

1,000,000 Shares
EXELIXIS, INC.
Common Stock

This prospectus supplement supplements the prospectus dated October 20, 2008 (the "Prospectus"), as supplemented by that certain Prospectus Supplement No. 1 dated October 30, 2008 ("Supplement No. 1"), which forms a part of our Registration Statement on Form S-1 (Registration No. 333-152166). This prospectus supplement is being filed to update and supplement the information in the Prospectus and Supplement No. 1, with the information contained in our current report on Form 8-K, filed with the Securities and Exchange Commission on November 7, 2008 (the "Current Report"). Accordingly, we have attached the Current Report to this prospectus supplement.

The Prospectus, Supplement No. 1 and this prospectus supplement relate to the offer and sale of up to 1,000,000 shares of our common stock by the selling security holders listed on page 23 of the Prospectus, including their transferees, pledgees or donees or their respective successors, which includes shares of our common stock issuable upon the exercise of warrants issued pursuant to a facility agreement dated as of June 4, 2008 between us and the lenders identified therein. We will not receive any proceeds from any resale of the shares of common stock being offered by the Prospectus, Supplement No. 1 and this prospectus supplement.

This prospectus supplement should be read in conjunction with the Prospectus and Supplement No. 1. This prospectus supplement updates and supplements the information in the Prospectus and Supplement No. 1. If there is any inconsistency between the information in the Prospectus, Supplement No. 1 and this prospectus supplement, you should rely on the information in this prospectus supplement.

Our common stock is traded on The Nasdaq Global Select Market under the trading symbol "EXEL." On November 11, 2008, the last reported sale price of our common stock was \$3.37 per share.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" beginning on page 3 of the Prospectus and beginning on page 24 of our quarterly report on Form 10-Q for the quarterly period ended September 26, 2008 before you decide whether to invest in shares of our common stock.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if the Prospectus, Supplement No. 1 or this prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus supplement is November 12, 2008

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

FORM 8-K

**CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934**

Date of Report (Date of earliest event reported): November 4, 2008

EXELIXIS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

0-30235
(Commission
File Number)

04-3257395
(IRS Employer
Identification No.)

**249 East Grand Ave.
P.O. Box 511
South San Francisco, California 94083-0511**
(Address of principal executive offices, and including zip code)

(650) 837-7000
(Registrant's telephone number, including area code)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 2.05. Costs Associated with Exit or Disposal Activities.

On November 4, 2008, Exelixis, Inc. (the "Company") implemented a restructuring plan that resulted in the reduction of approximately 10% of the Company's workforce. The 78 employees being terminated by the restructuring plan received notification on November 4, 2008. Each affected employee is eligible to receive a severance payment relative to the employee's length of service with the Company, a health benefit payment that may be used by such affected employee to pay the premiums required to continue health care coverage under COBRA and outplacement assistance. Payment of a portion of these severance benefits to each affected employee is contingent on the affected employee entering into a separation agreement with the Company, which agreement includes a general release of claims against the Company. The Company anticipates that the actions associated with the restructuring plan will be completed during the first quarter of 2009.

The decision to restructure the Company's operations was based on the Company's recently announced corporate strategy to bring the Company's net cash usage in line with the Company's available cash, with the goal of allowing the Company to operate independently of the capital markets for a substantial period of time. As a result of this restructuring plan, the Company expects to record a restructuring charge of approximately \$3.3 million in the fourth quarter of 2008. This represents the total estimated restructuring charge the Company anticipates in connection with this restructuring plan. The restructuring charge is associated with one-time termination benefits. The Company expects that approximately \$2.9 million of the restructuring charge will result in cash expenditures, which will be paid out during the fourth quarter of 2008 and the first quarter of 2009. The restructuring charge that the Company expects to incur in connection with the restructuring is subject to a number of assumptions, and actual results may materially differ. The Company may also incur other material charges not currently contemplated due to events that may occur as a result of, or associated with, the restructuring plan.

This current report on Form 8-K contains forward-looking statements, including, but not limited to, statements related to the timing of completion of the Company's restructuring plan, the expected costs of the Company's restructuring plan and the Company's goal of operating independently of the capital markets for a substantial period of time. Words such as "expects," "anticipates," "will," "may," "goal," and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon the Company's current plans, assumptions, beliefs, and expectations. Forward-looking statements involve risks and uncertainties. The Company's actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks related to: the Company's ability to implement the restructuring plan to the extent currently anticipated, the impact of the workforce reduction on the Company's business, unanticipated charges not currently contemplated that may occur as a result of the restructuring plan, the Company's ability to execute on its strategy and general business and economic conditions. These and other risk factors are discussed under "Risk Factors" and elsewhere in the Company's quarterly report on Form 10-Q for the quarter ended September 26, 2008, and other filings with the Securities and Exchange Commission. The Company expressly disclaims any duty, obligation, or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in the Company's expectations with regard thereto or any change in events, conditions, or circumstances on which any such statements are based.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: November 7, 2008

EXELIXIS, INC.

/s/ James B. Bucher

Vice President, Corporate Legal Affairs and Secretary