

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

**FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933**

PHIO PHARMACEUTICALS CORP.
(Exact name of Registrant as specified in its charter)

Delaware
*(State or other jurisdiction of
incorporation or organization)*

2834
*(Primary Standard Industrial
Classification Code Number)*

45-3215903
*(I.R.S. Employer
Identification Number)*

**257 Simarano Drive, Suite 101
Marlborough, Massachusetts 01752
(508) 767-3861**
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

**Gerrit Dispersyn, Dr. Med. Sc.
President & CEO
Phio Pharmaceuticals Corp.
257 Simarano Drive, Suite 101
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Approximate date of commencement of proposed sale to the public:
As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

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

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input type="checkbox"/>
Non-accelerated filer	<input checked="" type="checkbox"/>	Smaller reporting company	<input checked="" type="checkbox"/>
		Emerging growth company	<input type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of each class of securities to be registered	Amount to be registered (1)	Proposed maximum offering price per share (2)	Proposed maximum aggregate offering Price (2)	Amount of registration fee
Common stock, par value \$0.0001 per share	8,323,694	\$2.83	\$23,556,054.02	\$2,569.97

- (1) Represents (i) 4,420,863 shares of common stock, par value \$0.0001 per share, of the registrant (the “Common Stock”), (ii) 3,560,761 shares of Common Stock that are issuable upon the exercise of certain warrants that were acquired by the selling stockholders in a private placement transaction and (iii) 342,070 shares of Common Stock that are issuable upon exercise of certain warrants issued to the placement agent pursuant to an engagement letter in connection with such private placement transaction, each of which may be sold by the selling stockholders named in this registration statement. Pursuant to Rule 416 of the Securities Act of 1933, as amended, this registration statement also covers such an indeterminate amount of shares of Common Stock as may become issuable to prevent dilution resulting from stock splits, stock dividends and similar events.
- (2) Calculated pursuant to Rule 457(c), solely for the purpose of computing the amount of the registration fee, on the basis of the average of the high and low prices of the registrant’s Common Stock quoted on The Nasdaq Capital Market on January 25, 2021.

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities, and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated _____, 2021

Preliminary Prospectus



8,323,694 Shares of Common Stock

Pursuant to this prospectus, the selling stockholders identified herein (the “**Selling Stockholders**”) are offering on a resale basis an aggregate of 8,323,694 shares of common stock, par value \$0.0001 per share (the “**Common Stock**”), of Phio Pharmaceuticals Corp. (“**Phio**,” “**we**,” “**our**” or the “**Company**”), a Delaware corporation. 7,981,624 shares of Common Stock offered for resale hereby were deemed acquired by certain Selling Stockholders pursuant to a securities purchase agreement by and among the Company and the Selling Stockholders, dated January 21, 2021 (the “**Purchase Agreement**”), of which 4,420,863 shares are outstanding and held by the Selling Stockholders and 3,560,761 shares are issuable upon the exercise of warrants (the “**Warrants**”) held by the Selling Stockholders and issued pursuant to the Purchase Agreement. 342,070 shares of Common Stock are issuable upon the exercise of Warrants issued to the Company’s placement agent in connection with the Purchase Agreement. The shares of Common Stock issued and the Common Stock issuable upon the exercise of the Warrants were issued pursuant to an exemption from the registration requirements of the Securities Act of 1933, as amended (the “**Securities Act**”) provided in Section 4(a)(2) thereof and/or Rule 506 of Regulations D promulgated thereunder. We are registering the resale of the shares of Common Stock covered by this prospectus as required by the Purchase Agreement and registration rights agreement entered into by and among the Company and the Selling Stockholders.

We will not receive any of the proceeds from the sale by the Selling Stockholders of the Common Stock. Upon any exercise of the Warrants by payment of cash, however, we will receive the exercise price of the Warrants. We intend to use those proceeds, if any, for general corporate purposes.

The Selling Stockholders may sell or otherwise dispose of the Common Stock covered by this prospectus in a number of different ways and at varying prices. We provide more information about how the Selling Stockholders may sell or otherwise dispose of the Common Stock covered by this prospectus in the section entitled “[Plan of Distribution](#)” on page 12. Discounts, concessions, commissions and similar selling expenses attributable to the sale of Common Stock covered by this prospectus will be borne by the Selling Stockholders. We will pay all expenses (other than discounts, concessions, commissions and similar selling expenses) relating to the registration of the Common Stock with the Securities and Exchange Commission.

Our common stock is listed on The Nasdaq Capital Market under the symbol “PHIO.” On January 28, 2021, the last reported sale price of our common stock on The Nasdaq Capital Market was \$3.09 per share.

Investing in our securities involves a high degree of risk. Before making any investment in these securities, you should consider carefully the risks and uncertainties described in the section entitled “[Risk Factors](#)” beginning on page 7 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense. The securities are not being offered in any jurisdiction where the offer is not permitted.

The date of this prospectus is _____, 2021

TABLE OF CONTENTS

	<u>Page</u>
Cautionary Note Regarding Forward-Looking Statements	1
Prospectus Summary	2
The Offering	6
Risk Factors	7
Use of Proceeds	8
Selling Stockholders	9
Plan of Distribution	12
Legal Matters	14
Experts	14
Where You Can Find More Information	15
Incorporation of Certain Information by Reference	16

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission (the “SEC”) utilizing a shelf registration process. Under the shelf registration process, the Selling Stockholders may, from time to time, offer and sell the shares described in this prospectus in one or more offerings. Information about the Selling Stockholders may change over time.

This prospectus provides you with a general description of the shares the Selling Stockholders may offer. Each time the Selling Stockholders sell our shares using this prospectus, to the extent necessary and required by law, we will provide a prospectus supplement that will contain specific information about the terms of that offering, including the number of shares being offered, the manner of distribution, the identity of any underwriters or other counterparties and other specific terms related to the offering. The prospectus supplement may also add, update or change information contained in this prospectus. To the extent that any statement made in a prospectus supplement is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. You should read this prospectus, any applicable prospectus supplement and the information incorporated by reference in this prospectus before making an investment in shares of our common stock. See “[Where You Can Find More Information](#)” for more information.

