

EXACT SCIENCES CORP
Form 424B5
June 17, 2013

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The information contained in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. A registration statement relating to the securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-187000

SUBJECT TO COMPLETION, DATED JUNE 17, 2013

PROSPECTUS SUPPLEMENT
(To Prospectus dated May 2, 2013)

Shares

Exact Sciences Corporation

Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on the NASDAQ Capital Market under the symbol "EXAS." On June 14, 2013, the last reported sale price of our common stock on the NASDAQ Capital Market was \$12.34 per share.

Investing in our common stock involves a high degree of risk. Please read "Risk Factors" beginning on page S-5 of this prospectus supplement, on page 3 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

| | PER SHARE | TOTAL |
|--|--------------|-------|
| Public Offering Price | \$ | \$ |
| Underwriting Discounts and Commissions ⁽¹⁾ | | |
| Proceeds to Exact Sciences Corporation (Before Expenses) | | |

(1)

The underwriters will also be reimbursed for certain expenses incurred in this offering. See "Underwriting" for details.

Delivery of the shares of common stock is expected to be made on or about June , 2013. We have granted the underwriters an option for a period of 30 days to purchase an additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ and the total proceeds to us, before expenses, will be \$.

Joint Book-Running Managers

Jefferies

Baird

Prospectus Supplement dated June , 2013.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus form part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or the "SEC," using a "shelf" registration process. This document contains two parts. The first part consists of this prospectus supplement, which provides you with specific information about this offering. The second part, the accompanying prospectus, provides more general information, some of which may not apply to this offering. Generally, when we refer only to the "prospectus," we are referring to both parts combined.

In this prospectus supplement, the "Company," "we," "us" and "our" and similar terms refer to Exact Sciences Corporation. References to our "common stock" refer to the common stock of Exact Sciences Corporation.

This prospectus supplement, and the information incorporated herein by reference, may add, update or change information in the accompanying prospectus. You should read both this prospectus supplement and the accompanying prospectus together with additional information described under the headings "Where You Can Find More Information" and "Incorporation of Certain Information by Reference." If there is any inconsistency between the information in this prospectus supplement and the accompanying prospectus, you should rely on the information in this prospectus supplement.

You should rely only on the information contained in or incorporated by reference to this prospectus supplement and the accompanying prospectus. Neither we nor the underwriters have authorized any other person to provide information different from that contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein. If anyone provides you with different or inconsistent information, you should not rely on it. You should assume that the information appearing in the prospectus and this prospectus supplement is accurate as of the dates on their respective covers, regardless of time of delivery of the prospectus and this prospectus supplement or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since those dates.

All references in this prospectus supplement to our consolidated financial statements include, unless the context indicates otherwise, the related notes.

The industry and market data and other statistical information contained in this prospectus supplement, the accompanying prospectus and the documents we incorporate by reference are based on management's own estimates, independent publications, government publications, reports by market research firms or other published independent sources, and, in each case, are believed by management to be reasonable estimates. Although we believe these sources are reliable, we have not independently verified the information. None of the independent industry publications used in this prospectus supplement, the accompanying prospectus or the documents we incorporate by reference were prepared on our or our affiliates' behalf and none of the sources cited by us consented to the inclusion of any data from its reports, nor have we sought their consent.

CAUTIONARY STATEMENT ABOUT FORWARD LOOKING INFORMATION

Certain information set forth in this prospectus supplement, set forth in the accompanying prospectus or incorporated by reference herein or therein, may contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that are intended to be covered by the "safe harbor" created by those sections. Forward-looking statements, which are based on certain assumptions and describe our future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such as "believe," "expect," "may," "will," "should," "would," "could," "seek," "intend," "plan," "estimate," "goal," "anticipate," "project" or other comparable terms. Forward-looking statements involve inherent risks and uncertainties which could cause actual results to differ

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materially from those in the forward-looking statements, as a result of various factors including those risks and uncertainties included in this prospectus supplement under the caption "Risk Factors," and those risks and uncertainties described in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. We urge you to consider those risks and uncertainties in evaluating our forward-looking statements. All subsequent written and oral forward-looking statements attributable to us or to persons acting on our behalf are expressly qualified in their entirety by the applicable cautionary statements. We further caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made. Except as otherwise required by the federal securities laws, we disclaim any obligation or undertaking to publicly release any updates or revisions to any forward-looking statement contained herein or in the accompanying prospectus (or elsewhere) to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based.

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SUMMARY

The information below is only a summary of more detailed information included elsewhere in or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary may not contain all the information that is important to you or that you should consider before making a decision to invest in our common stock. Please read this entire prospectus supplement and the accompanying prospectus, including the risk factors, as well as the information incorporated by reference in this prospectus supplement and the accompanying prospectus, carefully.

Our Company

Exact Sciences Corporation ("we," "us," "our" or the "Company") is a molecular diagnostics company currently focused on the early detection and prevention of colorectal cancer. We have developed an accurate, non-invasive, patient-friendly screening test to meet our primary goal of becoming the market leader for a diagnostic screening product for the early detection of colorectal pre-cancer and cancer.

Our strategic roadmap to achieve this goal includes the following key components:

advance our product through U.S. Food and Drug Administration (FDA) clinical trials;

commercialize an FDA-approved product that detects colorectal pre-cancer and cancer; and

secure favorable reimbursement for our product from payors.

Our Cologuard® test is a non-invasive, stool-based DNA (sDNA) screening test designed to detect DNA markers, which in published studies have been shown to be associated with colorectal cancer. In addition to DNA markers, our test includes a protein marker to detect blood in the stool, utilizing an antibody-based fecal immunochemical test (FIT).

Our current focus is on seeking FDA approval for our Cologuard test. We believe obtaining FDA approval is important to building broad demand and successfully commercializing our sDNA colorectal cancer screening technology. We submitted the final module of our pre-market approval application to the FDA on June 7, 2013. We are also in the process of developing our strategy for the ultimate commercialization of our Cologuard test.

Corporate Information

Our executive offices are located at 441 Charmany Drive, Madison, Wisconsin 53719. Our telephone number is (608) 284-5700. Our Internet website address is www.exactsciences.com. Our Internet website and the information contained therein or connected thereto are not part of this prospectus supplement or the accompanying prospectus.

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THE OFFERING

The summary below describes some of the terms of the offering. For a more complete description of our common stock, see "Description of Capital Stock" in the accompanying prospectus.

Issuer: Exact Sciences Corporation
Shares of common stock offered by us: _____ shares.
Shares of common stock outstanding after the offering: _____ shares (or _____ shares if the underwriters' option to purchase additional shares is exercised in full).
Underwriters' Option to Purchase Additional Shares

We have granted the underwriters an option to purchase up to _____ additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.

Use of Proceeds

We intend to use the net proceeds from this offering for general corporate and working capital purposes, including for product development and in furtherance of our efforts to obtain FDA approval of our sDNA colorectal cancer screening product and product commercialization activities. See "Use of Proceeds."

NASDAQ Capital Market Listing

Our common stock is listed on the NASDAQ Capital Market under the symbol "EXAS."

Risk Factors

Investing in our common stock involves a high degree of risk. You should carefully consider all the information included or incorporated by reference in this prospectus supplement prior to investing in our common stock. In particular, we urge you to carefully consider the information contained in or incorporated by reference under "Risk Factors" beginning on page S-5 of this prospectus supplement, page 3 of the accompanying prospectus and in the documents incorporated by reference into this prospectus supplement.

Outstanding Shares

The number of shares outstanding after the offering is based on 64,093,730 shares outstanding as of March 31, 2013, and includes 111,678 shares of unvested restricted stock issued to employees and directors. The number of outstanding shares after the offering does not include, in each case as of March 31, 2013:

6,378,946 shares subject to outstanding stock options at a weighted average exercise price of \$2.89 per share;

890,883 shares subject to outstanding restricted stock unit awards;

1,076,154 additional shares of common stock reserved for issuance under our equity incentive plans; or

240,000 shares reserved for issuance upon the exercise of outstanding stock purchase warrants at a weighted average exercise price of \$1.31 per share.

If the underwriters' option to purchase additional shares is exercised in full, we will issue and sell an additional _____ shares of our common stock and will have _____ shares outstanding after the offering.

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Except as otherwise noted, all information in this prospectus supplement assumes no exercise of the underwriters' option to purchase additional shares.

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RISK FACTORS

Investing in our securities involves risk. You should carefully review the risk factors described in our Annual Report on Form 10-K for our most recent fiscal year (together with any material changes thereto contained in subsequent filed Quarterly Reports on Form 10-Q) and those contained in our other filings with the SEC, which are incorporated by reference in this prospectus supplement.

