limitations and restrictions thereof, applicable to the shares of each series. Our Board will be able to, without stockholder approval, issue preferred stock with voting and other rights that could adversely affect the voting power and other rights of the holders of the common stock and could have anti-takeover effects. The ability of our Board to issue preferred stock without stockholder approval could have the effect of delaying, deferring or preventing a change of control of the Company or the removal of existing management.

Our Transfer Agent

The transfer agent for our common stock is Continental Stock Transfer & Trust Company. We have agreed to indemnify Continental Stock Transfer & Trust Company in its role as transfer agent, its agents and each of its stockholders, directors, officers and employees against all liabilities, including judgments, costs and reasonable counsel fees that may arise out of acts performed or omitted for its activities in that capacity, except for any liability due to any gross negligence, willful misconduct or bad faith of the indemnified person or entity.

Certain Anti-Takeover Provisions of Delaware Law and our Charter and Bylaws

We are subject to the provisions of Section 203 of the Delaware General Corporation Law (the “DGCL”) regulating corporate takeovers. This statute prevents certain Delaware corporations, under certain circumstances, from engaging in a “business combination” with:

- a stockholder who owns 15% or more of our outstanding voting stock (otherwise known as an “interested stockholder”);
- an affiliate of an interested stockholder; or
- an associate of an interested stockholder, for three years following the date that the stockholder became an interested stockholder.

A “business combination” includes a merger or sale of more than 10% of our assets. However, the above provisions of Section 203 do not apply if:

- our Board approves the transaction that made the stockholder an “interested stockholder,” prior to the date of the transaction;
- after the completion of the transaction that resulted in the stockholder becoming an interested stockholder, that stockholder owned at least 85% of our voting stock outstanding at the time the transaction commenced, other than statutorily excluded shares of common stock; or
- on or subsequent to the date of the transaction, the business combination is approved by our Board and authorized at a meeting of our stockholders, and not by written consent, by an affirmative vote of at least two-thirds of the outstanding voting stock not owned by the interested stockholder.

Our second amended and restated certificate of incorporation provides that our Board be classified into two classes of directors. As a result, in most circumstances, a person can gain control of our Board only by successfully engaging in a proxy contest at two or more annual meetings.

Our authorized but unissued common stock and preferred stock are available for future issuances without stockholder approval and could be utilized for a variety of corporate purposes, including future offerings to raise additional capital, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could render more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Stock Exchange Listing

Our common stock is currently listed on Nasdaq under the symbol “ATNF”.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee to be identified in an accompanying prospectus supplement. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement of which this prospectus forms a part and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer’s certificate or by a supplemental indenture. The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit upon the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;

- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;
- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be United States dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees.

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of a clearing agency registered under the Exchange Act, which we refer to as the depositary, or a nominee of the depositary (we will refer to any debt security represented by a global debt security as a “book-entry debt security”), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a “certificated debt security”) as set forth in the applicable prospectus supplement. Except as set forth under the heading “*Global Debt Securities and Book-Entry System*” below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities

You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange.

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System

Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the depository, and registered in the name of the depository or a nominee of the depository.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities.

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person, which we refer to as a successor person, unless:

- we are the surviving corporation or the successor person (if other than us) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and
- immediately after giving effect to the transaction, no default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us.

Events of Default

“Event of Default” means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee, or we and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of us; and
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement.

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any default or Event of Default within 30 days of becoming aware of the occurrence of such default or Event of Default, which notice will describe in reasonable detail the status of such default or Event of Default and what action we are taking or propose to take in respect thereof.

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. Subject to certain rights of the trustee, 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.

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days.

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment.

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. If a default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall send to each securityholder of the securities of that series notice of a default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities.

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

- to cure any ambiguity, defect or inconsistency;
- to comply with covenants in the indenture described above under the heading “*Consolidation, Merger and Sale of Assets*”;
- to provide for uncertificated securities in addition to or in place of certificated securities;

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- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depository;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act of 1939 (the Trust Indenture Act”).

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

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Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance

The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred.

Defeasance of Certain Covenants

The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading “*Consolidation, Merger and Sale of Assets*” and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and
- any omission to comply with those covenants will not constitute a default or an Event of Default with respect to the debt securities of that series.

We refer to this as covenant defeasance. The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities;
- such deposit will not result in a breach or violation of, or constitute a default under the indenture or any other agreement to which we are a party;
- no default or Event of Default with respect to the applicable series of debt securities shall have occurred or is continuing on the date of such deposit; and
- delivering to the trustee an opinion of counsel to the effect that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred.

No Personal Liability of Directors, Officers, Employees or Stockholders

None of our past, present or future directors, officers, employees or stockholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum.

We may issue additional warrants to purchase common stock, preferred stock and debt securities. Each such additional warrant will entitle the holder to purchase for cash a number of shares of common stock, preferred stock or the principal amount of debt securities at the exercise price as, in each case, will be described in, or can be determined from, the applicable prospectus supplement relating to the offered warrants.

Such additional warrants may be issued independently or together with any securities and may be attached to or separate from the securities. Such warrants will be issued under warrant agreements to be entered into between us and a bank or trust company, as warrant agent. You should read the particular terms of such warrants, which will be described in more detail in the applicable prospectus supplement. The particular terms of any such warrants offered by any prospectus supplement, and the extent to which the general provisions summarized below may apply to the offered securities, will be described in the prospectus supplement.