Neither we nor the Selling Stockholders have authorized anyone to provide any information other than that contained in this prospectus or in any free writing prospectus prepared by or on behalf of us or to which we may have referred you. Neither we nor the Selling Stockholders take any responsibility for, nor can provide assurance as to the reliability of, any other information that others may give you. Neither we nor the Selling Stockholders have authorized any other person to provide you with different or additional information, and neither of us are making an offer to sell the shares in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of the prospectus or any sale of the ordinary shares. Our business, financial condition, results of operations and prospects may have changed since the date on the front cover of this prospectus.

For investors outside of the United States, neither we nor the Selling Stockholders have done anything that would permit the offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to the offering and the distribution of this prospectus outside of the United States.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as “intends,” “believes,” “anticipates,” “indicates,” “plans,” “expects,” “suggests,” “may,” “would,” “should,” “potential,” “designed to,” “will,” “ongoing,” “estimate,” “forecast,” “predict,” “could,” and similar references, although not all forward-looking statements contain these words. Forward-looking statements are neither historical facts nor assurances of future performance. These statements are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Risks that could cause actual results to vary from expected results expressed in our forward-looking statements include, but are not limited to:

- our business and operations may be materially and adversely affected by the recent coronavirus outbreak;
- our product candidates are in an early stage of development and may fail or experience significant delays or may never advance to the clinic, which may materially and adversely impact our business;
- we are dependent on collaboration partners for the successful development of our adoptive cell therapy product candidates;
- the approach we are taking to discover and develop novel therapeutics using RNAi may never lead to marketable products;
- a number of different factors could prevent us from advancing into clinical development, obtaining regulatory approval, and ultimately commercializing our product candidates on a timely basis, or at all;
- the FDA could impose a unique regulatory regime for our therapeutics;
- we may be unable to protect our intellectual property rights licensed from other parties; our intellectual property rights may be inadequate to prevent third parties from using our technologies or developing competing products; and we may need to license additional intellectual property from others;
- we are subject to significant competition and may not be able to compete successfully;
- if we fail to attract, hire and retain qualified personnel, we may not be able to design, develop, market or sell our products or successfully manage our business;
- future financing may be obtained through, and future development efforts may be paid for by, the issuance of debt or equity, which may have an adverse effect on our stockholders or may otherwise adversely affect our business; and
- the price of our common stock has been and may continue to be volatile.

Our actual results and financial condition may differ materially from those indicated in the forward-looking statements as a result of the foregoing factors, as well as those identified in this prospectus under the heading “[Risk Factors](#)” and in other filings the Company periodically makes with the SEC. Therefore, you should not rely unduly on any of these forward-looking statements. Forward-looking statements contained in this prospectus speak as of the date hereof and the Company does not undertake to update any of these forward-looking statements to reflect a change in its views or events or circumstances that occur after the date of this report.

PROSPECTUS SUMMARY

The following summary highlights certain information contained elsewhere in this prospectus and the documents incorporated by reference herein. This summary provides an overview of selected information and does not contain all of the information you should consider in making your investment decision. Therefore, you should read the entire prospectus and the documents incorporated by reference herein carefully before investing in our securities. Investors should carefully consider the information set forth under “[Risk Factors](#)” beginning on page 7 of this prospectus and the financial statements and other information incorporated by reference in this prospectus. In this prospectus, unless otherwise noted, (1) the term “Phio” refers to Phio Pharmaceuticals Corp. and our subsidiary, MirImmune, LLC and (2) the terms “Company,” “we,” “us,” and “our” refer to the ongoing business operations of Phio and MirImmune, LLC, whether conducted through Phio or MirImmune, LLC.

Overview

Phio Pharmaceuticals Corp. is a biotechnology company developing the next generation of immuno-oncology therapeutics based on our self-delivering RNAi (“**INTASYL™**”) therapeutic platform. Our efforts are focused on silencing tumor-induced suppression of the immune system through our proprietary INTASYL platform with utility in immune cells and the tumor micro-environment. Our goal is to develop powerful INTASYL therapeutic compounds that can weaponize immune effector cells to overcome tumor immune escape, thereby providing patients a potentially powerful new treatment option that goes beyond current treatment modalities.

Our development efforts are based on our broadly patented INTASYL technology platform. Our INTASYL compounds do not require a delivery vehicle to penetrate into tissues and cells and are designed to “silence” or down-regulate, the expression of a specific gene which is over-expressed in cancer. We believe that our INTASYL platform has the potential to uniquely position the Company in the field of immuno-oncology because of this and the following reasons:

- Efficient uptake of INTASYL to immune cells obviating the need for facilitated delivery (mechanical or formulation);
- Does not require permanent genetic modification;
- Can target multiple genes (i.e. multiple immunosuppression pathways) in a single therapeutic entity;
- Gene silencing by INTASYL has been shown to have a sustained, or long-term, effect *in vivo*;
- Favorable clinical safety profile of INTASYL with local administration; and
- Can be readily manufactured under current good manufacturing practices.

The self-delivering nature of our compounds makes INTASYL ideally suited for use with adoptive cell transfer (“**ACT**”) treatments and direct therapeutic use. ACT consists of the infusion of immune cells with antitumor properties, after growing them in a lab to large numbers. These cells can be derived from unmodified (i.e. naturally occurring) immune cells, immune cells isolated from resected tumors, or genetically engineered immune cells recognizing tumor cells.

Regardless of the source of immune cells (ACT or naturally occurring immune cells), in patients with solid tumors, these cells face several hurdles. Multiple inhibitory mechanisms restrain immune cells from effectively eradicating tumors, including immune checkpoints, reduced cell fitness and cell persistence. Furthermore, the immunosuppressive tumor micro-environment (the “**TME**”) can pose a formidable barrier to immune cell infiltration and function.

We have developed a product platform based on our INTASYL technology that allows easy, precise, rapid, and selective non-genetically modified programming of ACT cells (*ex vivo*, during manufacturing) and of the TME (*in vivo*, by local application), resulting in reduced immune inhibition and in improved immunotherapy.

ACT includes a number of different types of immunotherapy treatments. These treatments use immune cells, isolated from patients, donors or retrieved from allogeneic immune cell banks. They are grown in a lab to large numbers, followed by administering them to the body to fight the cancer cells. Sometimes, immune cells that naturally recognize a tumor are used, while other times immune cells are modified or “genetically engineered” to make them recognize and kill the cancer cells. There are several types of ACT, including: a.) non-engineered cell therapy in which immune cells are grown from the patient’s tumor or blood, such as tumor infiltrating lymphocytes (“**TILs**”), or from donor blood or tissue such as natural killer (“**NK**”) cells, dendritic cells (“**DC**”) and macrophages, and b.) genetically engineered immune cells that are genetically modified to recognize specific tumor proteins and to remain in an activated state (such as T cell receptor technology (“**TCRs**”), chimeric antigen receptor (“**CAR**”) T cells, or CAR-NK cells).