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USE OF PROCEEDS

We estimate that our net proceeds from the sale of our common stock in this offering will be approximately \$ million, after deducting the underwriting discount and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that our net proceeds from the sale of our common stock in this offering will be approximately \$ million, after deducting the underwriting discount and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for general corporate and working capital purposes, including for product development and in furtherance of our efforts to obtain FDA approval of our Cologuard colorectal cancer screening product and product commercialization activities.

The amounts and timing of our use of proceeds will vary depending on a number of factors, including the amount of cash generated or used by our operations, and the rate of growth, if any, of our business. As a result, we will retain broad discretion in the allocation of the net proceeds of this offering.

Until we use the net proceeds of this offering, we intend to invest the funds in short-term, investment-grade, interest-bearing securities.

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DILUTION

Our net tangible book value as of March 31, 2013, was \$89.1 million, or \$1.39 per share of common stock. Net tangible book value per share represents total tangible assets less total liabilities, divided by the number of shares of common stock outstanding as of March 31, 2013. After giving effect to our sale of _____ shares of common stock in this offering at the public offering price of per \$ _____ share, and after deduction of the underwriters fees and estimated offering expenses payable by us, our net tangible book value as of March 31, 2013, would have been \$ _____, or \$ _____ per share. This represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution in net tangible book value of \$ _____ per share to purchasers of common stock in this offering. The following table illustrates this calculation.

| | |
|--|---------|
| Public offering price per share of common stock | |
| Net tangible book value per share as of March 31, 2013 | \$ 1.39 |
| Increase per share attributable to this offering | |

As adjusted tangible book value per share after this offering

Dilution per share to new investors in this offering

If the underwriters exercise their option to purchase additional shares in full, our as adjusted net tangible book value per share at March 31, 2013, after giving effect to this offering, would have been \$ _____ per share, and the dilution to purchasers in this offering would have been \$ _____ per share.

The number of shares outstanding after the offering is based on 64,093,730 shares outstanding as of March 31, 2013, and includes 111,678 shares of unvested restricted stock issued to employees and directors. The number of outstanding shares after the offering does not include, in each case as of March 30, 2013:

6,378,946 shares subject to outstanding stock options at a weighted average exercise price of \$2.89 per share;

890,883 shares subject to outstanding restricted stock unit awards;

1,076,154 additional shares of common stock reserved for issuance under our equity incentive plans; or

240,000 shares reserved for issuance upon the exercise of outstanding stock purchase warrants at a weighted average exercise price of \$1.31 per share.

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**MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS
FOR NON-U.S. HOLDERS**

The following discussion summarizes certain material U.S. federal income and estate tax considerations relating to the acquisition, ownership and disposition of our common stock purchased in this offering by a non-U.S. holder (as defined below). This discussion is based on the provisions of the Internal Revenue Code of 1986, as amended (Code), final, temporary and proposed U.S. Treasury regulations promulgated thereunder and current administrative rulings and judicial decisions, all as in effect as of the date hereof. All of these authorities may be subject to differing interpretations or repealed, revoked or modified, possibly with retroactive effect, which could materially alter the tax consequences to non-U.S. holders described in this prospectus.

There can be no assurance that the IRS will not take a contrary position to the tax consequences described herein or that such position will not be sustained by a court. No ruling from the IRS has been obtained with respect to the U.S. federal income or estate tax consequences to a non-U.S. holder of the purchase, ownership or disposition of our common stock.

This discussion is for general information only and is not tax advice. All prospective non-U.S. holders of our common stock should consult their own tax advisors with respect to the U.S. federal, state, local and non-U.S. tax consequences of the purchase, ownership and disposition of our common stock.

As used in this discussion, the term "non-U.S. holder" means a beneficial owner of our common stock that is not any of the following for U.S. federal income tax purposes:

an individual who is a citizen or a resident of the United States;

a corporation or other entity taxable as a corporation for U.S. federal income tax purposes that was created or organized in or under the laws of the United States, any state thereof or the District of Columbia;

an estate whose income is subject to U.S. federal income taxation regardless of its source;

a trust (a) if a U.S. court is able to exercise primary supervision over the trust's administration and one or more U.S. persons have the authority to control all of the trust's substantial decisions or (b) that has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person; or

an entity that is disregarded as separate from its owner for U.S. federal income tax purposes if all of its interests are owned by a single person described above.

An individual may be treated, for U.S. federal income tax purposes, as a resident of the United States in any calendar year by being present in the United States on at least 31 days in that calendar year and for an aggregate of at least 183 days during a three-year period ending in the current calendar year. The 183-day test is determined by counting all of the days the individual is treated as being present in the current year, one-third of such days in the immediately preceding year and one-sixth of such days in the second preceding year. Residents are subject to U.S. federal income tax as if they were U.S. citizens.

This discussion assumes that a prospective non-U.S. holder will hold shares of our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances. In addition, this discussion does not address any aspect of U.S. federal alternative minimum, U.S. state or U.S. local or non-U.S. taxes, or the special tax rules applicable to particular non-U.S. holders, such as:

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insurance companies and financial institutions;

tax-exempt organizations;

partnerships or other pass-through entities;

regulated investment companies or real estate investment trusts;

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pension plans;

persons who received our common stock as compensation;

brokers and dealers in securities;

owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and

former citizens or residents of the United States subject to tax as expatriates.

If a partnership or other entity treated as a partnership for U.S. federal income tax purposes is an owner of our common stock, the treatment of a partner in the partnership generally will depend on the status of the partner and the activities of the partnership. We urge any owner of our common stock that is a partnership and partners in that partnership to consult their tax advisors regarding the U.S. federal income tax consequences of acquiring, owning and disposing of our common stock.

Distributions on Our Common Stock

Any distribution on our common stock paid to non-U.S. holders will generally constitute a dividend for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Distributions in excess of our current and accumulated earnings and profits will generally constitute a return of capital to the extent of the non-U.S. holder's adjusted tax basis in our common stock, and will be applied against and reduce the non-U.S. holder's adjusted tax basis. Any remaining excess will be treated as capital gain, subject to the tax treatment described below in " Gain on Sale, Exchange or Other Disposition of Our Common Stock."

Subject to the discussions below regarding backup withholding and the Foreign Account Tax Compliance Act, dividends paid to a non-U.S. holder that are not treated as effectively connected with the non-U.S. holder's conduct of a trade or business in the United States generally will be subject to withholding of U.S. federal income tax at a rate of 30% on the gross amount paid, unless the non-U.S. holder is entitled to an exemption from or reduced rate of withholding under an applicable income tax treaty. In order to claim the benefit of a tax treaty, a non-U.S. holder must provide a properly executed IRS Form W-8BEN (or successor form) prior to the payment of dividends. A non-U.S. holder eligible for a reduced rate of withholding pursuant to an income tax treaty may be eligible to obtain a refund of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

Dividends paid to a non-U.S. holder that are treated as effectively connected with a trade or business conducted by the non-U.S. holder within the United States (and, if an applicable income tax treaty so provides, are also attributable to a permanent establishment or a fixed base maintained within the United States by the non-U.S. holder) are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. To obtain the exemption, a non-U.S. holder must provide us with a properly executed IRS Form W-8ECI (or successor form) prior to the payment of the dividend. Dividends received by a non-U.S. holder that are treated as effectively connected with a U.S. trade or business generally are subject to U.S. federal income tax at rates applicable to U.S. persons. A non-U.S. holder that is a corporation may, under certain circumstances, be subject to an additional "branch profits tax" imposed at a rate of 30%, or such lower rate as specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder who provides us with an IRS Form W-8BEN, Form W-8ECI or other form must update the form or submit a new form, as applicable, if there is a change in circumstances that makes any information on such form incorrect.

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Gain On Sale, Exchange or Other Disposition of Our Common Stock

Subject to the discussions below regarding backup withholding and the Foreign Account Tax Compliance Act, a non-U.S. holder will generally not be subject to any U.S. federal income tax or withholding on any gain realized from the non-U.S. holder's sale, exchange or other disposition of shares of our common stock unless:

the gain is effectively connected with a U.S. trade or business (and, if an applicable income tax treaty so provides, is also attributable to a permanent establishment or a fixed base maintained within the United States by the non-U.S. holder), in which case the gain will be taxed on a net income basis generally in the same manner as if the non-U.S. holder were a U.S. person, and, if the non-U.S. holder is a corporation, the additional branch profits tax described above in "Distributions on Our Common Stock" may also apply;

the non-U.S. holder is an individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax on the net gain derived from the disposition, which may be offset by U.S.-source capital losses of the non-U.S. holder, if any; or

we are, or have been at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter), a "United States real property holding corporation."

