

	Unit(3)(4)	Price
Common Stock, par value \$0.01 per share		
Preferred Stock, par value \$0.01 per share		
Warrants		
Subscription Rights		
Units		
Total:		\$25,000,000.00
		\$2,897.50

- (1) This registration statement also covers (i) common stock and preferred stock that may be issued upon exercise of warrants and/or subscription rights and (ii) such indeterminate amount of securities as may be issued in exchange for or upon conversion of, as the case may be, the securities registered hereunder. In addition, securities registered hereunder may be sold separately or as units with other securities registered hereunder.
- (2) An indeterminate number of the securities is being registered as may at various times be issued at indeterminate prices, with an aggregate public offering price not to exceed \$25,000,000 or the equivalent thereof in one or more currencies.
- (3) Not specified as to each class of securities to be registered pursuant to General Instruction II.D of Form S-3 under the Securities Act.
- (4) The proposed maximum offering price per unit will be determined from time to time by the registrant in connection with, and at the time of, the issuance of the securities registered hereunder.
- (5) Calculated pursuant to Rule 457(o) under the Securities Act, based on the proposed maximum aggregate offering price.

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 or until this Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.



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

SUBJECT TO COMPLETION, DATED MARCH 30, 2017

PROSPECTUS

YIELD10 BIOSCIENCE, INC.

\$25,000,000

Common Stock

Preferred Stock

Warrants

Subscription Rights

Units

This prospectus relates to common stock, preferred stock, warrants and subscription rights that we may sell from time to time in one or more offerings up to a total public offering price of \$25,000,000 on terms to be determined at the time of sale, which securities may be sold either individually or in units. We will provide specific terms of these securities in supplements to this prospectus. You should read this prospectus and any supplement carefully before you invest. This prospectus may not be used to offer and sell securities unless accompanied by a prospectus supplement for those securities.

Our common stock is traded on The NASDAQ Capital Market under the symbol "YTEN."

These securities may be sold directly by us, through dealers or agents designated from time to time, to or through underwriters or through a combination of these methods. See "Plan of Distribution" in this prospectus. We may also describe the plan of distribution for any particular offering of these securities in any applicable prospectus supplement. If any agents, underwriters or dealers are involved in the sale of any securities in respect of which this prospectus is being delivered, we will disclose their names and the nature of our arrangements with them in a prospectus supplement. The net proceeds we expect to receive from any such sale will also be included in a prospectus supplement.

As of March 20, 2017, the aggregate market value of the voting and non-voting common equity held by non-affiliates, computed by reference to the price at which the common equity was last sold or the average bid and asked price of such common equity on that date, was approximately \$3,833,886, based on 28,402,471 shares of outstanding common stock, of which 10,361,855 were held by non-affiliates. Pursuant to General Instruction I.B.6 of Form S-3, in no event will we sell securities in a public primary offering with a value exceeding more than one-third of our public float in any 12-month period so long as our public float remains below \$75.0 million. We have not offered any securities pursuant to General Instruction I.B.6 of Form S-3 during the 12 calendar months prior to and including the date of this prospectus.

Investing in our securities involves a high degree of risk. See "Risk Factors" on page 4 of this prospectus. We may include additional risk factors in an applicable prospectus supplement under the heading "Risk Factors." You should review that section of the prospectus supplement for a discussion of matters that investors in our securities should consider.

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 or any accompanying prospectus supplement. Any representation to the contrary is a criminal offense.

Our principal executive office is at 19 Presidential Way, Woburn, Massachusetts 01801, and our telephone number is (617) 583-1700. The date of this prospectus is March [], 2017.

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YOU SHOULD RELY ONLY ON THE INFORMATION CONTAINED IN THIS PROSPECTUS, ANY PROSPECTUS SUPPLEMENT OR ANY DOCUMENT TO WHICH WE HAVE REFERRED YOU. WE HAVE NOT AUTHORIZED ANYONE ELSE TO PROVIDE YOU WITH INFORMATION THAT IS DIFFERENT. THIS PROSPECTUS AND ANY PROSPECTUS SUPPLEMENT MAY BE USED ONLY WHERE IT IS LEGAL TO SELL THESE SECURITIES. THE INFORMATION IN THIS PROSPECTUS OR ANY PROSPECTUS SUPPLEMENT IS CURRENT ONLY AS OF THE DATE ON THE FRONT OF THESE DOCUMENTS.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a "shelf" registration process. Under this shelf process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total public offering price of \$25,000,000.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the securities being offered and the terms of that offering. The prospectus supplement may also add to, 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 heading "Where You Can Find More Information" carefully before making an investment decision.

Unless the context otherwise requires, in this prospectus, "Yield10," "the Company," "we," "us," "our" and similar names refer to Yield10 Bioscience, Inc. and its subsidiaries.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement (including any document incorporated by reference herein or therein) contain statements with respect to the Company which constitute "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and are intended to be covered by the "safe harbor" created by those sections. Forward-looking statements, which are based on certain assumptions and reflect our plans, estimates and beliefs, can generally be identified by the use of forward-looking terms such as "believes," "expects," "may," "will," "should," "could," "seek," "intends," "plans," "estimates," "anticipates" or other comparable terms. These forward looking statements include, but are not limited to, statements concerning potential future collaborations and objectives for research and development, product development, and commercialization of current and future products. Our actual results could differ materially from those discussed in the forward-looking statements. Factors that could cause or contribute to these differences include those discussed in "Risk Factors" in any prospectus supplement and in the documents incorporated by reference herein or therein.

We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date they are made. We disclaim any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in company expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

You should read this prospectus and any accompanying prospectus supplement and the documents that we reference herein and therein and have filed as exhibits to the registration statement, of which this prospectus is part, completely and with the understanding that our actual future results may be materially different from what we expect. You should assume that the information appearing in this prospectus and any accompanying prospectus supplement is accurate as of the date on the front cover of this prospectus or such prospectus supplement only. Our business, financial condition, results of operations and prospects may change. We may not update these forward-looking statements, even though our situation may change in the future, unless we have obligations under the Federal securities laws to update and disclose material developments related to previously disclosed information. We qualify all of the information presented in this prospectus and any accompanying prospectus supplement, and particularly our forward-looking statements, by these cautionary statements.