In ACT, immune cells are then expanded and modified before being returned and used to treat the patient. Multiple inhibitory mechanisms restrain immune cells used in ACT from effectively eradicating tumors, including immune checkpoints, reduced cell fitness and cell persistence, and other barriers to immune cell infiltration and function mainly in solid tumors. We believe our INTASYL compounds are ideally suited to be used in combination with ACT, in order to make these immune cells more effective without the need for additional complicated manufacturing steps and/or genetic engineering.

Our approach builds on well-established methodologies of ACT and involves the treatment of immune cells with our INTASYL compounds *ex vivo* while they are grown in the lab and before administering them to the patient. Because our INTASYL compounds do not require a delivery vehicle to penetrate into the cells, we are able to enhance the function of these cells by merely adding our INTASYL compounds during the expansion process and without the need for genetic engineering and without additional needed complex manufacturing steps. By adding INTASYL to the cell culture media used during the cell expansion, we can reduce or eliminate the expression of genes that make the immune cells less effective. For example, with our INTASYL compounds, we can reduce the expression of immunosuppressive proteins by the therapeutic immune cells, potentially enabling them to overcome tumor resistance mechanisms and thus improving their ability to destroy the tumor cells. In various types of immune cells tested to date, INTASYL treatment results in potent silencing with close to 100% transfection efficiency and while maintaining nearly full cell viability. After expanding these cells and enhancing them with INTASYL *ex vivo*, they are returned to the patient for treatment.

Our lead product candidate and most advanced program being developed in ACT is PH-762, an INTASYL compound that targets the checkpoint protein PD-1. Checkpoint proteins, such as PD-1, normally act as a type of “off switch” that prevents T cells from attacking certain cells, such as cancer cells, in the body. Our T cells are immune cells that protect the body from cancer cells and infections.

Data developed by Phio and with collaborators has shown that PH-762 silences PD-1 checkpoint expression, thereby removing the “off switch” and resulting in enhanced T cell activation and tumor cytotoxicity. Experimental data shows that PH-762 can silence the expression of PD-1 in target human T cells in a potent and durable manner, and can increase function of patient derived TILs for use in ACT, showing that PH-762 is suitable for use both in ACT and as a standalone therapeutic through intra-tumoral injection. This supports the application of INTASYL technology in immunotherapy of cancer.

Our second ACT product candidate PH-894, an INTASYL compound that targets BRD4, is a regulator of gene expression impacting cell differentiation. In previous studies, PH-894 has been shown to improve T cell function and persistence by differentiating T cells into a more active state (stem-cell like memory phenotype). Data, completed in partnership with the Karolinska Institutet, demonstrated that the application of PH-894, was shown to silence BRD4 in human T cells during expansion for ACT, which has the potential to confer superior anti-tumor activity, for example by improving T cell persistence. With this data we expanded our collaboration with the Karolinska Institutet to build upon these findings and develop INTASYL compounds for additional targets and cell types toward clinical application in areas of the Karolinska Institutet’s ongoing clinical research.

We are also developing our INTASYL compound PH-804 for use in ACT. PH-804 targets the suppressive immune receptor TIGIT, which is a checkpoint protein present on T cells and NK cells. To date, we have shown that PH-804 can silence the expression of TIGIT in NK cells and T cells, overcoming their “off switch” and the cells becoming “weaponized” to kill cancer cells.

In March 2020, we entered into a collaboration and option agreement with Medigene AG and the Helmholtz Zentrum München (“HMGU”). This three-way collaboration expands upon our outstanding research agreement with HMGU to design and develop novel candidates for the use of INTASYL compounds in ACT to enhance immune cell function. Under the agreement, Medigene AG will contribute expertise regarding clinical development, as well as proprietary research material and has the option to an exclusive license for the clinical and/or commercial development of the potential immune cell enhancers.

Tumor Micro-Environment

The TME is the environment that surrounds and feeds a tumor, including normal cells, blood vessels, immune cells, and the extracellular matrix. The TME is an immunosuppressive microenvironment that inhibits the immune system’s natural ability to recognize and destroy tumor cells by negatively impacting how immunosuppressive cells are being attracted and activated. Reprogramming different components of the TME may overcome resistance to immunotherapy. Such reprogramming of the TME by INTASYL compounds through direct local administration into the tumor, could potentially become an important form of therapy. The Company has previously shown in a clinical setting that our INTASYL compounds are safe and well-tolerated following local administration, therefore we believe that our INTASYL technology can not only be used with ACT, but can also be used as an independent therapeutic platform.

We have pipeline programs in place for the development of INTASYL compounds for direct administration into the tumor, including the use of PH-762, PH-804 and PH-894 for *in situ* transfection and activation of immune cells in the TME.

Data presented in January 2020 from *in vivo* studies performed by the Company showed that intra-tumoral injection of a mouse version of PH-804 reduced the tumor growth in colorectal carcinoma tumor bearing mice, which was shown to inhibit tumor growth and was correlated with the silencing of TIGIT mRNA expression and an increase in cytotoxic effector T cells in the TME.

Building on the animal data with PH-804, the Company conducted several animal studies with a mouse version of PH-762 and with PH-894 in a validated mouse model of hepatocellular carcinoma. These studies showed that local administration of the mouse version of PH-762 or PH-894 through intra-tumoral injection resulted in potent anti-tumoral effects. The treated animals showed a complete and statistically significant inhibition of tumor growth, whereas placebo treated animals displayed exponential tumor growth. The combined PH-804, PH-762, and PH-894 data further shows that INTASYL compounds can trigger associated changes in the TME such as an increase of TILs, including CD8+ T cells responsible for tumor cell killing, and an increase of activation markers on these cells. These preclinical findings demonstrate that direct injection of INTASYL compounds can successfully infiltrate solid tumors and impact the TME by activating the immune response in animal models of solid tumors resulting in reduced tumor growth. This is one of the key challenges for many other immunotherapy platforms to be able to achieve an adequate therapeutic effect in solid tumors.