Generally, we will be a "United States real property holding corporation" (USRPHC) if the fair market value of our U.S. real property interests equals or exceeds 50% of the sum of the fair market values of our worldwide real property interests and other assets used or held for use in a trade or business, all as determined under applicable U.S. Treasury regulations. We believe that we have not been and are not currently, and do not anticipate becoming in the future, a USRPHC for U.S. federal income tax purposes. However, because the determination of whether we are a USRPHC depends on the fair market value of our United States real property relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, such common stock will be treated as United States real property interests only if you actually or constructively hold more than five percent of such regularly traded common stock at any time during the applicable period that is specified in the Code.

Backup Withholding and Information Reporting

We must report annually to the IRS and to each non-U.S. holder the amount of distributions paid to such holder and the amount of tax withheld, if any. Copies of the information returns filed with the IRS to report the distributions and withholding may also be made available to the tax authorities in a country in which the non-U.S. holder is a resident under the provisions of an applicable income tax treaty or agreement.

The United States imposes a backup withholding tax on the gross amount of dividends and certain other types of payments. Dividends paid to a non-U.S. holder will not be subject to backup withholding if proper certification of foreign status (usually on IRS Form W-8BEN) is provided, and we do not have actual knowledge or reason to know that the non-U.S. holder is a U.S. person. In addition, no backup withholding or information reporting will be required regarding the proceeds of a disposition of our common stock made by a non-U.S. holder within the United States or conducted through certain U.S. financial intermediaries if the payor receives the certification of foreign status described in the preceding sentence and the payor does not have actual knowledge or reason to know that such non-U.S. holder is a U.S. person or the non-U.S. holder otherwise establishes an exemption. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Backup withholding is not an additional tax. Amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal

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income tax liability, if any, provided that certain required information is furnished to the IRS in a timely manner.

U.S. Federal Estate Tax

An individual non-U.S. holder who is treated as the owner, or who has made certain lifetime transfers, of an interest in our common stock will be required to include the value of the common stock in his or her gross estate for U.S. federal estate tax purposes and may be subject to U.S. federal estate tax, unless an applicable estate tax treaty provides otherwise.

Recently-Enacted Legislation Relating to Foreign Accounts

In addition to the withholding described above, legislation enacted in 2010, known as the Foreign Account Tax Compliance Act ("FATCA"), generally imposes a withholding tax of 30% on dividends paid with respect to our common stock and on the gross proceeds of a sale or other disposition of our common stock, if the payments are made to a foreign entity, unless certain diligence, reporting, withholding and certification obligations and requirements are met. Subsequent U.S. Treasury regulations have delayed the implementation of withholding under FATCA with respect to dividends until after December 31, 2013, and with respect to payments of gross proceeds until after December 31, 2016.

The withholding under FATCA may be avoided if (i) the foreign entity is a "foreign financial institution" (as defined in the Code) and such institution enters into an agreement with the U.S. government to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which would include certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or (ii) the foreign entity is not a "foreign financial institution" and makes a certification identifying its substantial U.S. owners (as defined in the Code) or makes a certification that such foreign entity does not have any substantial U.S. owners. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules. Under certain circumstances, a non-U.S. holder of our common stock might be eligible for refunds or credits of such withholding taxes, and a non-U.S. holder might be required to file a U.S. federal income tax return to claim such refunds or credits.

Non-U.S. holders should consult their own tax advisors regarding the implications of this legislation on their investment in our common stock.

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UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, to be dated on or about June 18, 2013, between us and Jefferies LLC and Robert W. Baird & Co. Incorporated, as the representatives of the underwriters named below and the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

| Underwriter | Number of Shares |
|------------------------------------|-----------------------------|
| Jefferies LLC | |
| Robert W. Baird & Co. Incorporated | |
| Total | |

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriters have advised us that they do not intend to confirm sales to any account over which they exercise discretionary authority.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ _____ per share of common stock. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of \$ _____ per share of common stock to certain brokers and dealers. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such

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amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

| | Per Share | | Total | |
|---|--|---|--|---|
| | Without Option to Purchase Additional Shares | With Option to Purchase Additional Shares | Without Option to Purchase Additional Shares | With Option to Purchase Additional Shares |
| Public offering price | \$ | \$ | \$ | \$ |
| Underwriting discounts and commissions paid by us | | | | |
| Proceeds to us, before expenses | | | | |

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$175,000. We also have agreed to reimburse the underwriters for their FINRA counsel fee up to \$10,000. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Listing

Our common stock is listed on the NASDAQ Capital Market under the trading symbol "EXAS."

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of _____ shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus.

No Sales of Similar Securities

We and our officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

sell, offer, contract or grant any option to sell (including without limitation any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Exchange Act, as amended, or

otherwise dispose of any common stock, options or warrants to acquire common stock, or securities exchangeable or exercisable for or convertible into common stock currently or hereafter owned either of record or beneficially (as defined in Rule 13d-3 under the Exchange Act, as amended), or

publicly announce an intention to do any of the foregoing for a period of 90 days after the date of the underwriting agreement relating to this offering without the prior written consent of Jefferies LLC and Robert W. Baird & Co. Incorporated.

This restriction terminates after the close of trading of the common stock on and including the 90 day after the date of the underwriting agreement relating to this offering. However, subject to certain exceptions, in the event that either:

during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or

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prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period,

then in either case the expiration of the 90-day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of an earnings release or the occurrence of the material news or event, as applicable, unless Jefferies LLC and Robert W. Baird & Co. Incorporated waive, in writing, such an extension.

Jefferies LLC and Robert W. Baird & Co. Incorporated may, in their sole discretion and at any time or from time to time before the termination of the 90-day period release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters 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 our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

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The underwriters may also engage in passive market making transactions in our common stock on the NASDAQ Capital Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

In connection with this offering, XMS Capital Partners, LLC, a FINRA member, will be paid a fee of \$300,000 for providing advisory services to us. This fee is deemed to constitute underwriting compensation under Rule 5110 of the rules of The Financial Industry Regulatory Authority, Inc.

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

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

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NOTICE TO INVESTORS

Australia

This prospectus and the accompanying prospectus are not disclosure documents for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, have not been lodged with the Australian Securities & Investments Commission and are only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus supplement in Australia:

A.

You confirm and warrant that you are either a:

"sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

"sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the Company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or

"professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act, any offer made to you under this prospectus is void and incapable of acceptance.

B.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the "Relevant Implementation Date"), no offer of any securities which are the subject of the offering contemplated by this prospectus supplement has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;

to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive;

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provided that no such offer of securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus

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Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus and the accompanying prospectus have not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus supplement may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus supplement and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the underwriters will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus supplement and the accompanying prospectus have not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

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Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;

where no consideration is given for the transfer; or

where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This prospectus supplement has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus supplement nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus supplement nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA ("FINMA"), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus supplement only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated (each such person being referred to as a "relevant person").

This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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LEGAL MATTERS

K&L Gates LLP, Raleigh, North Carolina, will pass upon certain legal matters relating to this offering. Covington & Burling LLP, New York, New York, is counsel to the underwriters in connection with this offering.

EXPERTS

The financial statements as of December 31, 2012 and 2011 and for each of the three years in the period ended December 31, 2012 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2012 incorporated by reference in this prospectus supplement have been so incorporated in reliance on the reports of BDO USA LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We are currently subject to the information requirements of the Exchange Act, and in accordance therewith, file periodic reports, proxy statements and other information with the SEC. We also filed a registration statement on Form S-3, including exhibits, under the Securities Act, with respect to the securities offered by this prospectus supplement. This prospectus supplement and the accompanying prospectus are a part of the registration statement but do not contain all of the information included in the registration statement or the exhibits. You may read and copy the registration statement, and any other document that we file, at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. You can call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference room. You can also find our public filings with the SEC on the internet at a website maintained by the SEC located at www.sec.gov.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus supplement and the accompanying prospectus, which means that we can disclose important information about us by referring you to another document filed separately with the SEC. The information incorporated by reference is considered to be a part of this prospectus supplement and the accompanying prospectus. We incorporate by reference the documents and reports listed below:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2012, filed with the SEC on March 1, 2013;

Our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2013 filed on May 3, 2013;

Our Current Reports on Form 8-K filed on May 3, 2013 and June 7, 2013;

The description of our common stock contained in our Registration Statement on Form S-1, filed with the SEC on January 30, 2001, including any amendment or reports filed for the purpose of updating such description (Registration No. 333-48812);

The description of our preferred stock purchase rights contained in our Registration Statement on Form 8-A filed with the SEC on February 23, 2011; and

all documents filed after the date of this prospectus supplement and prior to the termination of the offering hereunder pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934.

