EXELIXIS INC
Form 8-K
October 31, 2011

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): October 28, 2011

EXELIXIS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**0-30235**	**04-3257395**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

210 East Grand Ave.

South San Francisco, California 94080

(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))

Item 8.01 Other Events.

Decision to Initiate Cabozantinib Pivotal Trials in Metastatic Castration-Resistant Prostate Cancer

On October 31, 2011, Exelixis, Inc. (the Company) announced that it has decided to initiate the 306 trial, the Company s first planned phase 3 pivotal trial of cabozantinib in patients with metastatic castration-resistant prostate cancer (CRPC). Based on the regulatory feedback obtained from both the United States Food and Drug Administration (the FDA) and the European Medicines Agency to date, the Company has determined that pain will be the primary efficacy endpoint for the 306 trial. The Company was not able to reach a timely agreement with the FDA under a special protocol assessment (a SPA) on the proposed design and analysis of the 306 trial. The Company expects to initiate the 306 trial by the end of 2011. As previously announced, the Company plans to initiate the 307 trial, a phase 3 pivotal trial in metastatic CRPC patients with an overall survival endpoint, in the first half of 2012 as part of the Company s comprehensive development plan for cabozantinib in CRPC.

SPA Process

The Company originally submitted the proposed protocol for the 306 trial using primary endpoints of pain reduction and bone scan response to the FDA in June 2011 with a request for a SPA. The Company received the FDA s initial response to the protocol in August 2011. The Company responded to the FDA in September 2011, agreeing to substantially all of the FDA s requested changes to the protocol and resubmitting the request for a SPA. The FDA s latest response, which the Company received on October 28, 2011 (the October FDA Response), raised the following concerns regarding the 306 trial design in the context of its consideration of a SPA for the trial, among other comments:

- A concern about the ability to maintain blinding of the trial due to differences in toxicity profiles between cabozantinib and mitoxantrone.
- A view that the assumed magnitude of pain improvement is modest and could represent a placebo effect or be attained with less toxicity by opioid therapy.
- A view that symptomatic improvement should be supported by evidence of anti-tumor activity, an acceptable safety profile and lack of survival decrement. The FDA also expressed the view that if the effect that the Company believes cabozantinib will have on pain is mediated by anti-tumor activity, that anti-tumor activity should translate into an improvement in overall survival.
- A recommendation that if the Company uses pain response as a primary efficacy endpoint, that it conduct two adequate and well-controlled trials to demonstrate effectiveness as, according to the FDA, a conclusion based on two persuasive studies will always be more secure. The FDA advised that for a single randomized trial to support a new drug application, the trial must be well designed, well conducted, internally consistent and provide statistically persuasive efficacy findings so that a second trial would be ethically or practically impossible to perform.

In the context of its consideration of a SPA for the 306 trial, the FDA also recommended in the October FDA Response that overall survival be the primary efficacy endpoint. The October FDA Response stated that the Company could choose to conduct the 306 trial in the absence of a SPA agreement. The Company believes that it will address the recommendation regarding overall survival through the 307 trial, which the Company plans to initiate in the first half of 2012. The Company believes that the other concerns in the October FDA Response are difficult to address in the absence of a complete set of clinical data. As a result, the Company has elected to proceed with initiation of the 306 and 307 trials, and to discontinue further attempts to secure a SPA agreement with respect to the 306 trial.

306 Trial Design

The double-blind 306 trial is designed to enroll 246 patients with CRPC that is metastatic to the bone, who are suffering from moderate to severe bone pain despite optimized narcotic medication, and who have failed prior docetaxel and abiraterone in no particular order. The 306 trial will be conducted in English speaking regions including the United States, Canada and the United Kingdom. Patients will be randomized 1:1 to receive either cabozantinib or mitoxantrone/prednisone. Alleviation of bone pain will be the primary endpoint, and will be measured by comparing the percentage of patients in the two treatment arms who achieve a pain response at Week 9 that is confirmed at Week 15. The trial design assumes that 25% of patients in the cabozantinib arm will have a pain response while 8% of patients in the mitoxantrone/prednisone arm will have a pain response. Prior to randomization, patients will undergo a period during which their pain medication is optimized using one long acting narcotic and one immediate release narcotic medication. This optimization is following a standard approach defined in the National Comprehensive

Cancer Network guidelines. Patients in the cabozantinib arm will be dosed at 60 mg per day until the patient no longer receives clinical benefit. The definition of a responder with respect to the bone pain endpoint is a ³30% decrease from baseline in the average of the daily worst pain intensity collected over 7 days in Week 9 and confirmed in Week 15, with neither a concomitant increase in average daily dose of any narcotic pain medication, nor addition of any new narcotic pain medication.

Overall survival will be a secondary endpoint of the 306 trial. The 306 trial will be deemed successful if the primary endpoint of statistically significant pain improvement is met and the overall survival analysis demonstrates that there is no adverse impact on overall survival in the cabozantinib arm. In light of not proceeding under an SPA, the Company has decided to evaluate bone scan response as a secondary endpoint rather than as an exploratory endpoint, with evaluation by an independent radiology facility (IRF). A response per bone scan will be a ³30% decrease in the lesion area of all bone lesions on bone scan determined by automated computer-aided lesion detection (CAD) system as compared to the baseline bone scan per an IRF analysis. To be a bone-scan responder, patients must have both a response on bone scan and the absence of soft tissue progression.

307 Trial Design

In the context of the Company s comprehensive development plan for cabozantinib in CRPC, the Company expects to initiate the 307 trial in the first half of 2012. The primary endpoint of 307 trial will be overall survival. The trial will be conducted in patients with CRPC with bone metastases who have failed prior docetaxel and abiraterone therapies. Patients will be randomized to receive cabozantinib at 60 mg daily or prednisone. The 307 trial is expected be executed globally and at non-overlapping sites with the 306 trial.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements, including, without limitation, statements related to: the continued development of cabozantinib; plans to initiate the XL184-306 trial and the timing thereof; plans to initiate the XL184-307 trial and the timing thereof; the design and conduct of the XL184-306 and XL184-307 trials; the potential success of the XL184-306 and XL184-307 trials; the Company s ability to address the FDA s concerns and recommendations set forth in the October FDA Response Letter and prior communications; and a potential regulatory submission for product approval and the FDA s response thereto. Words such as expects, plans, believes, designed, will, expected and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon Exelixis current plans, assumptions, beliefs and expectations. Forward-looking statements involve risks and uncertainties. Exelixis 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 potential failure of cabozantinib to demonstrate safety and efficacy in clinical testing; Exelixis ability to conduct clinical trials of cabozantinib sufficient to achieve a positive completion; the sufficiency of Exelixis capital and other resources; the uncertain timing and level of expenses associated with the development of cabozantinib; the uncertainty of the FDA approval process; market competition; and changes in economic and business conditions. These and other risk factors are discussed under Risk Factors and elsewhere in Exelixis quarterly report on Form 10-Q for the quarter ended September 30, 2011 and Exelixis other filings with the Securities and Exchange Commission. Exelixis 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 Exelixis 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: October 31, 2011

EXELIXIS, INC.

/s/ James B. Bucher
Vice President, Corporate Legal Affairs and Secretary