We are also investigating other relevant compounds for TME targets, such as PH-790, an INTASYL compound targeting PD-L1. PD-L1 is a protein formed by cancer cells that activate the PD-1 “off switch” on immune cells. Our approach with PH-790 is to block the formation of the PD-L1 protein, which may prevent cancer cells from inactivating T cells and attack the cancer, and will be evaluated alongside PH-762. Previously, a series of preclinical *in vivo* studies in tumor models showed dose-dependent attenuated tumor growth for the INTASYL compounds compared to control groups. Recent data presented at the 35th Annual Meeting of Society for Immunotherapy of Cancer in November 2020 demonstrated that the antitumoral efficacy of our individual pipeline products, PH-762, PH-790 and PH-804, can be further improved by combining them in a single drug treatment. This data showed that the combination of our INTASYL compounds inhibited tumor growth without having a negative impact on the tolerability of the treatment.

Corporate Information

We were incorporated in the state of Delaware in 2011 as RXi Pharmaceuticals Corporation. On November 19, 2018, the Company changed its name to Phio Pharmaceuticals Corp., to reflect its transition from a platform company to one that is fully committed to developing groundbreaking immuno-oncology therapeutics. Our executive offices are located at 257 Simarano Drive, Suite 101, Marlborough, MA 01752, and our telephone number is (508) 767-3861. The Company's website address is <http://www.phiopharma.com>. Our website and the information contained on that site, or connected to that site, is not part of or incorporated by reference into this prospectus.

Our certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings: any derivative action or proceeding brought on behalf of the Company, any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of the Company to the Company or the Company's stockholders, any action asserting a claim against the Company arising pursuant to any provision of the Delaware General Corporation Law or the Company's certificate of incorporation or bylaws, or any action asserting a claim against the Company governed by the internal affairs doctrine. Despite the fact that our certificate of incorporation provides for this exclusive forum provision to be applicable to the fullest extent permitted by applicable law, Section 27 of the Securities Act and Exchange Act of 1934, as amended (the "**Exchange Act**"), creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder and Section 22 of the Securities Act, creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. As a result, this provision of our certificate of incorporation would not apply to claims brought to enforce a duty or liability created by the Securities Act, Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

THE OFFERING

Pursuant to this prospectus, the Selling Stockholders are offering on a resale basis an aggregate of 8,323,694 shares of Common Stock. 7,981,624 shares of Common Stock offered for resale hereby were acquired by certain Selling Stockholders pursuant to the Purchase Agreement by and among the Company and the Selling Stockholders, dated January 21, 2021, of which 4,420,863 shares are outstanding and held by the Selling Stockholders and 3,560,761 shares are issuable upon the exercise of the Warrants held by the Selling Stockholders and issued pursuant to the Purchase Agreement. 342,070 shares of Common Stock are issuable upon the exercise of Warrants issued to the Company's placement agent in connection with the Purchase Agreement

Common Stock to be offered by the Selling Stockholders	4,420,863 shares of Common Stock and 3,902,831 shares of Common Stock issuable upon the exercise of Warrants.
Common Stock outstanding prior to this offering	10,201,836 shares.
Common Stock to be outstanding after this offering	14,104,667 shares (assuming the exercise of all Warrants).
Use of proceeds:	We will not receive any of the proceeds from the sale by the Selling Stockholders of the Common Stock. Upon any exercise of the Warrants by payment of cash, however, we will receive the exercise price of the Warrants. See " Use of Proceeds " on page 8 of this prospectus.
Risk factors:	You should read the " Risk Factors " section beginning on page 7 of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our securities.
Nasdaq Capital Market symbol:	Our common stock is listed on The Nasdaq Capital Market under the symbol "PHIO." We do not intend to apply for listing of the Warrants on any securities exchange or nationally recognized trading system.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before investing in our securities, you should carefully consider the risks, uncertainties and assumptions contained in this prospectus and discussed under the heading “[Risk Factors](#)” included in our Annual Report on Form 10-K for the year ended December 31, 2019 and subsequent Quarterly Reports on Form 10-Q, 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, including any accompanying prospectus supplement and the documents incorporated by reference therein. Our business, financial condition, results of operations and future growth prospects could be materially and adversely affected by any of these risks. In these circumstances, the market price of our Common Stock could decline, and you may lose all or part of your investment.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of the Common Stock by the Selling Stockholders. Some of the shares offered hereby are issuable upon the exercise of the Warrants. Upon exercise of such Warrants for cash, we will receive the applicable cash exercise price paid by the holders of the Warrants. We intend to use those proceeds, if any, for general corporate purposes.

SELLING STOCKHOLDERS

The Common Stock being offered by the Selling Stockholders are those previously issued to the Selling Stockholders, and those issuable to the Selling Stockholders, upon exercise of the Warrants. The Selling Stockholders acquired the Common Stock and the Warrants pursuant to the Purchase Agreement. We are registering the shares of Common Stock in order to permit the Selling Stockholders to offer the shares for resale from time to time. The Selling Stockholders may sell some, all or none of their shares of Common Stock. We do not know how long the Selling Stockholders will hold the Warrants, whether any will exercise the Warrants, and upon such exercise, how long such Selling Stockholders will hold the shares of Common Stock before selling them, and we currently have no agreements, arrangements or understandings with the Selling Stockholders regarding the sale of any of the shares. Except for the ownership of the shares of Common stock and the Warrants, the Selling Stockholders have not had any material relationship with us within the past three years.

The table below lists the Selling Stockholders and other information regarding the beneficial ownership of the shares of Common Stock by each of the Selling Stockholder based on information supplied to us by the Selling Stockholders. The second column lists the number of shares of Common Stock beneficially owned by each Selling Stockholder, based on its ownership of the shares of Common Stock and warrants, as of the date such information was provided to us, assuming exercise of the warrants held by the selling shareholders on that date, without regard to any limitations on exercises. The third column lists the number shares of Common Stock being offered by this prospectus by the Selling Stockholders.