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Information in this prospectus supplement supersedes related information in the documents listed above, and information in subsequently filed documents supersedes related information in each of this prospectus supplement, the prospectus and the incorporated documents.

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We will promptly provide, without charge to you, upon written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus supplement or the prospectus, other than exhibits to those documents, unless the exhibits are specifically incorporated by reference in those documents. Requests should be directed to:

Corporate Secretary
Exact Sciences Corporation
441 Charmany Drive
Madison, Wisconsin 53719
(608) 284-5700

You can also find these filings on our website at www.exactsciences.com. We are not incorporating the information on our website other than these filings into this prospectus supplement or the prospectus.

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\$200,000,000

**Common Stock
Preferred Stock
Debt Securities
Warrants**

This prospectus relates to common stock, preferred stock, debt securities and warrants that Exact Science Corporation may sell from time to time in one or more offerings up to a total public offering price of \$200,000,000 on terms to be determined at the time of sale. 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 trades on the NASDAQ Capital Market under the symbol "EXAS."

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.

INVESTING IN OUR SECURITIES INVOLVES RISKS. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES DESCRIBED UNDER THE HEADING "RISK FACTORS" CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND ANY RELATED FREE WRITING PROSPECTUS, AND UNDER SIMILAR HEADINGS IN OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS. SEE "RISK FACTORS" ON PAGE 3 OF THIS PROSPECTUS.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is May 2, 2013.

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WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission (the "SEC"). You can inspect and copy these reports, proxy statements and other information 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 further information on the Public Reference Room. The SEC also maintains a web site that contains reports, proxy and information statements and other information regarding issuers, such as Exact Sciences Corporation (www.sec.gov). Our web site is located at www.exactsciences.com. The information contained on our web site is not part of this prospectus.

This prospectus "incorporates by reference" certain information that we have filed with the SEC under the Securities Exchange Act of 1934. This means we are disclosing important information to you by referring you to those documents. We incorporate by reference the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until the offering is terminated:

Annual Report on Form 10-K for the fiscal year ended December 31, 2012 as filed on March 1, 2013; and

The description of the Company's Common Stock contained in the Company's Registration Statement on Form 8-A, filed with the SEC pursuant to Section 12(g) of the Exchange Act on December 26, 2000, including any further amendment or report filed hereafter for the purpose of updating such description.

You should rely only on the information incorporated by reference or provided in this prospectus. We have authorized no one to provide you with different information. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of this document. All documents that we file pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus or after the date of the registration statement of which this prospectus forms a part and prior to the termination of the offering will be deemed to be incorporated in this prospectus by reference and will be a part of this prospectus from the date of the filing of the document. Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or in any other subsequently filed document which also is or is deemed to be incorporated by reference in this prospectus modifies or supersedes that statement. Any statement that is modified or superseded will not constitute a part of this prospectus, except as modified or superseded.

We will provide, upon written or oral request, without charge to you, including any beneficial owner to whom this prospectus is delivered, a copy of any or all of the documents incorporated herein by reference other than the exhibits to those documents, unless the exhibits are specifically incorporated by reference into the information that this prospectus incorporates. You should direct a request for copies to us at Attention: Secretary, 441 Charmany Drive, Madison, WI 53719 or you may call us at 608.284.5700.

FORWARD-LOOKING STATEMENTS

Certain information set forth in this prospectus or incorporated by reference in this prospectus may contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), that are intended to be covered by the "safe harbor" created by those sections. Forward-looking statements, which are based on certain assumptions and describe our future plans, strategies and expectations, can generally be identified by the use of forward-looking terms such

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as "believe," "expect," "may," "will," "should," "would," "could," "seek," "intend," "plan," "estimate," "goal," "anticipate," "project" or other comparable terms. Forward-looking statements involve inherent risks and uncertainties which could cause actual results to differ materially from those in the forward-looking statements, as a result of various factors including those risks and uncertainties included in this prospectus under the caption "Risk Factors," and those risks and uncertainties described in the documents incorporated by reference into this prospectus. We urge you to consider those risks and uncertainties in evaluating our forward-looking statements. All subsequent written and oral forward-looking statements attributable to us or to persons acting on our behalf are expressly qualified in their entirety by the applicable cautionary statements. We further caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made. Except as otherwise required by the federal securities laws, we disclaim any obligation or undertaking to publicly release any updates or revisions to any forward-looking statement contained herein or in the accompanying prospectus (or elsewhere) to reflect any change in our expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based.

PROSPECTUS SUMMARY

This prospectus is part of a registration statement on Form S-3 that we filed with the SEC utilizing a "shelf" registration process. Under this shelf process, we may from time to time, sell any combination of securities described in this prospectus in one or more offerings.

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 terms of the securities being offered. That prospectus supplement may include a discussion of any risk factors or other special consideration that apply to those securities. The prospectus supplement may also add, update or change information contained in this prospectus. If there is any inconsistency between the information in this prospectus and a prospectus supplement, you should rely on the information in that prospectus supplement. You should read both this prospectus and any applicable prospectus supplement together with additional information described above under the heading "Where You Can Find More Information."

When acquiring any securities discussed in this prospectus, you should rely on the information provided in this prospectus and the prospectus supplement, including the information incorporated by reference. Neither we, nor any underwriters or agents, have authorized anyone to provide you with different information. We are not offering the securities in any state where such an offer is prohibited. You should not assume that the information in this prospectus, any prospectus supplement, or any document incorporated by reference, is truthful or complete at any date other than the date mentioned on the cover page of those documents. You should also carefully review the section entitled "Risk Factors", which highlights certain risks associated with an investment in our securities, to determine whether an investment in our securities is appropriate for you.

References in this prospectus to "Exact", the "Company", "we", "us" and "our" are to Exact Sciences Corporation and its subsidiaries.

THE COMPANY

Exact Sciences Corporation ("we," "us," "our" or the "Company") is a molecular diagnostics company currently focused on the early detection and prevention of colorectal cancer. We have developed an accurate, non-invasive, patient friendly screening test to meet our primary goal of becoming the market leader for a diagnostic screening product for the early detection of colorectal pre-cancer and cancer.

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Our strategic roadmap to achieve this goal includes the following key components:

advance our product through U.S. Food and Drug Administration (FDA) clinical trials;

commercialize an FDA-approved product that detects colorectal pre-cancer and cancer; and

secure favorable reimbursement for our product from payors.

Our Cologuard® test is a non-invasive, stool-based DNA (sDNA) screening test designed to detect DNA markers, which in published studies have been shown to be associated with colorectal cancer. In addition to DNA markers, our test includes a protein marker to detect blood in the stool, utilizing an antibody-based fecal immunochemical test (FIT).

USE OF PROCEEDS

We currently intend to use the estimated net proceeds from the sale of these securities for general corporate and working capital purposes, including to fund strategic initiatives that we may undertake from time to time, for product development and in furtherance of our efforts to obtain FDA clearance of our sDNA colorectal cancer screening product and product commercialization activities. 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. 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.

RATIO OF EARNINGS TO FIXED CHARGES

Our earning are inadequate to cover fixed charges. The following table sets forth the dollar amount of the coverage deficiency (in thousands) for the periods indicated.

| | Fiscal Year Ended December 31 | | | | |
|---|-------------------------------|----------|----------|---------|---------|
| | 2012 | 2011 | 2010 | 2009 | 2008 |
| Ratio of Earnings to Fixed Charges | * | * | * | * | * |
| Deficiency of Earnings to Cover Fixed Charges | (52,421) | (28,675) | (11,556) | (9,128) | (9,741) |

*
During each of these periods, our earnings were less than our fixed charges. The amount of the deficiency for each period is set forth in the above table under the caption "Deficiency of Earnings to Cover Fixed Charges."

RISK FACTORS

Investing in our securities involves risk. See the risk factors described in our Annual Report on Form 10-K for our most recent fiscal year (together with any material changes thereto contained in subsequent filed Quarterly Reports on Form 10-Q) and those contained in our other filings with the SEC, which are incorporated by reference in this prospectus and any accompanying prospectus supplement.

The prospectus supplement applicable to each type or series of securities we offer may contain a discussion of risks applicable 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 caption "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained in the prospectus supplement or appearing or incorporated by reference in this prospectus. These risks could materially affect our business, results of operations or financial condition and cause the value of our securities to decline. You could lose all or part of your investment.