A prospectus supplement relating to any new series of warrants being offered will include specific terms relating to the offering. They will include, where applicable:

- the title of the warrants;
- the aggregate number of warrants;
- the price or prices at which the warrants will be issued;
- the currency or currencies, including composite currencies or currency units, in which the price or prices of the warrants may be payable;
- the designation, number or aggregate principal amount and terms of the securities purchasable upon exercise of the warrants, and the procedures and conditions relating to the exercise of the warrants;
- the date on which the right to exercise the warrants will commence, and the date on which the right will expire;
- the designation and terms of any related securities with which the warrants are issued, and the number of the warrants issued with each security;
- the date, if any, on and after which the warrants and the related securities will be separately transferable;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreement and the warrants;
- the maximum or minimum number of warrants which may be exercised at any time; and
- if appropriate, a discussion of material United States federal income tax considerations.

DESCRIPTION OF UNITS

We may issue units comprising two or more securities described in this prospectus in any combination. For example, we might issue units consisting of a combination of debt securities and warrants to purchase common stock. The following description sets forth certain general terms and provisions of the units that we may offer pursuant to this prospectus. The particular terms of the units and the extent, if any, to which the general terms and provisions may apply to the units so offered will be described in the applicable prospectus supplement.

Each unit will be issued so that the holder of the unit also is the holder of each security included in the unit. Thus, the unit will have the rights and obligations of a holder of each included security. Units will be issued pursuant to the terms of a unit agreement, which may provide that the securities included in the unit may not be held or transferred separately at any time or at any time before a specified date. A copy of the forms of the unit agreement and the unit certificate relating to any particular issue of units will be filed with the SEC each time we issue units, and you should read those documents for provisions that may be important to you. For more information on how you can obtain copies of the forms of the unit agreement and the related unit certificate, see the section of this prospectus captioned "*Where You Can Find More Information.*"

The prospectus supplement relating to any particular issuance of units will describe the terms of those units, including, to the extent applicable, the following:

- the designation and terms of the units and the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provision for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units; and
- whether the units will be issued in fully registered or global form.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution to our existing securityholders.

We may directly solicit offers to purchase securities or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering,

name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price or prices that may be changed from time to time;
- 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 Nasdaq 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 Nasdaq 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.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions. The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

Agents, underwriters, dealers and other persons may be entitled under agreements that they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery.

The underwriters and other persons acting as agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over-allot in connection with the offering, creating a short position for their own accounts. In addition, to cover over-allotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the third business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than three scheduled business days after the trade date for your securities, to

make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

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WHERE YOU CAN FIND MORE INFORMATION

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 filed electronically with the SEC, which is available at <http://www.sec.gov>. We also make these documents available on our website at www.180lifesciences.com. Our website and the information contained, or connected to, our website is not incorporated by reference in this prospectus or any prospectus supplement, and you should not consider it part of this prospectus or any prospectus supplement.

This prospectus forms part of the registration statement on Form S-3 we filed with the SEC under the Securities Act. Whenever a reference is made in this prospectus to a contract or other document that is an exhibit to the registration statement, the reference is only a summary and you should refer to the exhibits that are a part of the registration statement for a copy of the contract or other document. You may review a copy of the registration statement and the documents incorporated by reference herein through the SEC's website listed above.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows the Company to "incorporate by reference" information into this prospectus, which means important information may be disclosed to you by referring you to another document filed separately with the SEC. Any information incorporated by reference is deemed to be part of this prospectus.

The Company incorporates by reference in this prospectus the documents set forth below that have been previously filed with the SEC as well as any filings the Company makes with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, on or after the date of this prospectus and before the termination of the applicable offering; provided, however, that, except as specifically provided below, we are not incorporating any documents or information deemed to have been furnished rather than filed in accordance with SEC rules:

- our Annual Report on [Form 10-K](#) for the year ended December 31, 2021, filed with the SEC on March 31, 2022 (as amended by Amendment No. 1 to our Annual Report on [Form 10-K](#) filed with the SEC on April 28, 2022);
- our Definitive Proxy Statement on [Schedule 14A](#) filed on April 28, 2022 (to the extent incorporated by reference into our Annual Report on Form 10-K);
- our Quarterly Report on [Form 10-Q](#) for the quarter ended March 31, 2022, filed with the SEC on May 16, 2022;
- our Current Reports on Form 8-K filed with the SEC on [March 28, 2022](#), [April 14, 2022](#), [April 28, 2022](#) and [May 27, 2022](#); and
- the description of our common stock contained in the registration statement on [Form 8-A](#) (File No. 001-38105) filed with the SEC on May 31, 2017, including any amendments or reports filed for the purpose of updating such description.

Any statement contained in a document incorporated by reference in this prospectus shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained herein or in any other subsequently filed document that also is incorporated by reference in this prospectus modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus or any prospectus supplement.

Information furnished under Items 2.02 and 7.01 of any Current Report on Form 8-K of the Company, including any related exhibits under Item 9.01, will not be incorporated by reference in this prospectus.

To obtain copies of these filings, see "*Where You Can Find More Information.*" You may also request a copy of these filings, at no cost, by writing or telephoning to the address and telephone number set forth below:

180 Life Sciences Corp.
3000 El Camino Real, Bldg. 4, Suite 200
Palo Alto, California 94306
(650) 507-0669

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LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by DLA Piper LLP (US). Additional legal matters may be passed on for us, or any underwriters, dealers, or agents by counsel we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of 180 Life Sciences Corp. and Subsidiaries as of December 31, 2021 and 2020 and for each of the two years in the period ended December 31, 2021, incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2021, have been so incorporated in reliance on the report, which includes an explanatory paragraph as to the 180 Life Sciences Corp.'s ability to continue as a going concern, of Marcum LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

3,500,000 Shares of Common Stock
Pre-Funded Warrants to Purchase up to 2,632,076 Shares of Common Stock
Warrants to Purchase up to 6,132,076 Shares of Common Stock



PROSPECTUS SUPPLEMENT

A.G.P.

July 17, 2022
