# Spectrum Pharmaceuticals Provides Strategy Update for Poziotinib Development Program

April 28, 2020

*ZENITH20 Phase 2 clinical trial amended to include new dosing regimens aimed at improving therapeutic index*

*Management to host webcast and conference call today to review data and program strategy at 8:30 a.m. ET*

HENDERSON, Nev.--(BUSINESS WIRE)--Apr. 28, 2020-- Spectrum Pharmaceuticals (NasdaqGS: SPPI), a biopharmaceutical company focused on novel and targeted oncology therapies, today provided an update on its ZENITH20 Phase 2 clinical trial evaluating poziotinib in non-small cell lung cancer (NSCLC) patients with EGFR and HER2 exon 20 insertion mutations. The protocol has been amended to explore additional twice daily dosing regimens as well as lower single daily dosage amounts. Earlier use of corticosteroids has also been added to the protocol in an effort to help patients better tolerate poziotinib and stay on therapy for a longer time. Previously announced results for Cohort 1 of the SPECTRUM20 trial were presented yesterday during the oral plenary of the Lung Cancer Targeted Therapy session at the American Association for Cancer Research (AACR) Virtual Annual Meeting. Although the results for Cohort 1 did not meet the primary endpoint, as previously announced, poziotinib demonstrated a positive treatment effect with a 68.7% disease control rate.

“Based on our analysis of the data, we believe that dose reductions and interruptions may have negatively impacted the treatment effect of poziotinib in this trial, and we are moving forward to further test this hypothesis with additional dose exploration in various cohorts. Pharmacologic modeling suggests that BID dosing can significantly lower Cmax, potentially reducing toxicity, and at the same time, maintain serum concentration above the IC50 value, therefore retaining anti-tumor activity,” said Francois Lebel, M.D., Chief Medical Officer of Spectrum Pharmaceuticals. “Cohort 5 already included lower daily doses of poziotinib and we now have added twice daily regimens with a goal of providing a greater therapeutic window. Additionally, we are incorporating earlier use of corticosteroids for better control of the observed treatment related rash.”

“Our data clearly shows that poziotinib produces a positive treatment effect and we are exploring changes in its dosing to allow patients to stay on drug longer and therefore derive the full potential benefits of treatment,” stated Joe Turgeon, CEO of Spectrum Pharmaceuticals. “These seriously ill cancer patients urgently need alternative treatment options.”

**ZENITH20 Trial Design and Results from Cohort 1**

Cohort 1 of the ZENITH20 trial enrolled 115 patients who received 16 mg/day of poziotinib. The intent-to-treat analysis showed that 17 patients had a response (by RECIST) and 62 patients had stable disease for a 68.7% disease control rate (DCR). The confirmed objective response rate (ORR) was 14.8% (95% Confidence Interval (CI) 8.9%-22.6%). Based on the FDA reviewed protocol, an observed ORR of 30%, with 17% as the lower bound for 95% CI was considered to be the clinically meaningful efficacy in our study. The median duration of response was 7.4 months with progression free survival of 4.2 months.

The safety profile was in-line with the type of adverse events seen with other second-generation EGFR tyrosine kinase inhibitors. Approximately 63% of patients experienced a grade 3 or 4 adverse event, the most common of which was rash and diarrhea. Tolerability may have led to reduced drug exposure as 68% of patients were dose reduced and 88% of patients had a temporary drug/dosing interruption. The median relative dose intensity was 72%. The high incidence of dose reductions and interruptions may indicate that the once daily starting dose of 16 mg was high and the resulting reduced dose intensity could have impaired the efficacy results. The company believes that a reduction in dose interruptions and daily dosing could lead to a greater number of deeper and more durable responses.

Cohort 5 is evaluating patients using a range of different doses compared to Cohort 1. Patients are randomized to 10, 12 or 16 mg administered once daily, and with the amended protocol, the trial will also explore 6 and 8 mg administered twice daily. Cohorts 4, 6 and 7 have also been amended to use 8 mg twice daily dosing.