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DESCRIPTION OF DEBT SECURITIES WE MAY OFFER

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 initial 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.

General

The debt securities that we may issue will constitute debentures, notes, bonds or other evidences of indebtedness of Exact, to be issued in one or more series, which may include senior debt securities, subordinated debt securities and senior subordinated debt securities. The particular terms of any series of debt securities we offer, including the extent to which the general terms set forth below may be applicable to a particular series, will be described in a prospectus supplement relating to such series.

Debt securities that we may issue will be issued under an indenture between us and a trustee qualified to act as such under the Trust Indenture Act of 1939. We have filed the form of the indenture as an exhibit to the registration statement of which this prospectus is a part. When we refer to the "indenture" in this prospectus, we are referring to the indenture under which your debt securities are issued as supplemented by any supplemental indenture applicable to your debt securities. We will provide the name of the trustee in any prospectus supplement related to the issuance of debt securities, and we will also provide certain other information related to the trustee, including describing any relationship we have with the trustee, in such prospectus supplement.

THE FOLLOWING DESCRIPTION IS A SUMMARY OF THE MATERIAL PROVISIONS OF THE INDENTURE. IT DOES NOT RESTATE THE INDENTURE IN ITS ENTIRETY. THE INDENTURE IS GOVERNED BY THE TRUST INDENTURE ACT OF 1939. THE TERMS OF THE DEBT SECURITIES INCLUDE THOSE STATED IN THE INDENTURE AND THOSE MADE PART OF THE INDENTURE BY REFERENCE TO THE TRUST INDENTURE ACT. WE URGE YOU TO READ THE INDENTURE BECAUSE IT, AND NOT THIS DESCRIPTION, DEFINES YOUR RIGHTS AS A HOLDER OF THE DEBT SECURITIES.

Information You Will Find In The Prospectus Supplement

The indenture provides that we may issue debt securities from time to time in one or more series and that we may denominate the debt securities and make them payable in foreign currencies. The indenture does not limit the aggregate principal amount of debt securities that can be issued thereunder. The prospectus supplement for a series of debt securities will provide information relating to the terms of the series of debt securities being offered, which may include:

the title and denominations of the debt securities of the series;

any limit on the aggregate principal amount of the debt securities of the series;

the date or dates on which the principal and premium, if any, with respect to the debt securities of the series are payable or the method of determination thereof;

the rate or rates, which may be fixed or variable, at which the debt securities of the series shall bear interest, if any, or the method of calculating and/or resetting such rate or rates of interest;

the dates from which such interest shall accrue or the method by which such dates shall be determined and the duration of the extensions and the basis upon which interest shall be calculated;

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the interest payment dates for the series of debt securities or the method by which such dates will be determined, the terms of any deferral of interest and any right of ours to extend the interest payments periods;

the place or places where the principal and interest on the series of debt securities will be payable;

the terms and conditions upon which debt securities of the series may be redeemed, in whole or in part, at our option or otherwise;

our obligation, if any, to redeem, purchase, or repay debt securities of the series pursuant to any sinking fund or other specified event or at the option of the holders and the terms of any such redemption, purchase, or repayment;

the terms, if any, upon which the debt securities of the series may be convertible into or exchanged for other securities, including, among other things, the initial conversion or exchange price or rate and the conversion or exchange period;

if the amount of principal, premium, if any, or interest with respect to the debt securities of the series may be determined with reference to an index or formula, the manner in which such amounts will be determined;

if any payments on the debt securities of the series are to be made in a currency or currencies (or by reference to an index or formula) other than that in which such securities are denominated or designated to be payable, the currency or currencies (or index or formula) in which such payments are to be made and the terms and conditions of such payments;

any changes or additions to the provisions of the indenture dealing with defeasance, including any additional covenants that may be subject to our covenant defeasance option;

the currency or currencies in which payment of the principal and premium, if any, and interest with respect to debt securities of the series will be payable, or in which the debt securities of the series shall be denominated, and the particular provisions applicable thereto in accordance with the indenture;

the portion of the principal amount of debt securities of the series which will be payable upon declaration of acceleration or provable in bankruptcy or the method by which such portion or amount shall be determined;

whether the debt securities of the series will be secured or guaranteed and, if so, on what terms;

any addition to or change in the events of default with respect to the debt securities of the series;

the identity of any trustees, authenticating or paying agents, transfer agents or registrars;

the applicability of, and any addition to or change in, the covenants currently set forth in the indenture;

the subordination, ranking or priority, if any, of the debt securities of the series and terms of the subordination;

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any other terms of the debt securities of the series which are not prohibited by the indenture; and

whether securities of the series shall be issuable as registered securities or bearer securities (with or without interest coupons), and any restrictions applicable to the offering, sale or delivery of such bearer securities and the terms upon which such bearer securities of a series may be exchanged for registered securities, and vice versa.

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Holders of debt securities may present debt securities for exchange in the manner, at the places, and subject to the restrictions set forth in the debt securities, the indenture, and the prospectus supplement. We will provide these services without charge, other than any tax or other governmental charge payable in connection therewith, but subject to the limitations provided in the indenture, any board resolution establishing such debt securities and any applicable indenture supplement. Debt securities in bearer form and the coupons, if any, appertaining thereto will be transferable by delivery.

Senior Debt

We may issue senior debt securities under the indenture and any coupons that will constitute part of our senior debt. Unless otherwise set forth in the applicable indenture supplement and described in a prospectus supplement, the senior debt securities will be senior unsecured obligations, ranking equally with all of our existing and future senior unsecured debt. The senior debt securities will be senior to all of our subordinated debt and junior to any secured debt we may incur as to the assets securing such debt.

Subordinated Debt

We may issue subordinated debt securities under the indenture and any coupons that will constitute part of such subordinated debt. These subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner set forth in the indenture and any applicable indenture supplement, to all of our senior indebtedness.

If this prospectus is being delivered in connection with a series of subordinated debt securities, the accompanying prospectus supplement or the information incorporated by reference will set forth the approximate amount of senior indebtedness outstanding as of the end of the most recent fiscal quarter.

Senior Subordinated Debt

We may issue senior subordinated debt securities under the indenture and any coupons that will constitute part of our senior subordinated debt. These senior subordinated debt securities will be, to the extent and in the manner set forth in the applicable indenture supplement, subordinate and junior in right of payment to all of our "senior indebtedness" and senior to our other subordinated debt. See the discussions above under " Senior Debt" and " Subordinated Debt" for a more detailed explanation of our senior and subordinated indebtedness.

Interest Rate

Debt securities that bear interest will do so at a fixed rate or a floating rate. We may sell, at a discount below the stated principal amount, any debt securities which bear no interest or which bear interest at a rate that at the time of issuance is below the prevailing market rate. The relevant prospectus supplement will describe the special United States federal income tax considerations applicable to:

any discounted debt securities; and

any debt securities issued at par which are treated as having been issued at a discount for United States federal income tax purposes.

Registered Global Securities

We may issue registered debt securities of a series in the form of one or more fully registered global securities. We will deposit the registered global security with a depository or with a nominee for a depository identified in the prospectus supplement relating to such series. The global security or global securities will represent and will be in a denomination or aggregate denominations equal to the

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portion of the aggregate principal amount of outstanding registered debt securities of the series to be represented by the registered global security or securities. Unless it is exchanged in whole or in part for debt securities in definitive registered form, a registered global security may not be transferred, except as a whole in three cases:

by the depository for the registered global security to a nominee of the depository;

by a nominee of the depository to the depository or another nominee of the depository; and

by the depository or any nominee to a successor of the depository or a nominee of the successor.

The prospectus supplement relating to a series of debt securities will describe the specific terms of the depository arrangement concerning any portion of that series of debt securities to be represented by a registered global security. We anticipate that the following provisions will generally apply to all depository arrangements.

Upon the issuance of a registered global security, the depository will credit, on its book-entry registration and transfer system, the principal amounts of the debt securities represented by the registered global security to the accounts of persons that have accounts with the depository. These persons are referred to as "participants." Any underwriters, agents or debtors participating in the distribution of debt securities represented by the registered global security will designate the accounts to be credited. Only participants or persons that hold interests through participants will be able to beneficially own interests in a registered global security. The depository for a global security will maintain records of beneficial ownership interests in a registered global security for participants. Participants or persons that hold through participants will maintain records of beneficial ownership interests in a global security for persons other than participants. These records will be the only means to transfer beneficial ownership in a registered global security.

The laws of some states may require that specified purchasers of securities take physical delivery of the securities in definitive form. These laws may limit the ability of those persons to own, transfer or pledge beneficial interests in global securities.