ABOUT YIELD10 BIOSCIENCE, INC.

Overview

Yield10 Bioscience, Inc. is an agricultural bioscience company focusing on the development of new technologies to enable step-change increases in crop yield to enhance global food security. According to a United Nations report, food production must be increased by over 70 percent in the next 35 years to feed the growing global population, which is expected to increase from 7 billion to more than 9.6 billion by 2050. During that time period, there will be a reduction in available arable land as a result of infrastructure growth and increased pressure on scarce water resources. Harvestable food production per acre and per growing season must be increased to meet this demand.

Yield10 is using two proprietary advanced biotechnology trait gene discovery platforms to improve fundamental crop yield through enhanced photosynthetic carbon capture and increased carbon utilization efficiency to increase seed yield. These platforms are based on the principle that plants which capture and utilize carbon more efficiently will enable more robust crops capable of increased seed yield. Yield10 is working to develop, translate and demonstrate the commercial value of new genetically engineered yield trait genes in major crops and to identify additional genome editing targets for improved crop performance in several key food and feed crops, including canola, soybean, rice and corn. Yield10 Bioscience is headquartered in Woburn, Massachusetts and has an additional agricultural science facility with greenhouses in Saskatoon, Saskatchewan, Canada.

Yield10 was founded as Metabolix, Inc. in 1992 and originally focused on redirecting carbon flow in living systems to produce bioplastics and biobased chemicals. In 1997, Metabolix started a crop science research program with the intent to produce the microbial bioplastic polyhydroxybutyrate ("PHB") in high concentration in the seeds of oilseed crops or in the leaves of biomass crops where it acts as an additional carbon sink or carbon store. As we made progress on our crop program, we learned that the rate of carbon supply from photosynthesis was a bottleneck and we initiated a series of exploratory programs to develop new technologies to fundamentally increase the plants' ability to fix and capture more carbon. These early research programs resulted in the establishment of our crop yield trait gene discovery platforms and the identification of a series of promising proprietary yield trait genes.

Based on encouraging early results from these gene discovery programs, we refocused our crop science efforts to yield improvement in major food and feed crops in 2015 and rebranded the effort as Yield10 Bioscience. In 2016, we sold our biopolymers assets and restructured the Company around our crop science mission. In January 2017, we completed this transition and changed the name of the company to Yield10 Bioscience, Inc. We are developing proprietary, breakthrough plant biotechnologies to improve crop productivity and seed yield based on two proprietary discovery platforms:

- the "Smart Carbon Grid for Crops Platform,"—in which we are working to eliminate bottlenecks in plant photosynthesis and carbon metabolism by harnessing new metabolic capabilities from non-plant systems including microbes and algae; and
- the "T3 Platform,"—in which we have identified three powerful global regulator genes in plants which control complex regulatory networks and gene cascades resulting in step-change increases in photosynthetic carbon fixation and biomass yields. Molecular genomic analysis of high yielding plants developed using these genes has identified a series of additional crop trait gene targets. Genetic engineering of this new series of crop trait gene targets can be accomplished using only DNA sequences from the crop target species or through genome editing potentially reducing regulatory costs and timelines.

In our work to date, our team has demonstrated step-change yield increases in Camelina seed production and in switchgrass biomass production. We are currently progressing the development of our

lead yield trait genes in canola, soybean, rice and corn to provide step-change crop yield solutions for enhancing global food security.

With these two platforms, we have established a series of proprietary trait genes to enhance carbon dioxide capture and fixation in both C3 and C4 photosynthetic plants for yield improvement. C3 photosynthesis, the simplest type of plant photosynthetic system, exists in most agricultural crops used for human consumption, and includes canola, soybean, rice, wheat and potato. C4 photosynthesis is a more complex system. Plants using the C4 system have evolved an additional distinctive cellular structure, in which carbon dioxide is concentrated for the main photosynthesis enzyme RUBISCO through a series of metabolic and metabolite transports known as the C4 pathway. Corn and sugarcane are part of the C4 photosynthetic plant family. In general, C4 photosynthetic plants have up to five times inherently higher plant yield than plants in the C3 photosynthetic family. This difference in plant yield is a result of evolution, which has led plant scientists to consider the possibility that new genetic enhancements can be created to fundamentally improve the photosynthetic system in C3 plants.

Over the last 18 months, we have consolidated our crop science intellectual property position with approximately ten patent filings in prosecution, identified additional novel gene targets for improving crop performance and yield through genetic engineering or genome editing, formed a scientific advisory board with leaders in plant science, conducted several greenhouse studies and conducted our first Fast Field Testing of traits from our "Smart Carbon Grid for Crops" discovery platform. We have reported encouraging data for our lead yield trait gene, C3003 in Camelina from greenhouse and field tests and are conducting additional studies in Camelina, canola, soybean and rice.

Crop yield is the primary driver of the agriculture value chain. Yield can make the difference between a profitable season and losses for growers. As such, technologies to protect crop yield or increase it are the primary determinant of the seed the growers buy for planting at the start of the season. This in turn determines both revenue and market share for the major seed players. Yield10's goal is to discover, optimize and translate our yield trait gene innovations into major food and feed crops and demonstrate the economic value to growers and seed companies. In all cases our trait genes will be introduced using genetic engineering technologies either to introduce new genes, to introduce additional copies of genes from the same crop species with modified regulatory sequences from that crop species or by using genome editing technologies to reduce or eliminate the function of specific plant gene targets in individual crops. The method by which we deploy our yield trait genes has significant regulatory implications, which, in turn can affect the timelines and cost of their commercialization. We intend to create high-value assets in the form of proprietary yield gene technologies and to de-risk these assets by progressing them along the path to commercial development with increasingly larger scale field tests and multi-site field trials in major crops. We are deploying our yield trait genes into canola, soybean and corn. We are engineering these traits into the major crops with the goal that they will be suitable for the regulatory approval process and in crop varieties (germplasm) such that our traits can be readily introduced into the industry's elite crop lines by plant breeding.