In accordance with the terms of a registration rights agreement with the Selling Stockholders, this prospectus generally covers the resale of the sum of (i) the number of shares of Common Stock issued to the Selling Stockholders pursuant to the Purchase Agreement and (ii) the maximum number of shares of Common Stock issuable upon exercise of the Warrants, determined as if the outstanding Warrants were exercised in full as of the trading day immediately preceding the date this registration statement was initially filed with the SEC, each as of the trading day immediately preceding the applicable date of determination and all subject to adjustment as provided in the registration right agreement, without regard to any limitations on the exercise of the Warrants. The fourth and fifth columns assume the sale of all of the shares of Common Stock offered by the Selling Stockholders pursuant to this prospectus. Except as noted below, beneficial ownership is determined in accordance with Section 13(d) of the Exchange Act and Rule 13d-3 thereunder. The percentage of shares beneficially owned prior to the offering is based on 10,201,836 shares of our Common Stock actually outstanding as of January 25, 2021.

Under the terms of the Warrants and other warrants held by the Selling Stockholders, a Selling Stockholder may not exercise such securities to the extent such exercise would cause such Selling Stockholder, together with its affiliates and attribution parties, to beneficially own a number of shares of Common Stock which would exceed 4.99% of our then outstanding Common Stock following such exercise, excluding for purposes of such determination shares of common stock issuable upon exercise of the warrants which have not been exercised. The number of shares in the second and fourth columns do not reflect this limitation. The Selling Stockholders may sell all, some or none of their shares in this offering. See "[Plan of Distribution](#)."

Selling Stockholder	Number of Shares Beneficially Owned Before this Offering ⁽¹⁾	Number of Shares to be Sold in this Offering	Shares Beneficially Owned After this Offering	
			Number of Shares	Percentage of Total Outstanding Common Stock
Alpha Capital Anstalt ⁽²⁾	427,525	427,525	–	*
Altium Growth Fund, LP ⁽³⁾	1,140,066	1,140,066	–	*
Anson Investments Master Fund LP ⁽⁴⁾	353,949	262,500	91,499	*
Anson East Master Fund LP ⁽⁵⁾	87,500	87,500	–	*
Armistice Capital Master Fund, Ltd. ⁽⁶⁾	2,612,213	1,995,113	617,100	4.19%
Bigger Capital Fund, LP ⁽⁷⁾	379,563	288,750	90,813	*
Brio Capital Master Fund LTD. ⁽⁸⁾	175,000	175,000	–	*
Empery Asset Master, LTD ⁽⁹⁾	1,024,090	878,930	145,160	1.02%
Empery Tax Efficient, LP ⁽¹⁰⁾	284,889	259,947	24,942	*
Empery Tax Efficient III, LP ⁽¹¹⁾	286,206	286,206	–	*
Intracoastal Capital, LLC ⁽¹²⁾	1,360,204	855,048	505,156	3.46%
Iroquois Master Fund, Ltd. ⁽¹³⁾	668,176	478,826	189,350	1.32%
Iroquois Capital Investment Group LLC ⁽¹⁴⁾	315,996	233,713	82,283	*
MMCAP International Inc. SPC ⁽¹⁵⁾	612,500	612,500	–	*
Noam Rubinstein ⁽¹⁶⁾	214,061	107,752	106,309	*
Craig Schwabe ⁽¹⁶⁾	20,944	11,545	9,399	*
Michael Vasinkevich ⁽¹⁶⁾	435,974	219,352	216,622	1.51%
Charles Worthman ⁽¹⁶⁾	6,796	3,421	3,375	*

*Represents beneficial ownership of less than one percent.

(1) The ability to exercise warrants held by the Selling Stockholders is subject to a beneficial ownership limitation that, at the time of initial issuance of the warrants, was capped at either 4.99% or 9.99% beneficial ownership of the Company's issued and outstanding common stock (post-exercise). These beneficial ownership limitations may be adjusted up or down, subject to providing advanced notice to the Company, provided that any increases in beneficial ownership limitations only take effect upon 61 days advance notice. Beneficial ownership as reflected in the selling stockholder table reflects the total number of shares potentially issuable underlying warrants and does not give effect to these beneficial ownership limitations. Accordingly, actual beneficial ownership, as calculated in accordance with Section 13(d) and Rule 13d-3 thereunder may be lower than as reflected in the table.

(2) Nicola Feuerstein has sole voting and dispositive power over the securities held for the account of this Selling Stockholder. The Selling Stockholder's address is Lettstrasse 32, 9490 Vaduz, Principality of Liechtenstein.

(3) Jacob Gottlieb has sole voting and dispositive power over the securities held by Altium Growth Fund, LP. The principal business address of Altium Growth Fund, LP is 152 West 57th Street, Floor 20, New York, New York 10019.

(4) Anson Advisors Inc and Anson Funds Management LP, the Co-Investment Advisers of Anson Investments Master Fund LP ("Anson"), hold voting and dispositive power over the Common Shares held by Anson. Bruce Winson is the managing member of Anson Management GP LLC, which is the general partner of Anson Funds Management LP. Moez Kassam and Amin Nathoo are directors of Anson Advisors Inc. Mr. Winson, Mr. Kassam and Mr. Nathoo each disclaim beneficial ownership of these Common Shares except to the extent of their pecuniary interest therein. The principal business address of Anson is Walkers Corporate Limited, Cayman Corporate Centre, 27 Hospital Road, George Town, Grand Cayman KY1-9008, Cayman Islands.

(5) Anson Advisors Inc and Anson Funds Management LP, the Co-Investment Advisers of Anson East Master Fund LP (“**Anson**”), hold voting and dispositive power over the Common Shares held by Anson. Bruce Winson is the managing member of Anson Management GP LLC, which is the general partner of Anson Funds Management LP. Moez Kassam and Amin Nathoo are directors of Anson Advisors Inc. Mr. Winson, Mr. Kassam and Mr. Nathoo each disclaim beneficial ownership of these Common Shares except to the extent of their pecuniary interest therein. The principal business address of Anson is Walkers Corporate Limited, Cayman Corporate Centre, 27 Hospital Road, George Town, Grand Cayman KY1-9008, Cayman Islands.

(6) The shares are directly held by Armistice Capital Master Fund Ltd., a Cayman Islands exempted company (the “Master Fund”), and may be deemed to be indirectly beneficially owned by: (i) Armistice Capital, LLC (“Armistice Capital”), as the investment manager of the Master Fund; and (ii) Steven Boyd, as the Managing Member of Armistice Capital. The number of shares includes 1,612,213 shares of common stock issuable upon exercise of the pre-funded warrants and the warrants, both of which are subject to certain beneficial ownership limitations. Armistice Capital and Steven Boyd disclaim beneficial ownership of the securities except to the extent of their respective pecuniary interests therein.