So long as the depository, or its nominee, is the registered owner of a registered global security, the depository or its nominee will be considered the sole owner or holder of the debt securities represented by the registered global security for all purposes under the indenture. Except as set forth below, owners of beneficial interests in a registered global security:

may not have the debt securities represented by a registered global security registered in their names;

will not receive or be entitled to receive physical delivery of debt securities represented by a registered global security in definitive form; and

will not be considered the owners or holders of debt securities represented by a registered global security under the indenture.

Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depository for the registered global security and, if the person is not a participant, on the procedures of the participant through which the person owns its interests, to exercise any rights of a holder under the indenture applicable to the registered global security.

We understand that, under existing industry practices, if we request any action of holders, or if an owner of a beneficial interest in a registered global security desires to give or take any action which a holder is entitled to give or take under the indenture, the depository for the registered global security would authorize the participants holding the relevant beneficial interests to give or take the action, and the participants would authorize beneficial owners owning through the participants to give or take the action or would otherwise act upon the instructions of beneficial owners holding through them.

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Payment of Interest on and Principal of Registered Global Securities

We will make principal, premium, if any, and interest payments on debt securities represented by a registered global security registered in the name of a depository or its nominee to the depository or its nominee as the registered owner of the registered global security. None of Exact, the trustee, or any paying agent for debt securities represented by a registered global security will have any responsibility or liability for:

any aspect of the records relating to, or payments made on account of, beneficial ownership interests in such registered global security;

maintaining, supervising, or reviewing any records relating to beneficial ownership interests;

the payments to beneficial owners of the global security of amounts paid to the depository or its nominee; or

any other matter relating to the actions and practices of the depository, its nominee or any of its participants.

We expect that the depository, upon receipt of any payment of principal, premium or interest in respect of the global security, will immediately credit participants' accounts with payments in amounts proportionate to their beneficial interests in the principal amount of a registered global security as shown on the depository's records. We also expect that payments by participants to owners of beneficial interests in a registered global security held through participants will be governed by standing instructions and customary practices. This is currently the case with the securities held for the accounts of customers registered in "street name." Such payments will be the responsibility of participants.

Exchange of Registered Global Securities

We may issue debt securities in definitive form in exchange for the registered global security if both of the following occur:

the depository for any debt securities represented by a registered global security is at any time unwilling or unable to continue as depository or ceases to be a clearing agency registered under the Exchange Act; and

we do not appoint a successor depository within 90 days.

In addition, we may, at any time, determine not to have any of the debt securities of a series represented by one or more registered global securities. In this event, we will issue debt securities of that series in definitive form in exchange for all of the registered global security or securities representing those debt securities.

Covenants by Exact

The indenture includes covenants by us, including among other things that we will make all payments of principal and interest at the times and places required. The supplemental indenture establishing each series of debt securities may contain additional covenants, including covenants which could restrict our right to incur additional indebtedness or liens and to take certain actions with respect to our businesses and assets.

Events of Default

Unless otherwise indicated in the applicable prospectus supplement, the following will be events of default under the indenture with respect to each series of debt securities issued under the indenture:

failure to pay when due any interest on any debt security of that series, continued for 30 days;

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failure to pay when due the principal of, or premium, if any, on, any debt security of that series;

default in the payment of any sinking fund installment with respect to any debt security of that series when due and payable;

failure to perform any other covenant or agreement of ours under the indenture or the supplemental indenture with respect to that series or the debt securities of that series, continued for 90 days after written notice to us by the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the series to which the covenant or agreement relates;

certain events of bankruptcy, insolvency or similar proceedings affecting us; and

any other event of default specified in any supplemental indenture under which such series of debt securities is issued.

Except as to certain events of bankruptcy, insolvency or similar proceedings affecting us and except as provided in the applicable prospectus supplement, if any event of default shall occur and be continuing with respect to any series of debt securities under the indenture, either the trustee or the holders of at least 25% in aggregate principal amount of outstanding debt securities of such series may accelerate the maturity of all debt securities of such series. Upon certain events of bankruptcy, insolvency or similar proceedings affecting us, the principal, premium, if any, and interest on all debt securities of each series shall be immediately due and payable.

After any such acceleration, but before a judgment or decree based on acceleration has been obtained by the trustee, the holders of a majority in aggregate principal amount of each affected series of debt securities may waive all defaults with respect to such series and rescind and annul such acceleration if all events of default, other than the non-payment of accelerated principal, have been cured, waived or otherwise remedied.

No holder of any debt securities will have any right to institute any proceeding with respect to the indenture or for any remedy under the indenture, unless such holder shall have previously given to the trustee written notice of a continuing event of default and the holders of at least 25% in aggregate principal amount of the outstanding debt securities of the relevant series shall have made written request and offered indemnity satisfactory to the trustee to institute such proceeding as trustee, and the trustee shall not have received from the holders of a majority in aggregate principal amount of the outstanding debt securities of such series a direction inconsistent with such request and shall have failed to institute such proceeding within 60 days. However, such limitations do not apply to a suit instituted by a holder of a debt security for enforcement of payment of the principal of and premium, if any, or interest on such debt security on or after the respective due dates expressed in such debt security.

Supplemental Indentures

We and the trustee may, at any time and from time to time, without prior notice to or consent of any holders of debt securities, enter into one or more indentures supplemental to the indenture, among other things:

to add guarantees to or secure any series of debt securities;

to provide for the succession of another person pursuant to the provisions of the indenture relating to consolidations, mergers and sales of assets and the assumption by such successor of our covenants, agreements, and obligations, or to otherwise comply with the provisions of the indenture relating to consolidations, mergers, and sales of assets;

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to surrender any right or power conferred upon us under the indenture or to add to our covenants further covenants, restrictions, conditions or provisions for the protection of the holders of all or any series of debt securities;

to cure any ambiguity or to correct or supplement any provision contained in the indenture, in any supplemental indenture or in any debt securities that may be defective or inconsistent with any other provision contained therein;

to modify or amend the indenture in such a manner as to permit the qualification of the indenture or any supplemental indenture under the Trust Indenture Act;

to add to or change any of the provisions of the indenture to supplement any of the provisions of the indenture in order to permit the defeasance and discharge of any series of debt securities pursuant to the indenture, so long as any such action does not adversely affect the interests of the holders of debt securities of any series in any material respect;

to add to, change, or eliminate any of the provisions of the indenture with respect to one or more series of debt securities, so long as any such addition, change or elimination shall not apply to any debt securities of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision;

to evidence and provide for the acceptance of appointment by a successor or separate trustee; and

to establish the form or terms of debt securities of any series and to make any change that does not adversely affect the interests of the holders of debt securities.

With the consent of the holders of at least a majority in principal amount of debt securities of each series affected by such supplemental indenture (each series voting as one class), we and the trustee may enter into one or more supplemental indentures for the purpose of adding any provisions to or changing in any manner or eliminating any of the provisions of the indenture or modifying in any manner the rights of the holders of debt securities of each such series.

Notwithstanding our rights and the rights of the trustee to enter into one or more supplemental indentures with the consent of the holders of debt securities of the affected series as described above, no such supplemental indenture shall, without the consent of the holder of each outstanding debt security of the affected series, among other things:

change the final maturity of the principal of, or any installment of interest on, any debt securities;

reduce the principal amount of any debt securities or the rate of interest on any debt securities;

change the currency in which any debt securities are payable;

impair the right of the holders to conduct a proceeding for any remedy available to the trustee;

reduce the percentage in principal amount of any series of debt securities whose holders must consent to an amendment or supplemental indenture;

modify the ranking or priority of the securities;

reduce any premium payable upon the redemption of any debt securities; or

make any change that adversely affects the relative rights of holders of subordinated debt securities with respect to senior debt securities.

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Satisfaction and Discharge of the Indenture; Defeasance

Except to the extent set forth in a supplemental indenture with respect to any series of debt securities, we, at our election, may discharge the indenture and the indenture shall generally cease to be of any further effect with respect to that series of debt securities if (a) we have delivered to the trustee for cancellation all debt securities of that series (with certain limited exceptions) or (b) all debt securities of that series not previously delivered to the trustee for cancellation shall have become due and payable, or are by their terms to become due and payable within one year or are to be called for redemption within one year, and we have deposited with the trustee the entire amount sufficient to pay at maturity or upon redemption all such debt securities.