Liquidity and Capital Resources

The Company held unrestricted cash, cash equivalents and investments of \$7,309,000 at December 31, 2016. We believe that these resources will be sufficient to meet our projected operating requirements into the fourth quarter of 2017. We have recently changed the focus of our business and are developing disruptive technologies for step-change improvements to crop yield to enhance global food security. We continue to face significant challenges and uncertainties in this new and developing area and, as a result, our available capital resources may be consumed more rapidly than currently expected due to: (a) increases in costs and operating expenses related to research and development activities; (b) changes we may make to the business that affect ongoing operating expenses; (c) additional changes we may make to our business strategy; (d) changes in our research and

development spending plans; and (e) other items affecting our forecasted level of expenditures and use of cash resources. Accordingly, we will need to raise additional funds to support our operating and capital needs. We will attempt to obtain additional funding through public or private financing, collaborative arrangements with strategic partners, or through additional credit lines or other debt financing sources to increase the funds available to support operations. However, there is uncertainty regarding whether we can successfully execute these actions, and we can provide no assurance that we will be able to do so. Furthermore, if we issue equity or debt securities to raise additional funds, our existing stockholders may experience dilution, and the new equity or debt securities may have rights, preferences and privileges senior to those of our existing stockholders. If we raise additional funds through collaboration, licensing or other similar arrangements, it may be necessary to relinquish valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us. Without additional funds, we will be forced to delay, scale back or eliminate some of our research and development activities or other operations and potentially delay product development in an effort to provide sufficient funds to continue our operations. If any of these events occurs, our ability to achieve our development goals would be adversely affected.

CORPORATE INFORMATION

We were incorporated in Massachusetts in June 1992 under the name of Metabolix, Inc. In September 1998, we reincorporated in Delaware. On January 9, 2017, we changed our name to Yield10 Bioscience, Inc. Our principal executive offices are located at 19 Presidential Way, Woburn, Massachusetts 01801, and our telephone number is (617) 583-1700. Our internet website is www.yield10bio.com. The information on our website is not incorporated by reference into this prospectus or any prospectus supplement and should not be considered to be part of this prospectus or any prospectus supplement. Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as well as reports relating to our securities filed by others pursuant to Section 16 of such act, are available through the investor relations page of our Internet website free of charge as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission (the "SEC"). The SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that website is www.sec.gov.

RISK FACTORS

Investing in our securities involves risk. The prospectus supplement applicable to each type or series of securities we offer will contain a discussion of the risks applicable to an investment in Yield10 and to the particular types of securities that we are offering under that prospectus supplement. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. 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.

USE OF PROCEEDS

We currently intend to use the estimated net proceeds from the sale of these securities for working capital and other general corporate purposes, and possibly acquisitions of other companies, products or technologies. Working capital and other general corporate purposes may include research and development expenditures, capital expenditures, operating and administrative expenditures, and any other purpose that we may specify in any prospectus supplement. While we have no current plans for any specific acquisitions at this time, we believe opportunities may exist from time to time to expand our current business through strategic alliances or acquisitions with other companies, products or technologies. We have not yet determined the amount of net proceeds to be used specifically for any of the foregoing purposes. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of these securities. Pending any use, as described above, we intend to invest the net proceeds in high-quality, short-term, interest-bearing securities. Our plans to use the estimated net proceeds from the sale of these securities may change, and if they do, we will update this information in a prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information included in any applicable prospectus supplements, summarizes the material terms and provisions of these types of securities but is not complete. For the complete terms of our common stock and preferred stock, please refer to our Amended and Restated Certificate of Incorporation, as amended to date, which we refer to as our Certificate of Incorporation, and our Amended and Restated By-laws, which we refer to as our By-laws, each of which is incorporated by reference into the registration statement of which this prospectus is a part and, with respect to any new shares of preferred stock, the certificate of designation which will be filed with the SEC for each new series of preferred stock we may designate, if any.

General

We will describe in a prospectus supplement the specific terms of any common stock or preferred stock we may offer pursuant to this prospectus. If indicated in a prospectus supplement, the terms of such common stock or preferred stock may differ from the terms described below.

We have 255,000,000 shares of capital stock authorized under our Certificate of Incorporation, consisting of 250,000,000 shares of common stock, par value \$0.01 per share and 5,000,000 shares of undesignated preferred stock, par value \$0.01 per share. The authorized shares of common stock and undesignated preferred stock are available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange or automated quotation system on which our securities may be listed or traded. If the approval of our stockholders is not so required, our board of directors may determine not to seek stockholder approval.

Common Stock

As of March 20, 2017, there were 28,402,471 shares of our common stock outstanding held by 44 stockholders of record.

Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our

common stock have no preemptive, subscription, redemption or conversion rights. However, each outstanding share of our common stock currently has attached to it one Preferred Stock Purchase Right issued under the shareholder rights plan, which is summarized below. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described below in "Provisions of our Certificate of Incorporation and By-Laws and Delaware Anti-Takeover Law," a majority vote of common stockholders is generally required to take action under our certificate of incorporation and by-laws.

Preferred Stock

Our board of directors is authorized, without action by the stockholders, to designate and issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series. The board of directors can fix the rights, preferences and privileges of the shares of each series and any of its qualifications, limitations or restrictions. Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of common stock. The issuance of preferred stock, while providing flexibility in connection with possible future financings and acquisitions and other corporate purposes could, under certain circumstances, have the effect of delaying, deferring or preventing a change in control of our company and might harm the market price of our common stock. There are no restrictions on our ability to repurchase or reclaim our preferred shares while there is any arrearage in the payment of dividends on our preferred stock.

Our board of directors will make any determination to issue such shares based on its judgment as to our company's best interests and the best interests of our stockholders.

Provisions of our Certificate of Incorporation and By-Laws and Delaware Anti-Takeover Law

Our certificate of incorporation and by-laws includes a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

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

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

Meetings of Stockholders. Our by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements. Our by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder

proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the by-laws.