(7) Michael Bigger is a managing member of Bigger Capital Fund, LP and has sole voting and dispositive power over the securities held by Bigger Capital Fund, LP. The principal business address of Bigger Capital Fund, LP is 11434 Glowing Sunset, Las Vegas, NV 89135.

(8) Shaye Hirsch has sole voting and dispositive power over the securities held by Brio Capital Master Fund Ltd. The principal business address of Brio Capital Master Fund Ltd. is c/o Brio Capital Management LLC, 100 Merrick Road, Suite 401W, Rockville Centre, New York 11570.

(9) Empery Asset Management LP, the authorized agent of Empery Asset Master, Ltd (“**EAM**”), has discretionary authority to vote and dispose of the securities listed in the table above held by EAM and may be deemed to be the beneficial owner of such securities. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over such securities held by EAM. EAM, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of such securities.

(10) Empery Asset Management LP, the authorized agent of Empery Tax Efficient, LP (“**ETE**”), has discretionary authority to vote and dispose of the securities listed in the table above held by ETE and may be deemed to be the beneficial owner of such securities. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over such securities held by ETE. ETE, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of such securities.

(11) Empery Asset Management LP, the authorized agent of Empery Tax Efficient III, LP (“**ETE III**”), has discretionary authority to vote and dispose of the securities listed in the table listed above held by ETE III and may be deemed to be the beneficial owner of such securities. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP, may also be deemed to have investment discretion and voting power over such securities held by ETE III. ETE III, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of such securities.

(12) Mitchell P. Kopin (“**Mr. Kopin**”) and Daniel B. Asher (“**Mr. Asher**”), each of whom are managers of Intracoastal Capital LLC (“**Intracoastal**”), have shared voting control and investment discretion over the securities reported herein that are held by Intracoastal. As a result, each of Mr. Kopin and Mr. Asher may be deemed to have beneficial ownership (as determined under Section 13(d) of the Exchange Act) of the securities reported herein that are held by Intracoastal.

(13) Iroquois Capital Management L.L.C. is the investment manager of Iroquois Master Fund, Ltd. Iroquois Capital Management, LLC has voting control and investment discretion over securities held by Iroquois Master Fund. As Managing Members of Iroquois Capital Management, LLC, Richard Abbe and Kimberly Page make voting and investment decisions on behalf of Iroquois Capital Management, LLC in its capacity as investment manager to Iroquois Master Fund Ltd. As a result of the foregoing, Mr. Abbe and Mrs. Page may be deemed to have beneficial ownership (as determined under Section 13(d) of the Exchange Act) of the shares held by Iroquois Capital Management and Iroquois Master Fund. The Selling Stockholder’s address is 125 Park Avenue, 25th Floor, New York, New York 10017.

(14) Richard Abbe is the managing member of Iroquois Capital Investment Group LLC. Mr. Abbe has voting control and investment discretion over securities held by Iroquois Capital Investment Group LLC. As such, Mr. Abbe may be deemed to be the beneficial owner (as determined under Section 13(d) of the Securities Exchange Act of 1934, as amended (the “Exchange Act”)) of the shares held by Iroquois Capital Investment Group LLC. The Selling Stockholder’s address is 125 Park Avenue, 25th Floor, New York, New York 10017.

(15) Matthew MacIssac is the Secretary of MM Asset Management Inc. and an investment advisor to MMCAP International Inc. SPC and has shared voting and dispositive power over the securities held by MMCAP International Inc. SPC. The principal business address of MMCAP International Inc. SPC is Mount Governance Services (Cayman), 94 Solaris Avenue, Camana Bay, P.O. Box 1348, Grand Cayman, Cayman Islands KY1-1108.

(16) The Selling Stockholder was issued Warrants as a representative of H.C. Wainwright, the Company’s placement agent, in connection with the Purchase Agreement and each representative has sole voting and dispositive power over the securities held. The business address is c/o H.C. Wainwright, 430 Park Avenue, 3rd Floor, New York, New York 10128.

PLAN OF DISTRIBUTION

Each Selling Stockholder of the securities and any of their pledgees, assignees and successors-in-interest may, from time to time, sell any or all of their securities covered hereby on the principal Trading Market or any other stock exchange, market or trading facility on which the securities are traded or in private transactions. These sales may be at fixed or negotiated prices. A Selling Stockholder may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- in transactions through broker-dealers that agree with the Selling Stockholders to sell a specified number of such securities at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The Selling Stockholders may also sell securities under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the Selling Stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the Selling Stockholders (or, if any broker-dealer acts as agent for the purchaser of securities, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440.

In connection with the sale of the securities or interests therein, the Selling Stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the securities in the course of hedging the positions they assume. The Selling Stockholders may also sell securities short and deliver these securities to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these securities. The Selling Stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The Selling Stockholders and any broker-dealers or agents that are involved in selling the securities may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the securities purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Each Selling Stockholder has informed the Company that it does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities.

The Company is required to pay certain fees and expenses incurred by the Company incident to the registration of the securities. The Company has agreed to indemnify the Selling Stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to keep this prospectus effective until the earlier of (i) the date on which the securities may be resold by the Selling Stockholders without registration and without regard to any volume or manner-of-sale limitations by reason of Rule 144, without the requirement for the Company to be in compliance with the current public information under Rule 144 under the Securities Act or any other rule of similar effect or (ii) all of the securities have been sold pursuant to this prospectus or Rule 144 under the Securities Act or any other rule of similar effect. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states, the resale securities covered hereby may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the resale securities may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the Selling Stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the common stock by the Selling Stockholders or any other person. We will make copies of this prospectus available to the Selling Stockholders and have informed them of the need to deliver a copy of this prospectus to each purchaser at or prior to the time of the sale (including by compliance with Rule 172 under the Securities Act).

Our common stock is quoted on The NASDAQ Capital Market under the symbol “PHIO.”

LEGAL MATTERS

Certain legal matters relating to the issuance of the securities offered by this prospectus will be passed upon for us by Gibson, Dunn & Crutcher LLP, San Francisco, California.