In addition, we have a "legal defeasance option" (pursuant to which we may terminate, with respect to the debt securities of a particular series, all of our obligations under such debt securities and the indenture with respect to such debt securities) and a "covenant defeasance option" (pursuant to which we may terminate, with respect to the debt securities of a particular series, our obligations with respect to such debt securities under certain specified covenants contained in the indenture). If we exercise our legal defeasance option with respect to a series of debt securities, payment of such debt securities may not be accelerated because of an event of default. If we exercise our covenant defeasance option with respect to a series of debt securities, payment of such debt securities may not be accelerated because of an event of default related to the specified covenants.

We may exercise our legal defeasance option or our covenant defeasance option with respect to the debt securities of a series only if we irrevocably deposit in trust with the trustee cash or U.S. government obligations (as defined in the indenture) for the payment of principal, premium, if any, and interest with respect to such debt securities to maturity or redemption, as the case may be. In addition, to exercise either of our defeasance options, we must comply with certain other conditions, including the delivery to the trustee of an opinion of counsel to the effect that the holders of debt securities of such series will not recognize income, gain or loss for Federal income tax purposes as a result of such defeasance and will be subject to Federal income tax on the same amounts, in the same manner and at the same times as would have been the case if such defeasance had not occurred (and, in the case of legal defeasance only, such opinion of counsel must be based on a ruling from the Internal Revenue Service or other change in applicable Federal income tax law).

The trustee will hold in trust the cash or U.S. government obligations deposited with it as described above and will apply the deposited cash and the proceeds from deposited U.S. government obligations to the payment of principal, premium, if any, and interest with respect to the debt securities of the defeased series.

Mergers, Consolidations and Certain Sales of Assets

We may not

consolidate with or merge into any other person or entity or permit any other person or entity to consolidate with or merge into us in a transaction in which we are not the surviving entity, or

transfer, lease or dispose of all or substantially all of our assets to any other person or entity

unless:

the resulting, surviving or transferee entity shall be a corporation organized and existing under the laws of the United States or any state thereof and such resulting, surviving or transferee entity shall expressly assume, by supplemental indenture, executed and delivered in form satisfactory to the trustee, all of our obligations under the debt securities and the indenture;

immediately after giving effect to such transaction (and treating any indebtedness which becomes an obligation of the resulting, surviving or transferee entity as a result of such transaction as

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having been incurred by such entity at the time of such transaction), no default or event of default would occur or be continuing; and

we shall have delivered to the trustee an officers' certificate and an opinion of counsel, each stating that such consolidation, merger or transfer and such supplemental indenture (if any) comply with the indenture.

Governing Law

The indenture and the debt securities will be governed by the laws of the State of New York.

No Personal Liability of Directors, Officers, Employees and Stockholders

No director, officer, incorporator or stockholder of Exact, as such, shall have any liability for any obligations of Exact under the debt securities or the indenture or for any claim based on, in respect of, or by reason of, such obligations or their creation, solely by reason of his, her, or its status as director, officer, incorporator or stockholder of Exact. By accepting a debt security, each holder waives and releases all such liability, but only such liability. The waiver and release are part of the consideration for issuance of the debt securities. Nevertheless, such waiver may not be effective to waive liabilities under the federal securities laws and it has been the view of the SEC that such a waiver is against public policy.

Conversion or Exchange Rights

Any debt securities offered hereby may be convertible into or exchangeable for shares of our equity or other securities. The terms and conditions of such conversion or exchange will be set forth in the applicable prospectus supplement. Such terms may include, among others, the following:

the conversion or exchange price;

the conversion or exchange period;

provisions regarding our ability or that of the holder to convert or exchange the debt securities;

events requiring adjustment to the conversion or exchange price; and

provisions affecting conversion or exchange in the event of our redemption of such debt securities.

Concerning the Trustee

The indenture provides that there may be more than one trustee with respect to one or more series of debt securities. If there are different trustees for different series of debt securities, each trustee will be a trustee of a trust under a supplemental indenture separate and apart from the trust administered by any other trustee under such indenture. Except as otherwise indicated in this prospectus or any prospectus supplement, any action permitted to be taken by a trustee may be taken by the trustee only with respect to the one or more series of debt securities for which it is the trustee under an indenture. Any trustee under the indenture or a supplemental indenture may resign or be removed with respect to one or more series of debt securities. All payments of principal of, premium, if any, and interest on, and all registration, transfer, exchange authentication and delivery (including authentication and delivery on original issuance of the debt securities) of, the debt securities of a series will be effected by the trustee with respect to such series at an office designated by the trustee.

The indenture contains limitations on the right of the trustee, should it become a creditor of Exact, to obtain payment of claims in certain cases or to realize on certain property received in respect of any such claim as security or otherwise. If the trustee acquires an interest that conflicts with any

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duties with respect to the debt securities, the trustee is required to either resign or eliminate such conflicting interest to the extent and in the manner provided by the indenture.

Limitations on Issuance of Bearer Debt Securities

Debt securities in bearer form are subject to special U.S. tax requirements and may not be offered, sold, or delivered within the United States or its possessions or to a U.S. person, except in certain transactions permitted by U.S. tax regulations. Investors should consult the relevant prospectus supplement, in the event that bearer debt securities are issued for special procedures and restrictions that will apply to such an offering.

DESCRIPTION OF PREFERRED STOCK WE MAY OFFER

This section describes the general terms and provisions of the preferred stock we may offer. This information may not be complete in all respects and is qualified entirely by reference to our certificate of incorporation, with respect to each series of preferred stock. The specific terms of any series will be described in a prospectus supplement. Those terms may differ from the terms discussed below. Any series of preferred stock we issue will be governed by our certificate of incorporation and by the certificate of designations relating to that series. We will file the certificate of designations with the SEC and incorporate it by reference as an exhibit to our registration statement at or before the time we issue any preferred stock of that series.

Authorized Preferred Stock

Our certificate of incorporation authorizes us to issue 5,000,000 shares of undesignated preferred stock, par value \$0.01 per share. We may issue preferred stock from time to time in one or more series, without shareholder approval, when authorized by our board of directors.

Upon issuance of a particular series of preferred stock, our board of directors is authorized, to specify:

the number of shares to be included in the series;

the annual dividend rate for the series, if any, and any restrictions or conditions on the payment of dividends;

the redemption price, if any, and the terms and conditions of redemption;

any sinking fund provisions for the purchase or redemption of the series;

if the series is convertible, the terms and conditions of conversion;

the amounts payable to holders upon our liquidation, dissolution or winding up; and

any other rights, preferences and limitations relating to the series, including voting rights.

Our board of director's ability to authorize, without shareholder approval, the issuance of preferred stock with conversion and other rights, may adversely affect the rights of holders of our common stock or other series of preferred stock that may be outstanding.

No shares of our preferred stock are currently issued and outstanding.

Specific Terms of a Series of Preferred Stock

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The preferred stock we may offer will be issued in one or more series. The preferred stock will have the dividend, liquidation, redemption and voting rights discussed below, unless otherwise described

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in a prospectus supplement relating to a particular series. A prospectus supplement will discuss the following features of the series of preferred stock to which it relates:

the designations and stated value per share;

the number of shares offered;

the amount of liquidation preference per share;

the public offering price at which the preferred stock will be issued;

the dividend rate, the method of its calculation, the dates on which dividends would be paid and the dates, if any, from which dividends would cumulate;

any redemption or sinking fund provisions;

any conversion or exchange rights; and

any additional voting, dividend, liquidation, redemption, sinking fund and other rights, preferences, privileges, limitations and restrictions.

Rank

Unless otherwise stated in the prospectus supplement, the preferred stock will have priority over our common stock with respect to dividends and distribution of assets, but will rank junior to all our outstanding indebtedness for borrowed money. Any series of preferred stock could rank senior, equal or junior to our other capital stock, as may be specified in a prospectus supplement, as long as our certificate of incorporation so permits.

Dividends

Holders of each series of preferred stock shall be entitled to receive cash dividends to the extent specified in the prospectus supplement when, as and if declared by our board of directors, from funds legally available for the payment of dividends. The rates and dates of payment of dividends of each series of preferred stock will be stated in the prospectus supplement. Dividends will be payable to the holders of record of preferred stock as they appear on our books on the record dates fixed by our board of directors. Dividends on any series of preferred stock may be cumulative or non-cumulative, as discussed in the applicable prospectus supplement.

Convertibility

Shares of a series of preferred stock may be exchangeable or convertible into shares of our common stock, another series of preferred stock or other securities or property. The conversion or exchange may be mandatory or optional. The prospectus supplement will specify whether the preferred stock being offered has any conversion or exchange features, and will describe all the related terms and conditions.

Redemption

The terms, if any, on which shares of preferred stock of a series may be redeemed will be discussed in the applicable prospectus supplement.