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

Blank Check Preferred Stock. Our certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of preferred stock or common stock. Warrants may be issued independently or together with preferred stock or common stock and may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and a warrant agent. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any registered holders of warrants or beneficial owners of warrants. This summary of some provisions of the warrants is not complete. You should refer to the warrant agreement, including the forms of warrant certificate representing the warrants, relating to the specific warrants being offered for the complete terms of the warrant agreement and the warrants. That warrant agreement, together with the terms of the warrant certificate and warrants, will be filed with the SEC in connection with the offering of the specific warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the title of such warrants;

- the aggregate number of such warrants;
- the price or prices at which such warrants will be issued;
- the terms of the securities purchasable upon exercise of such warrants and the procedures and conditions relating to the exercise of such warrants;
- the price at which the securities purchasable upon exercise of such warrants may be purchased;
- the date on which the right to exercise such warrants will commence and the date on which such right shall expire;
- any provisions for adjustment of the number or amount of securities receivable upon exercise of the warrants or the exercise price of the warrants;
- if applicable, the minimum or maximum amount of such warrants that may be exercised at any one time;
- if applicable, the designation and terms of the securities with which such warrants are issued and the number of such warrants issued with each such security;
- if applicable, the date on and after which such warrants and the related securities will be separately transferable;
- information with respect to book-entry procedures, if any; and
- any other terms of such warrants, including terms, procedures and limitations relating to the exchange or exercise of such warrants.

The prospectus supplement relating to any warrants to purchase equity securities may also include, if applicable, a discussion of certain U.S. federal income tax considerations.

Warrants for the purchase of preferred stock and common stock will be offered and exercisable for U.S. dollars only. Securities warrants will be issued in registered form only.

Each warrant will entitle its holder to purchase the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement.

After the close of business on the expiration date, unexercised warrants will become void. We will specify the place or places where, and the manner in which, warrants may be exercised in the applicable prospectus supplement.

Upon receipt of payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will, as soon as practicable, forward the purchased securities. If less than all of the warrants represented by the warrant certificate are exercised, a new warrant certificate will be issued for the remaining warrants.

Prior to the exercise of any warrants to purchase preferred stock or common stock, holders of the warrants will not have any of the rights of holders of preferred stock or common stock purchasable upon exercise, including the right to vote or to receive any payments of dividends on the preferred stock or common stock purchasable upon exercise.

DESCRIPTION OF SUBSCRIPTION RIGHTS

The following is a general description of the terms of the subscription rights we may issue from time to time. Particular terms of any subscription rights we offer will be described in the prospectus supplement or free writing prospectus relating to such subscription rights, and may differ from the terms described herein.

We may issue subscription rights to purchase our securities. These subscription rights may be issued independently or together with any other security offered hereby and may or may not be transferable by the stockholder receiving the subscription rights in such offering. In connection with any offering of subscription rights, we may enter into a standby arrangement with one or more underwriters or other purchasers pursuant to which the underwriters or other purchasers may be required to purchase any securities remaining unsubscribed for after such offering.

The applicable prospectus supplement will describe the specific terms of any offering of subscription rights for which this prospectus is being delivered, including the following:

- whether common stock, preferred stock, or warrants for those securities will be offered under the stockholder subscription rights;
- the price, if any, for the subscription rights;
- the exercise price payable for each security upon the exercise of the subscription rights;
- the number of subscription rights issued to each stockholder;
- the number and terms of the securities which may be purchased per each subscription right;
- the extent to which the subscription rights are transferable;
- any other terms of the subscription rights, including the terms, procedures and limitations relating to the exchange and exercise of the subscription rights;
- the date on which the right to exercise the subscription rights shall commence, and the date on which the subscription rights shall expire;
- the extent to which the subscription rights may include an over-subscription privilege with respect to unsubscribed securities;
- if appropriate, a discussion of material U.S. federal income tax considerations; and
- if applicable, the material terms of any standby underwriting or purchase arrangement entered into by us in connection with the offering of subscription rights.

The description in the applicable prospectus supplement of any subscription rights we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable subscription rights certificate or subscription rights agreement, which will be filed with the SEC if we offer subscription rights.

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements, summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of

units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of common stock, preferred stock, warrants, rights or purchase contracts for the purchase of common stock or preferred stock in one or more series, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued 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.

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

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under "Description of Common Stock," "Description of Preferred Stock," "Description of Warrants," "Description of Rights" and "Description of Purchase Contracts" will apply to each unit, as applicable, and to any common stock, preferred stock, warrant, right or purchase contract included in each unit, as applicable.

Unit Agent

The name and address of the unit agent for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

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

PLAN OF DISTRIBUTION

We may sell the securities being offered pursuant to this prospectus directly to purchasers, to or through underwriters, through dealers or agents, or through a combination of such methods. The prospectus supplement with respect to the securities being offered will set forth the terms of the offering of those securities, including the names of the underwriters, dealers or agents, if any, the purchase price, the net proceeds to us, any underwriting discounts and other items constituting

underwriters' compensation, the public offering price, any discounts or concessions allowed or reallocated or paid to dealers and any securities exchanges on which such securities may be listed.

If underwriters are used in an offering, we will execute an underwriting agreement with such underwriters and will specify the name of each underwriter and the terms of the transaction (including any underwriting discounts and other terms constituting compensation of the underwriters and any dealers) in a prospectus supplement. The securities may be offered to the public either through underwriting syndicates represented by managing underwriters or directly by one or more investment banking firms or others, as designated. If an underwriting syndicate is used, the managing underwriter(s) will be specified on the cover of the prospectus supplement. If underwriters are used in the sale, the offered securities will be acquired by the underwriters for their own accounts and may be resold from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time. Unless otherwise set forth in the prospectus supplement, the obligations of the underwriters to purchase the offered securities will be subject to conditions precedent and the underwriters will be obligated to purchase all of the offered securities if any are purchased.

We may grant to the underwriters options to purchase additional securities to cover over-allotments, if any, at the public offering price, with additional underwriting commissions or discounts, as may be set forth in a related prospectus supplement. The terms of any over-allotment option will be set forth in the prospectus supplement for those securities.