EXPERTS

The consolidated financial statements as of December 31, 2019 and 2018 and for each of the two years in the period ended December 31, 2019 incorporated by reference in this prospectus have been so incorporated in reliance on the report of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are required to file annual, quarterly and current reports, proxy statements and other information with the SEC. The SEC maintains an Internet site that contains all reports and other information that we file electronically with the SEC. The address of that website is www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.phioharma.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

We have filed a registration statement, of which this prospectus is a part, covering the securities offered hereby. As allowed by SEC rules, this prospectus does not include all of the information contained in the Registration Statement and the included exhibits, financial statements and schedules. You are referred to the Registration Statement, the included exhibits, financial statements and schedules for further information. Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete, and in each instance we refer you to the copy of the contract or document filed as an exhibit to the registration statement, each such statement being qualified in all respects by such reference. This prospectus is qualified in its entirety by such other information.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to “incorporate by reference” the information we have filed with them, which means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. The documents we are incorporating by reference are:

- Our Annual Report on [Form 10-K](#) for the year ended December 31, 2019, filed with the SEC on March 26, 2020;
- Our Quarterly Reports on Form 10-Q for the periods ended [March 31, 2020](#), [June 30, 2020](#) and [September 30, 2020](#) filed with the SEC respectively on May 12, 2020, August 12, 2020 and November 10, 2020;
- Our Current Reports on Form 8-K, filed with the SEC on [January 10, 2020](#), [January 14, 2020](#), [February 6, 2020](#), [February 10, 2020](#), [February 13, 2020](#), [March 12, 2020](#), [April 2, 2020](#), [October 13, 2020](#), and [January 25, 2021](#); and
- The description of our common stock contained in our registration statement on [Form 8-A12B](#) filed with the SEC on February 7, 2014, including any amendment or report filed for the purpose of updating such description.

All documents we file with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except as to any portion of any report or document that is not deemed filed under such provisions, (1) on or after the date of filing of the registration statement containing this prospectus and prior to the effectiveness of the registration statement and (2) on or after the date of this prospectus until the earlier of the date on which all of the securities registered hereunder have been sold or the registration statement of which this prospectus is a part has been withdrawn, shall be deemed incorporated by reference in this prospectus and to be a part of this prospectus from the date of filing of those documents and will be automatically updated and, to the extent described above, supersede information contained or incorporated by reference in this prospectus and previously filed documents that are incorporated by reference in this prospectus.

Nothing in this prospectus shall be deemed to incorporate information furnished but not filed with the SEC pursuant to Item 2.02, 7.01 or 9.01 of Form 8-K.

Upon written or oral request, we will provide without charge to each person, including any beneficial owner, to whom a copy of the prospectus is delivered a copy of any or all of the reports or documents incorporated by reference herein (other than exhibits to such documents, unless such exhibits are specifically incorporated by reference herein). You may request a copy of these filings, at no cost, by writing or telephoning us at the following address: Phio Pharmaceuticals Corp., 257 Simarano Drive, Suite 101, Marlborough, Massachusetts 01752 Attention: Investor Relations, telephone: (508) 767-3861. We maintain a website at www.phiopharma.com. You may access our definitive proxy statements on Schedule 14A, annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and periodic amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not incorporated by reference in, and is not part of, this prospectus. We have not authorized any one to provide you with any information that differs from that contained in this prospectus. Accordingly, you should not rely on any information that is not contained in this prospectus. You should not assume that the information in this prospectus is accurate as of any date other than the date of the front cover of this prospectus.

Phio Pharmaceuticals Corp.



Up to 8,323,694 Shares of Common Stock

PROSPECTUS

, 2021

PART II
Information Not Required in Prospectus

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The following table sets forth the fees and expenses payable in connection with the registration of the common stock hereunder. All amounts other than the SEC registration fees are estimates.

Item	Amount to be paid
SEC registration fees	\$ 2,569.97
Legal fees and expenses	10,000.00
Accounting fees and expenses	12,500.00
Printing and miscellaneous expenses	4,930.03
Total	\$ 30,000.00

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS

Section 145 of the Delaware General Corporation Law (“DGCL”) authorizes a corporation to indemnify its directors and officers against liabilities arising out of actions, suits and proceedings to which they are made or threatened to be made a party by reason of the fact that they have served or are currently serving as a director or officer to a corporation. The indemnity may cover expenses (including attorneys’ fees) judgments, fines and amounts paid in settlement actually and reasonably incurred by the director or officer in connection with any such action, suit or proceeding. Section 145 permits corporations to pay expenses (including attorneys’ fees) incurred by directors and officers in advance of the final disposition of such action, suit or proceeding. In addition, Section 145 provides that a corporation has the power to purchase and maintain insurance on behalf of its directors and officers against any liability asserted against them and incurred by them in their capacity as a director or officer, or arising out of their status as such, whether or not the corporation would have the power to indemnify the director or officer against such liability under Section 145.

Our certificate of incorporation provides that we will indemnify to the fullest extent authorized or permitted by the DGCL or any other applicable law as now or hereafter in effect any person made, or threatened to be made, a defendant or witness to any action, suit or proceeding (whether civil, criminal or otherwise) by reason of the fact that he is or was a director of our corporation or by reason of the fact that such director, at our request, is or was serving any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise in any capacity. Our certificate of incorporation also provides that no amendment or repeal of the certificate of incorporation will apply to or have any effect on any right to indemnification provided in the certificate of incorporation with respect to any acts or omissions occurring prior to such amendment or repeal.

As permitted by the DGCL, our bylaws, as amended, provide that we will indemnify to the fullest extent authorized or permitted by applicable law as now or hereafter in effect any person who was or is made, or is threatened to be made, a party or is otherwise involved in any action, suit or proceeding (whether civil, criminal, administrative or investigative), by reason of the fact that he (or a person for whom he is the legal representative) is or was a director or officer of our corporation, is or was serving at our request as a director, officer, employee, member, trustee or agent of another corporation or of a partnership, joint venture, trust, nonprofit entity or other enterprise.

Consequently, no director of the corporation will be personally liable to the corporation or its stockholders for monetary damages for any breach of fiduciary duty by such a director as a director. However, notwithstanding the preceding sentence, a director will be liable to the extent provided by Delaware law (1) for any breach of the director’s duty of loyalty to the corporation or its stockholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) for payments of unlawful dividends or for unlawful stock repurchases or redemption, or (4) for any transaction from which the director derived an improper personal benefit.

We have entered into indemnification agreements with each of our executive officers and directors. These agreements provide that, subject to limited exceptions and among other things, we will indemnify each of our executive officers and directors to the fullest extent permitted by law and advance expenses to each indemnitee in connection with any proceeding in which a right to indemnification is available.