Liquidation

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Upon any voluntary or involuntary liquidation, dissolution or winding up of the affairs of Exact, holders of each series of preferred stock will be entitled to receive distributions upon liquidation in the amount described in the related prospectus supplement. These distributions will be made before any

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distribution is made on any securities ranking junior to the preferred stock with respect to liquidation, including our common stock. If the liquidation amounts payable relating to the preferred stock of any series and any other securities ranking on a parity regarding liquidation rights are not paid in full, the holders of the preferred stock of that series will share ratably in proportion to the full liquidation preferences of each security. Holders of our preferred stock will not be entitled to any other amounts from us after they have received their full liquidation preference.

Voting

The holders of preferred stock of each series will have no voting rights, except as required by law and as described below or in a prospectus supplement. Our board of directors may, upon issuance of a series of preferred stock, grant voting rights to the holders of that series to elect additional board members if we fail to pay dividends in a timely fashion.

Without the affirmative vote of a majority of the shares of preferred stock of any series then outstanding, we may not:

increase or decrease the aggregate number of authorized shares of that series;

increase or decrease the par value of the shares of that series; or

alter or change the powers, preferences or special rights of the shares of that series so as to affect them adversely.

No Other Rights

The shares of a series of preferred stock will not have any preferences, voting powers or relative, participating, optional or other special rights except:

as discussed above or in the prospectus supplement;

as provided in our certificate of incorporation and in the certificate of designations; and

as otherwise required by law.

DESCRIPTION OF COMMON STOCK WE MAY OFFER

The following summary description of our common stock is based on the provisions of our certificate of incorporation or bylaws and the applicable provisions of the General Corporation Law of the State of Delaware. This information may not be complete in all respects and is qualified entirely by reference to the provisions of our certificate of incorporation, bylaws and the General Corporation Law of the State of Delaware. For information on how to obtain copies of our certificate of incorporation and bylaws, see the discussion above under the heading "Where You Can Find More Information."

We may offer our common stock issuable upon the conversion of debt securities or preferred stock and the exercise of warrants.

Authorized Capital

We currently have authority to issue 100,000,000 shares of our common stock, par value \$0.01 per share. As of February 26, 2013, 64,031,106 shares of our common stock were issued and outstanding.

Voting Rights

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Each outstanding share of our common stock is entitled to one vote on all matters submitted to a vote of shareholders. There is no cumulative voting.

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Dividend and Liquidation Rights

The holders of outstanding shares of our common stock are entitled to receive dividends out of assets legally available for the payment of dividends at the times and in the amounts as our board of directors may from time to time determine. The shares of our common stock are neither redeemable nor convertible. Holders of our common stock have no preemptive or subscription rights to purchase any securities of Exact. Upon the liquidation, dissolution or winding up of Exact, the holders of our common stock are entitled to receive pro rata the assets of Exact which are legally available for distribution, after payment of all debts and other liabilities and subject to the prior rights of any holders of preferred stock then outstanding.

We have never paid any cash dividends on our common stock.

DESCRIPTION OF WARRANTS WE MAY OFFER

We may issue warrants for the purchase of debt securities, preferred stock or common stock. Warrants may be issued independently or together with debt securities, preferred stock or common stock and may be attached to or separate from any offered securities. Any issue of warrants will be governed by the terms of the applicable form of warrant and any related warrant agreement which we will file as an exhibit to our registration statement at or before the time we issue any 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 currency or currencies (including composite currencies) in which the price of such warrants may be payable;

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;

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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 and ERISA considerations.

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Warrants for the purchase of preferred stock and common stock will be offered and exercisable for U.S. dollars only.

Each warrant will entitle its holder to purchase the principal amount of debt securities or 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.

Prior to the exercise of any warrants to purchase debt securities, preferred stock or common stock, holders of the warrants will not have any of the rights of holders of the debt securities, preferred stock or common stock purchasable upon exercise.

PLAN OF DISTRIBUTION

We may sell the securities offered by this prospectus to one or more underwriters or dealers for public offering, through agents, directly to purchasers or through a combination of any such methods of sale. The name of any such underwriters, dealers or agents involved in the offer and sale of the securities, the amounts underwritten and the nature of its obligation to take the securities will be specified in the applicable prospectus supplement. We have reserved the right to sell the securities directly to investors on our own behalf in those jurisdictions where we are authorized to do so. The sale of the securities may be effected in transactions (a) on any national or international securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, (b) in the over-the-counter market, (c) in transactions otherwise than on such exchanges or in the over-the-counter market or (d) through the writing of options.

We and our agents and underwriters, may offer and sell the securities at a fixed price or prices that may be changed, at market prices prevailing at the time of sale, at prices related to such prevailing market prices or at negotiated prices. The securities may be offered on an exchange, which will be disclosed in the applicable prospectus supplement. We may, from time to time, authorize dealers, acting as our agents, to offer and sell the securities upon such terms and conditions as set forth in the applicable prospectus supplement.

If we use underwriters to sell securities, we will enter into an underwriting agreement with them at the time of the sale to them. In connection with the sale of the securities, underwriters may receive compensation from us in the form of underwriting discounts or commissions and may also receive commissions from purchasers of the securities for whom they may act as agent. Any underwriting compensation paid by us to underwriters or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers, will be set forth in the applicable prospectus supplement to the extent required by applicable law. Underwriters may sell the securities to or through dealers, and such dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters or commissions (which may be changed from time to time) from the purchasers for whom they may act as agents.

Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions under the Securities Act. Unless otherwise indicated in the applicable prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase debt securities as a principal, and may then resell the debt securities at varying prices to be determined by the dealer.

If so indicated in the prospectus supplement, we will authorize underwriters, dealers or agents to solicit offers by certain specified institutions to purchase offered securities from us at the public

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offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. Such contracts will be subject to any conditions set forth in the applicable prospectus supplement and the prospectus supplement will set forth the commission payable for solicitation of such contracts. The underwriters and other persons soliciting such contracts will have no responsibility for the validity or performance of any such contracts.

Underwriters, dealers and agents may be entitled, under agreements entered into with us, to indemnification against and contribution towards certain civil liabilities, including any liabilities under the Securities Act.

To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain, or otherwise affect the price of the securities. These may include over-allotment, stabilization, syndicate short covering transactions and penalty bids. Over-allotment involves sales in excess of the offering size, which creates a short position. Stabilizing transactions involve bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Syndicate short covering transactions involve purchases of securities in the open market after the distribution has been completed in order to cover syndicate short positions. Penalty bids permit the underwriters to reclaim selling concessions from dealers when the securities originally sold by the dealers are purchased in covering transactions to cover syndicate short positions. These transactions may cause the price of the securities sold in an offering to be higher than it would otherwise be. These transactions, if commenced, may be discontinued by the underwriters at any time.

Any securities other than our common stock issued hereunder may be new issues of securities with no established trading market. Any underwriters or agents to or through whom such securities are sold for public offering and sale may make a market in such securities, but such underwriters or agents will not be obligated to do so and may discontinue any market making at any time without notice. No assurance can be given as to the liquidity of the trading market for any such securities. The amount of expenses expected to be incurred by us in connection with any issuance of securities will be set forth in the applicable prospectus supplement. Certain of the underwriters, dealers or agents and their associates may engage in transactions with, and perform services for, us and certain of our affiliates in the ordinary course of business.

During such time as we may be engaged in a distribution of the securities covered by this prospectus we are required to comply with Regulation M promulgated under the Exchange Act. With certain exceptions, Regulation M precludes us, any affiliated purchasers, and any broker-dealer or other person who participates in such distribution from bidding for or purchasing, or attempting to induce any person to bid for or purchase, any security which is the subject of the distribution until the entire distribution is complete. Regulation M also restricts bids or purchases made in order to stabilize the price of a security in connection with the distribution of that security. All of the foregoing may affect the marketability of our shares of common stock.

LEGAL MATTERS

The validity and legality of the securities offered hereby and certain other legal matters will be passed upon for the Company by K&L Gates LLP, Charlotte, North Carolina 28202.

EXPERTS

The financial statements as of December 31, 2012 and 2011 and for each of the three years in the period ended December 31, 2012 and management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2012 incorporated by reference in this Prospectus have been so incorporated in reliance on the reports of BDO USA, LLP, an independent registered public accounting firm, incorporated herein by reference, given on the authority of said firm as experts in auditing and accounting.

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Shares

Exact Sciences Corporation

Common Stock

PROSPECTUS SUPPLEMENT

Joint Book-Running Managers

Jefferies

Baird

June , 2013