If any underwriters are involved in the offer and sale, they will be permitted to engage in transactions that maintain or otherwise affect the price of the securities. These transactions may include over-allotment transactions, purchases to cover short positions created by the underwriter in connection with the offering and the imposition of penalty bids. If an underwriter creates a short position in the securities in connection with the offering by selling more securities than set forth on the cover page of the applicable prospectus supplement, the underwriter may reduce that short position by purchasing the securities in the open market. In general, purchases of a security to reduce a short position could cause the price of the security to be higher than it might be in the absence of such purchases. As noted above, underwriters may also choose to impose penalty bids on other underwriters and/or selling group members. This means that if underwriters purchase securities on the open market to reduce their short position or to stabilize the price of the securities, they may reclaim the amount of the selling concession from those underwriters and/or selling group members who sold such securities as part of the offering.

Neither we nor any underwriter make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of such securities. In addition, neither we nor any underwriter make any representation that such underwriter will engage in such transactions or that such transactions, once commenced, will not be discontinued without notice.

If dealers are used in an offering, we will sell the securities to the dealers as principals. The dealers then may resell the securities to the public at varying prices which they determine at the time of resale. The names of the dealers and the terms of the transaction will be specified in a prospectus supplement.

The securities may be sold directly by us or through agents we designate from time to time at a fixed price or prices, which may be changed, or at varying prices determined at the time of sale, such as in an at-the-market offering or arrangement. If agents are used in an offering, the names of the agents and the terms of the agency will be specified in a prospectus supplement. Unless otherwise indicated in a prospectus supplement, the agents will act on a best-efforts basis for the period of their appointment.

Dealers and agents named in a prospectus supplement may be deemed to be underwriters (within the meaning of the Securities Act of 1933, as amended, also referred to in this prospectus as the "Securities Act") of the securities described therein. In addition, we may sell the securities directly to institutional investors or others who may be deemed to be underwriters within the meaning of the Securities Act with respect to any resales thereof.

Underwriters, dealers and agents may be entitled to indemnification by us against specific civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the underwriters or agents may be required to make in respect thereof, under underwriting or other agreements. The terms of any indemnification provisions will be set forth in a prospectus supplement. Certain underwriters, dealers or agents and their associates may engage in transactions with and perform services for us in the ordinary course of business.

If so indicated in a prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by institutional investors to purchase securities pursuant to contracts providing for payment and delivery on a future date. We may enter into contracts with commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutional investors. The obligations of any institutional investor will be subject to the condition that its purchase of the offered securities will not be illegal at the time of delivery. The underwriters and other agents will not be responsible for the validity or performance of such contracts.

Direct sales to investors or our stockholders may be accomplished through subscription offerings or through subscription rights distributed to stockholders. In connection with subscription offerings or the distribution of subscription rights to stockholders, if all of the underlying securities are not subscribed for, we may sell any unsubscribed securities to third parties directly or through underwriters or agents. In addition, whether or not all of the underlying securities are subscribed for, we may concurrently offer additional securities to third parties directly or through underwriters or agents. If securities are to be sold through subscription rights, the subscription rights will be distributed as a dividend to the stockholders for which they will pay no separate consideration.

Any common stock sold pursuant to a prospectus supplement will be eligible for quotation and trading on NASDAQ, subject to official notice of issuance. Any underwriters to whom securities are sold by us for public offering and sale may make a market in the securities, but such underwriters will not be obligated to do so and may discontinue any market making at any time without notice.

In order to comply with the securities laws of some states, if applicable, the securities offered hereby will be sold in those jurisdictions only through registered or licensed brokers or dealers. In addition, in some states securities 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 complied with.

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C., Boston, Massachusetts. If the securities are being distributed in an underwritten offering, certain legal matters will be passed upon for the underwriters by counsel identified in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Yield10 Bioscience, Inc. as of December 31, 2016 and for the year then ended, incorporated in this Prospectus by reference from the Yield10 Bioscience, Inc. Annual Report on Form 10-K for the year ended December 31, 2016 have been audited by RSM US LLP, an independent registered public accounting firm, as stated in their report thereon (which

expresses an unqualified opinion and includes an explanatory paragraph relating to the Company's ability to continue as a going concern), incorporated herein by reference, and have been incorporated in this Prospectus and Registration Statement in reliance upon such reports and upon the authority of such firm as experts in accounting and auditing.

The consolidated financial statements incorporated in this Prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2016 have been so incorporated in reliance on the report (which contains an explanatory paragraph relating to the Company's ability to continue as a going concern as described in Note 1 to the financial statements) of PricewaterhouseCoopers 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

We are a public company and file annual, quarterly and current reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference room. Our SEC filings are also available to the public on the SEC's website at <http://www.sec.gov>, or on our website at <http://www.yield10bio.com/> under the "Investors" link. Information contained on our website is not part of this prospectus.

This prospectus is only part of a Registration Statement on Form S-3 that we have filed with the SEC under the Securities Act, and therefore omits certain information contained in the Registration Statement. We have also filed exhibits with the Registration Statement that are excluded from this prospectus, and you should refer to the applicable exhibit for a complete description of any statement referring to any contract or other document. You may:

- inspect a copy of this prospectus, including the exhibits and schedules, without charge at the public reference room;
- obtain a copy of this prospectus from the SEC upon payment of the fees prescribed by the SEC; or
- obtain a copy of this prospectus from the SEC website.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with them, which means that we can disclose important information in this prospectus by referring to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended. The documents we are incorporating by reference as of their respective dates of filing are:

- Our Annual Report on Form 10-K for the fiscal year ended December 31, 2016; and
- The description of our common stock contained in Item 1 of our Registration Statement on Form 8-A filed with the SEC on November 6, 2006, including any amendments or reports filed for the purpose of updating the description.