We also maintain insurance on behalf of any person who is or was our director, officer, trustee, employee or agent or serving at our request as a director, officer, trustee, employee or agent of another corporation, partnership, joint venture, trust, non-profit entity or other enterprise against any liability asserted against the person and incurred by the person in any such capacity, or arising out of his or her status as such.

ITEM 16. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

Exhibits

Exhibit Number	Description	Incorporated by Reference Herein	
		Form	Date
3.1	Amended and Restated Certificate of Incorporation of Phio Pharmaceuticals Corp.	Current Report on Form 8-K (File No. 001-36304)	November 19, 2018
3.2	Certificate of Amendment to the Amended and Restated Certificate of Incorporation of Phio Pharmaceuticals Corp.	Current Report on Form 8-K (File No. 001-36304)	January 14, 2020
3.3	Amended and Restated Bylaws of Phio Pharmaceuticals Corp.	Current Report on Form 8-K (File No. 001-36304)	October 13, 2020
4.1	Form of Warrant.	Amendment No. 3 to the Registration Statement on Form S-1 (File No. 333-214199)	December 14, 2016
4.2	Form of Warrant.	Current Report on Form 8-K (File No. 001-36304)	April 11, 2018
4.3	Form of Placement Agent Warrant.	Current Report on Form 8-K (File No. 001-36304)	April 11, 2018
4.4	Form of Warrant.	Amendment No. 1 to the Registration Statement on Form S-1 (File No. 333-221173)	September 28, 2018
4.5	Form of Underwriter Warrant.	Current Report on Form 8-K (File No. 001-36304)	October 5, 2018
4.6	Form of Placement Agent Warrant.	Current Report on Form 8-K (File No. 001-36304)	November 20, 2019
4.7	Form of Warrant.	Current Report on Form 8-K (File No. 001-36304)	February 6, 2020
4.8	Form of Warrant.	Current Report on Form 8-K (File No. 001-36304)	February 13, 2020
4.9	Form of Underwriter Warrant.	Current Report on Form 8-K (File No. 001-36304)	February 13, 2020
4.10	Form of Warrant.	Current Report on Form 8-K (File No. 001-36304)	April 2, 2020
4.11	Form of Common Stock Warrant	Current Report on Form 8-K (File No. 001-36304)	January 25, 2021
4.12	Form of Pre-Funded Warrant	Current Report on Form 8-K (File No. 001-36304)	January 25, 2021
5.1	Opinion of Gibson, Dunn & Crutcher LLP**		
23.1	Consent of BDO USA, LLP, an Independent Registered Public Accounting Firm.**		
23.2	Consent of Gibson, Dunn & Crutcher LLP (included in Exhibit 5.1). **		
24.1	Powers of Attorney (included on the signature page of Part II of this Registration Statement on Form S-3). **		

** Filed herewith.

ITEM 17. UNDERTAKINGS

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is therefore unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

- (i) To include any prospectus required by section 10(a)(3) of the Securities Act of 1933;
- (ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and
- (iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

Provided, however, that Paragraphs (a)(1)(i), (ii), and (iii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to section 13 or section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement.

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering;

(4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:

(A) Each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii), or (x) for the purpose of providing the information required by section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities: The undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

- (i) Any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424;
- (ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant;
- (iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and
- (iv) Any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.

The undersigned Registrant, hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the Registrant's annual report pursuant to section 13(a) or section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

The undersigned Registrant hereby undertakes that:

- (i) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act of 1933 shall be deemed to be part of this registration statement as of the time it was declared effective.
- (ii) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

GIBSON DUNN

Gibson, Dunn & Crutcher LLP
555 Mission Street
San Francisco, CA 94105-0921
Tel 415.393.8200
www.gibsondunn.com

January 29, 2021

Phio Pharmaceuticals Corp.
257 Simarano Drive, Suite 101
Marlborough, Massachusetts 01752

Re: *Phio Pharmaceuticals Corp.*
Registration Statement on Form S-3

Ladies and Gentlemen:

We have examined the Registration Statement on Form S-3 (the "Registration Statement") of Phio Pharmaceuticals Corp., a Delaware corporation (the "Company"), filed with the Securities and Exchange Commission (the "Commission") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), in connection with the offering by the Selling Stockholders identified in the Registration Statement (the "Selling Stockholders") of 4,420,863 shares (the "Shares") of the Company's common stock, par value \$0.0001 per share (the "Common Stock") and up to 3,902,831 shares (the "Warrant Shares") of Common Stock that are issuable upon the exercise of warrants (the "Warrants") that were acquired by the Selling Stockholders in connection with a January 25, 2021 private placement transaction.

In arriving at the opinion expressed below, we have examined originals, or copies certified or otherwise identified to our satisfaction as being true and complete copies of the originals, of specimen common stock certificates, the Warrants and such other documents, corporate records, certificates of officers of the Company and of public officials and other instruments as we have deemed necessary or advisable to enable us to render the opinions set forth below. In our examination, we have assumed without independent investigation the genuineness of all signatures, the legal capacity and competency of all natural persons, the authenticity of all documents submitted to us as originals and the conformity to original documents of all documents submitted to us as copies.

Based upon the foregoing, and subject to the assumptions, exceptions, qualifications and limitations set forth herein, we are of the opinion that the Shares are validly issued, fully paid and non-assessable and that the Warrant Shares, when issued in accordance with the terms of the Warrants, will be validly issued, fully paid and non-assessable.

We consent to the filing of this opinion as an exhibit to the Registration Statement, and we further consent to the use of our name under the caption "Legal Matters" in the Registration Statement and the prospectus that forms a part thereof. In giving these consents, we do not thereby admit that we are within the category of persons whose consent is required under Section 7 of the Securities Act or the Rules and Regulations of the Commission.

Very truly yours,

/s/ Gibson, Dunn & Crutcher LLP

Consent of Independent Registered Public Accounting Firm

Phio Pharmaceuticals Corp.
Marlborough, Massachusetts

We hereby consent to the incorporation by reference in the Prospectus constituting a part of this Registration Statement of our report dated March 26, 2020, relating to the consolidated financial statements of Phio Pharmaceuticals Corp. appearing in the Company's Annual Report on Form 10-K for the year ended December 31, 2019.

We also consent to the reference to us under the caption "Experts" in the Prospectus.

Boston, Massachusetts
January 29, 2021