The ZENITH20 trial is made up of seven independent cohorts. Cohorts 1 - 4 are each independently powered for a pre-specified statistical hypothesis with a primary endpoint of ORR. Cohorts 5 - 7 are exploratory studies. Cohort 3 is now fully enrolled and the company expects to report results for Cohort 2 in mid-2020 and Cohort 3 by the end of the year.

**Conference Call and Webcast**

Spectrum’s management will host a webcast and conference call today, April 28, 2020 at 8:30 a.m. ET / 5:30 a.m. PT to review the data and program strategy. The live call may be accessed by dialing (877) 837-3910 for domestic callers and (973) 796-5077 for international callers and entering the conference ID#: 5536065. A live webcast of the call will be available from the Investors and Media section of the company’s website at http://investor.sppirx.com/events-and-presentations and will be archived there shortly after the live event.

**About Spectrum Pharmaceuticals, Inc.**

Spectrum Pharmaceuticals is a biopharmaceutical company focused on acquiring, developing, and commercializing novel and targeted oncology therapies. Spectrum has a strong track record of successfully executing across the biopharmaceutical business model, from in-licensing and acquiring differentiated drugs, clinically developing novel assets, successfully gaining regulatory approvals and commercializing in a competitive healthcare marketplace. Spectrum has a late-stage pipeline with novel assets that serve areas of unmet need. This pipeline has the potential to transform the company in the near future. For additional information on Spectrum Pharmaceuticals please visit www.sppirx.com.

**Notice Regarding Forward-Looking Statements**

*Certain statements in this press release may constitute "forward-looking statements" within the meaning of the United States Private Securities Litigation Reform Act of 1995, as amended to date. These forward-looking statements relate to a variety of matters, including, without limitation, statements that relate to Spectrum's business and its future, including the company's ability to advance development of its late-stage pipeline assets; the ability of patients to better tolerate poziotinib and stay on the therapy for a longer time with a revised dosage protocol; the potential for the revised dosage protocol to reduce toxicity, maintain serum concentration above the IC50 value and retain anti-tumor activity; the effect of reduced dose intensity for patients in cohort 1 of Spectrum's ZENITH20 study on the overall efficacy of poziotinib; the likelihood that a reduction in dose interruptions and daily dosing could lead to a greater number of deeper and more durable responses to poziotinib; the timing of the results of cohort 2 and cohort 3 of Spectrum's ZENITH20 study; the ability of poziotinib to meet currently unaddressed medical needs and the size of the potential markets; the future potential of Spectrum's existing drug pipeline; the progression of the poziotinib development program and other statements that are not purely statements of historical fact. These forward-looking statements are made on the basis of the current beliefs, expectations, and assumptions of the management of Spectrum and are subject to significant risks and uncertainties that could cause actual results to differ materially from what may be expressed or implied in these forward-looking statements. Risks that could cause actual results to differ include the possibility that Spectrum's existing and new drug candidates may not prove safe or effective, the possibility that our existing and new applications to the FDA and other regulatory agencies may not receive approval in a timely manner or at all, the possibility that our existing and new drug candidates, if approved, may not be more effective, safer or more cost efficient than competing drugs, the possibility that our efforts to acquire or in-license and develop additional drug candidates may fail, our dependence on third parties for clinical trials, manufacturing, distribution and quality control and other risks that are described in further detail in the company's reports filed with the Securities and Exchange Commission. The company does not plan to update any such forward-looking statements and expressly disclaims any duty to update the information contained in this press release except as required by law. For a further discussion of risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of Spectrum in general, see the risk disclosures in the Annual Report on Form 10-K of Spectrum for the year ended December 31, 2019, and in subsequent reports on Forms 10-Q and 8-K and other filings made with the SEC by Spectrum.*



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