All documents and reports filed by us with the SEC pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than Current Reports on Form 8-K containing only information furnished under Item 2.02 or Item 7.01 of Form 8-K, unless otherwise indicated therein) after the date of this

prospectus and prior to the termination of the offering made hereby shall be deemed to be incorporated by reference into this prospectus and to be a part hereof from the date of filing of such documents. Any statement contained in a document incorporated or deemed to be incorporated by reference herein 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 which also is or is deemed to be incorporated by reference herein or in any 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. We will provide, without charge to each person, including any beneficial owner, to whom this prospectus is delivered, upon written or oral request of such person, a copy of any or all of the documents incorporated herein by reference other than exhibits, unless such exhibits are specifically incorporated by reference into such documents or this document. Requests for such documents should be addressed in writing or by telephone to:

Investor Relations
Yield10 Bioscience, Inc.
19 Presidential Way
Woburn, Massachusetts 01801
(617) 583-1700

You should rely only on the information contained in this prospectus, any prospectus supplement or any document to which we have referred you. We have not authorized anyone else to provide you with information that is different. This prospectus and any prospectus supplement may be used only where it is legal to sell these securities. The information in this prospectus or any prospectus supplement is current only as of the date on the front of these documents.

PART II**INFORMATION NOT REQUIRED IN PROSPECTUS****ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION**

The following table sets forth the costs and expenses payable by us in connection with the offerings described in this registration statement, other than underwriting discounts and commissions.

SEC Registration Fee	\$ 2,897.50
NASDAQ Capital Market Listing Fee	*
Printing Expenses	*
Accounting Fees and Expenses	*
Legal Fees and Expenses	*
Miscellaneous	*
TOTAL	\$ 2,897.50

* These fees are calculated based on the securities offered and the number of issuances and accordingly, cannot be estimated at this time.

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS

The Delaware General Corporation Law and our certificate of incorporation and by-laws provide for indemnification of our directors and officers for liabilities and expenses that they may incur in such capacities. In general, directors and officers are indemnified with respect to actions taken in good faith in a manner reasonably believed to be in, or not opposed to, the best interests of the registrant and, with respect to any criminal action or proceeding, actions that the indemnitee had no reasonable cause to believe were unlawful.

Our certificate of incorporation provides that no director shall be personally liable to us or to our stockholders for monetary damages for breach of fiduciary duty as a director, except that the limitation shall not eliminate or limit liability to the extent that the elimination or limitation of such liability is not permitted by the Delaware General Corporation Law as the same exists or may hereafter be amended.

Our by-laws further provide for the indemnification of our directors and officers to the fullest extent permitted by Section 145 of the Delaware General Corporation Law, including circumstances in which indemnification is otherwise discretionary. A principal effect of these provisions is to limit or eliminate the potential liability of our directors for monetary damages arising from breaches of their duty of care, subject to certain exceptions. These provisions may also shield directors from liability under federal and state securities laws.

We have entered into indemnification agreements with each of our directors and certain of our executive officers. These agreements provide that we will indemnify each of our directors and certain of our executive officers to the fullest extent permitted by law.

We also maintain a general liability insurance policy which covers certain liabilities of directors and officers of our company arising out of claims based on acts or omissions in their capacities as directors or officers.

ITEM 16. EXHIBITS

<u>Exhibit No.</u>	<u>Description</u>
1.1**	Form of Underwriting Agreement
4.1	Amended and Restated Certificate of Incorporation of the Company (incorporated by reference herein to the exhibits to the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2015 (File No. 001-33133))
4.2	Amended and Restated By-Laws of the Company (incorporated by reference herein to the exhibits to the Company's Registration Statement on Form S-1 (File No. 333-135760))
4.3	Amendment to Amended and Restated Certificate of Incorporation of the Company (incorporated by reference herein to the exhibit to the Company's Current Report on Form 8-K filed on January 6, 2017 (File No. 001-33133))
4.4	Specimen Stock Certificate for shares of the Company's Common Stock (incorporated by reference herein to the exhibits to the Company's Registration Statement on Form S-1 (File No. 333-135760))
4.5**	Form of Common Stock Warrant Agreement (together with form of Common Stock Warrant Certificate)
4.6**	Form of Preferred Warrant Agreement (together with form of Preferred Stock Warrant Certificate)
4.7**	Form of Certificate of Designation for the Preferred Stock (together with Preferred Stock Certificate)
4.8**	Form of Rights Agreement
4.9**	Form of Rights Certificate
5.1*	Legal Opinion of Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C.
23.1*	Consent of PricewaterhouseCoopers LLP, an independent registered public accounting firm
23.2*	Consent of RSM US LLP, an independent registered public accounting firm
23.3*	Consent of Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C. (included in the opinion filed as Exhibit 5.1)
24.1*	Power of Attorney (included on signature page to this Registration Statement)

* Filed herewith.

** To be subsequently filed, if applicable, by an amendment to the Registration Statement or by a Current Report on Form 8-K.

ITEM 17. UNDERTAKINGS

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 Securities and Exchange Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent 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 (1)(i), (1)(ii) and (1)(iii) do not apply if the information required to be included in a post-effective amendment by such clauses is contained in reports filed with or furnished to the Securities and Exchange Commission by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated herein by reference, 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:

(i) if the registrant is relying on Rule 430B:

(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; or

(ii) if the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness. 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 first use, 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 date of first use.

(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.

(6) 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 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.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 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 Securities Act of 1933, 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 Securities Act of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Woburn, Commonwealth of Massachusetts, on March 30, 2017.

YIELD10 BIOSCIENCE, INC.

By: /s/ OLIVER P. PEOPLES

Name: Oliver P. Peoples
Title: *President and Chief Executive Officer*

POWER OF ATTORNEY

We, the undersigned officers and directors of Yield10 Bioscience, Inc. hereby severally constitute and appoint Oliver P. Peoples, Charles B. Haaser, and Lynne H. Brum, and each of them singly, our true and lawful attorneys, with full power to them and each of them to sign for us in our names in the capacities indicated below, all pre-effective and post-effective amendments to this registration statement and any related subsequent registration statement pursuant to Rule 462(b) of the Securities Act of 1933, as amended, and generally to do all things in our names and on our behalf in such capacities to enable Yield10 Bioscience, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<hr/> /s/ OLIVER P. PEOPLES Oliver P. Peoples	President and Chief Executive Officer and Director (principal executive officer)	March 30, 2017
<hr/> /s/ CHARLES B. HAASER Charles B. Haaser	Chief Accounting Officer (principal accounting and financial officer)	March 30, 2017
<hr/> /s/ JOSEPH SHAULSON Joseph Shaulson	Director	March 30, 2017
<hr/> /s/ PETER N. KELLOGG Peter N. Kellogg	Director	March 30, 2017
<hr/> /s/ RICHARD HAMILTON Richard Hamilton	Director	March 30, 2017

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ ANTHONY J. SINSKEY</u> Anthony J. Sinskey	Director	March 30, 2017
<u>/s/ ROBERT L. VAN NOSTRAND</u> Robert L. Van Nostrand	Director	March 30, 2017

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<hr/>	
*	Filed herewith.
**	To be subsequently filed, if applicable, by an amendment to the Registration Statement or by a Current Report on Form 8-K.

Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C.

March 30, 2017

Yield10 Bioscience, Inc.
19 Presidential Way
Woburn, Massachusetts 01801

Ladies and Gentlemen,

We have acted as legal counsel to Yield10 Bioscience, Inc., a Delaware corporation (the "Company"), in connection with the preparation and filing with the Securities and Exchange Commission (the "Commission") of a Registration Statement on Form S-3 (the "Registration Statement"), pursuant to which the Company is registering under the Securities Act of 1933, as amended (the "Securities Act"), the following:

(i) common stock, \$0.01 par value per share (the "Common Stock");

(ii) preferred stock, \$0.01 par value per share (the "Preferred Stock");

(iii) warrants to purchase Common Stock or Preferred Stock (the "Warrants"), which may be issued under warrant agreements, to be dated on or about the date of the first issuance of the applicable Warrants thereunder, by and between the Company and a warrant agent to be selected by the Company (each, a "Warrant Agreement");

(iv) subscription rights to purchase Common Stock or Preferred Stock (the "Rights"), which may be issued pursuant to a rights agreement and certificates issued thereunder, to be dated on or about the date of the first issuance of the applicable Rights thereunder, by and between the Company and a rights agent to be selected by the Company (each, a "Rights Agreement"); and

(v) units comprised of one or more shares of Common Stock, shares of Preferred Stock, Rights and Warrants, in any combination (the "Units"), which may be issued under unit agreements, to be dated on or about the date of the first issuance of the applicable Units thereunder, by and between the Company and a unit agent to be selected by the Company (each, a "Unit Agreement").

The Common Stock, the Preferred Stock, the Warrants, the Rights, and the Units are collectively referred to herein as the "Securities." The Registration Statement relates to the registration of the Securities to be offered and sold by the Company from time to time on a delayed or continuous basis pursuant to Rule 415 under the Securities Act. The maximum aggregate public offering price of the Securities being registered is \$25,000,000. This opinion is being rendered in connection with the filing of the Registration Statement with the Commission. All capitalized terms used herein and not otherwise defined shall have the respective meanings given to them in the Registration Statement.

In connection with this opinion, we have examined the Company's Restated Certificate of Incorporation and Restated Bylaws, each as currently in effect; such other records of the corporate proceedings of the Company and certificates of the Company's officers as we have deemed relevant; and the Registration Statement and the exhibits thereto.

In our examination, we have assumed the genuineness of all signatures, the legal capacity of natural persons, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as certified or photostatic copies and the authenticity of the originals of such copies.

In our capacity as counsel to the Company in connection with such registration, we are familiar with the proceedings taken and proposed to be taken by the Company in connection with the authorization and issuance of the Securities. For purposes of this opinion, we have assumed that such proceedings will be timely and properly completed, in accordance with all requirements of applicable federal and Delaware laws, in the manner presently proposed.

The opinions set forth below are subject to the following exceptions, limitations and qualifications: (i) the effect of bankruptcy, insolvency, reorganization, fraudulent conveyance, moratorium or other similar laws now or hereafter in effect relating to or affecting the rights and remedies of creditors; (ii) the effect of general principles of equity, whether enforcement is considered in a proceeding in equity or at law, and the discretion of the court before which any proceeding therefor may be brought; (iii) the unenforceability under certain circumstances under law or court decisions of provisions providing for the indemnification of, or contribution to, a party with respect to a liability where such indemnification or contribution is contrary to public policy; and (iv) we express no opinion concerning the enforceability of any waiver of rights or defenses with respect to stay, extension or usury laws.

We have relied as to certain matters on information obtained from public officials, officers of the Company, and other sources believed by us to be responsible and we have assumed that the Warrant Agreement, Rights Agreement and Unit Agreement will each be duly authorized, executed, and delivered by the warrant agent, rights agent, and unit agent, respectively, thereunder. With respect to our opinion as to the Common Stock and Securities convertible into or exercisable for shares of Common Stock, we have assumed that, at the time of issuance and sale, a sufficient number of shares of Common Stock are authorized and available for issuance under the Company's Certificate of Incorporation as then in effect and that the consideration for the issuance and sale of the Common Stock (or Purchase Contracts, Preferred Stock, or Warrants or Rights exercisable for Common Stock) is in an amount that is not less than the par value of the Common Stock. With respect to our opinion as to the Preferred Stock and Securities convertible into or exercisable for shares of Preferred Stock, we have assumed that, at the time of issuance and sale, a sufficient number of shares of Preferred Stock are authorized, designated and available for issuance and that the consideration for the issuance and sale of the Preferred Stock (or Warrants or Rights exercisable for Preferred Stock) is in an amount that is not less than the par value of the Preferred Stock. We have also assumed that any Warrants, Rights or Units offered under the Registration Statement, and the related Warrant Agreement, Rights Agreement and Unit Agreement, as applicable, will be executed in the forms to be filed as exhibits to the Registration Statement or incorporated by reference therein. We have not independently verified any of the foregoing assumptions.

It is understood that this opinion is to be used only in connection with the offer and sale of Securities while the Registration Statement is effective under the Securities Act.

Our opinion is limited to the General Corporation Law of the State of Delaware and the laws of the State of New York. Without limiting the generality of the foregoing, we express no opinion with respect to (i) the qualification of the Shares under the securities or blue sky laws of any state or any foreign jurisdiction or (ii) the compliance with any federal or state law, rule or regulation relating to securities, or to the sale or issuance thereof.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. The Securities may be issued from time to time on a delayed or continuous basis, but this opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

Based upon the foregoing, we are of the opinion that:

1. With respect to the Common Stock, when (i) specifically authorized for issuance by the Company's Board of Directors or an authorized committee thereof (the "Authorizing Resolutions"), (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) an appropriate prospectus supplement with respect to the applicable shares of Common Stock has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations

thereunder, (iv) if the applicable shares of Common Stock are to be sold pursuant to a purchase, underwriting or similar agreement (an "Underwriting Agreement"), such Underwriting Agreement with respect to the applicable shares of Common Stock in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (v) the terms of the sale of the Common Stock have been duly established in conformity with the Company's then operative Certificate of Incorporation and By-laws and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding on the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vi) the Common Stock has been issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (vii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Common Stock will be validly issued, fully paid and nonassessable.

2. With respect to the Preferred Stock, when (i) specifically authorized for issuance by the Authorizing Resolutions, (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) an appropriate prospectus supplement with respect to the applicable shares of Preferred Stock has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (iv) if the applicable shares of Preferred Stock are to be sold pursuant to an Underwriting Agreement, such Underwriting Agreement with respect to the applicable shares of Preferred Stock in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (v) an appropriate Certificate or Certificates of Amendment or Designation relating to a class or series of the Preferred Stock to be sold under the Registration Statement has been duly authorized and adopted and filed with the Secretary of State of the State of Delaware prior to the issuance of the Preferred Stock, (vi) the terms of issuance and sale of shares of such class or series of Preferred Stock have been duly established in conformity with the Company's then operative Certificate of Incorporation and By-laws and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vii) shares of such class or series of Preferred Stock have been duly issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (viii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Preferred Stock will be validly issued, fully paid and nonassessable.

3. With respect to the Warrants, when (i) specifically authorized for issuance by the Authorizing Resolutions, (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) the Warrant Agreement relating to the Warrants has been duly authorized, executed, and delivered by the Company, (iv) an appropriate prospectus supplement with respect to the applicable Warrants has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (v) if the applicable Warrants are to be sold pursuant to an Underwriting Agreement, such Underwriting Agreement with respect to the applicable Warrants in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (vi) the terms of the Warrants and of their issuance and sale have been duly established in conformity with the Warrant Agreement and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding upon

the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vii) the Warrants have been duly executed and countersigned in accordance with the Warrant Agreement and issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (viii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Warrants will constitute valid and legally binding obligations of the Company.

5. With respect to the Rights, when (i) specifically authorized for issuance by the Authorizing Resolutions, (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) the Rights Agreement and any certificates relating to the Rights have been duly authorized, executed, and delivered by the Company, (iv) an appropriate prospectus supplement with respect to the applicable Rights has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (v) if the applicable Rights are to be sold pursuant to an Underwriting Agreement, such Underwriting Agreement with respect to the applicable Rights in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (vi) the terms of the Rights and of their issuance and sale have been duly established in conformity with the Rights Agreement and any rights certificates and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vii) the Rights have been duly executed and countersigned in accordance with the Rights Agreement and issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (viii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Rights will constitute valid and legally binding obligations of the Company.

6. With respect to the Units, when (i) specifically authorized for issuance by the Authorizing Resolutions, (ii) the Registration Statement, as finally amended (including all post-effective amendments), has become effective under the Securities Act, (iii) the Unit Agreement relating to the Units has been duly authorized, executed, and delivered by the Company, (iv) an appropriate prospectus supplement with respect to the applicable Units has been prepared, delivered and filed in compliance with the Securities Act and the applicable rules and regulations thereunder, (v) if the applicable Units are to be sold pursuant to an Underwriting Agreement, such Underwriting Agreement with respect to the applicable Units in the form filed as an exhibit to the Registration Statement, any post-effective amendment thereto or to a Current Report on Form 8-K, has been duly authorized, executed and delivered by the Company and the other parties thereto, (vi) the terms of the Units and of their issuance and sale have been duly established in conformity with the Unit Agreement and do not violate any applicable law or result in a default under or breach of any agreement or instrument binding upon the Company and comply with any requirement or restriction imposed by any court or governmental body having jurisdiction over the Company, (vii) the Units have been duly executed and countersigned in accordance with the Unit Agreement and issued and sold as contemplated by the Registration Statement and the prospectus included therein, and (viii) the Company has received the consideration provided for in the Authorizing Resolutions and, if applicable, the Underwriting Agreement, the Units will constitute valid and legally binding obligations of the Company.

We understand that you wish to file this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K promulgated under the Securities Act and to reference the firm's name under the caption "Legal

Matters" in the prospectus which forms part of the Registration Statement, and we hereby consent thereto. In giving this consent, we do not 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 promulgated thereunder.

Very truly yours,

/s/ Mintz, Levin, Cohn, Ferris,
Glovsky and Popeo, P.C.

Mintz, Levin, Cohn, Ferris,
Glovsky and Popeo, P.C.

QuickLinks

[Exhibit 5.1](#)

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report dated March 29, 2016, except for the effects of discontinued operations discussed in Note 15 to the consolidated financial statements as to which the date is March 30, 2017, relating to the financial statements which appear in Yield10 Bioscience, Inc.'s (formerly known as Metabolix, Inc.) Annual Report on Form 10-K for the year ended December 31, 2016. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 30, 2017

QuickLinks

[Exhibit 23.1](#)

[CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM](#)

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement on Form S-3 pertaining to the offering of up to \$25,000,000 of equity securities of Yield10 Bioscience, Inc. of our report dated March 30, 2017, relating to the consolidated financial statements of Yield10 Bioscience, Inc. (which report expresses an unqualified opinion and includes an explanatory paragraph relating to the company's ability to continue as a going concern), appearing in the Annual Report on Form 10-K of Yield10 Bioscience, Inc. for the year ended December 31, 2016.

We also consent to the reference to our firm under the heading "Experts" in such Registration Statement.

/s/ RSM US LLP
Boston, Massachusetts
March 30, 2017

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[Exhibit 23.2](#)

[CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM](#)