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Spark Therapeutics and Pfizer Present Updated Data from Hemophilia B Phase 1/2 Trial Suggesting Consistent and Sustained Levels of Factor IX Activity at Annual ASH Meeting

Saturday, December 03, 2016 - 08:00am

Together, all nine participants have reduced infusions of factor IX concentrates by 99 percent over cumulative 1,650 days

Seven infused participants who have progressed to at least 12 weeks post-vector administration as of Nov. 30, 2016, have a mean steady-state factor IX activity level greater than 28 percent

PHILADELPHIA, Dec. 3, 2016 (GLOBE NEWSWIRE) -- Spark Therapeutics (NASDAQ:ONCE) and Pfizer Inc. (NYSE:PFE) announced updated data today from the first nine infused participants in the ongoing Phase 1/2 clinical trial of investigational SPK-9001 for hemophilia B, who received a single administration of 5 x 1011 vector genomes (vg)/kg body weight. These data will be presented at today's media briefing and on Sunday, Dec. 4, at the Plenary Scientific Session of the 58th American Society of Hematology (ASH) Annual Meeting, in San Diego.

The first participant to reach one year in the study who has been followed for 52 weeks post-infusion of SPK-9001, has reduced to zero his number of intravenous factor IX infusions without having any bleeds. In the year before administration of SPK-9001, he infused factor IX concentrates prophylactically a total of 98 times and still experienced four traumatic bleeds. As of Nov. 30, 2016, his steady-state factor IX activity level was 33 percent of normal.

As of Nov. 30, 2016, the total clotting factor IX concentrate consumption in all nine infused participants over a cumulative 1,650 patient days following vector administration was reduced by 1.13 million international units based on their factor IX concentrate usage in the year before vector administration. Seven of the nine infused participants, who have progressed to at least 12 weeks post-vector administration as of Nov. 30, 2016, experienced consistent and sustained factor IX activity levels, with a mean steady-state level greater than 28 percent. In the study to date, no participants developed factor IX inhibitors or experienced thrombotic events after the vector administration. No serious adverse events after SPK-9001 administration have been reported.

Two of the nine participants experienced asymptomatic, transient elevation in liver enzymes associated with an immune response to the Spark100 vector capsid during the first four to eight weeks following administration. In one participant, this response was accompanied by a decline in factor IX activity level from 32 to 12 percent, as of Nov. 30, 2016. In the second participant, to whom steroids were 1 administered more promptly, this response

was accompanied by a decline from a peak factor IX activity level of 71 to 68 percent, as of Nov. 30, 2016. Both participants were put on a tapering course of corticosteroids, and, to date, neither participant has experienced any bleeds nor required infusion of replacement factor IX concentrate.

“We will monitor these two participants carefully as we continue to taper the corticosteroids,” said Katherine A. High, M.D., president and chief scientific officer at Spark Therapeutics. “It’s important to remember that the immune response to the capsid typically is transient, and in both cases, seems to have been arrested by corticosteroids. Once corticosteroids have been discontinued altogether, levels of expression will be the best measure of the efficacy of this approach. The experience we have gained in immuno-monitoring and in clinical management of the immune response in the hemophilia B trial will further inform our upcoming hemophilia studies.”

Eight of the infused participants have required no factor IX concentrates to prevent or control bleeding events since the day after vector administration. One participant with severe joint disease selfadministrated a precautionary infusion two days after administration of SPK-9001 for a suspected ankle bleed and again at week 35 post the data cut-off date and despite a factor IX activity level of 36 percent, for a suspected knee bleed.

“Giving people living with hemophilia B treatment options that potentially minimize or eliminate the need for infusions of factor concentrates is one of the main goals of conducting clinical studies of investigational gene therapies,” said Dr. High. “While continued observation and larger cohorts are needed, these updated interim data continue to be encouraging and suggest the potential of investigational SPK-9001 to deliver a consistent, sustained and therapeutically meaningful level of factor IX activity through a one-time intravenous administration.”

Additionally, to date, six of seven participants reported increased physical activity and improved quality of life based on the Haemophilia Quality of Life Questionnaire for Adults, a validated instrument that measures health-related quality of life in adults (? 17 years of age) with hemophilia. Two participants received the gene therapy product too recently to evaluate quality-of-life measures.

Presentation Details:
ASH Annual Meeting Media Briefing
Presenter: Katherine A. High, M.D., president and chief scientific officer at Spark Therapeutics
Date: Saturday, Dec. 3, 2016
Briefing time: 8-9 a.m. PST
Location: San Diego Convention Center, Room 22

*SPK-900*1: Adeno-Associated Virus Mediated Gene Transfer for Hemophilia B Achieves Sustained Mean Factor IX Activity Levels of >30% without Immunosuppression (Abstract # 91358)
Presenter: Lindsey George, M.D., Children’s Hospital of Philadelphia
Date: Sunday, Dec. 4, 2016
Session time: 2-4 p.m. PST
Location: San Diego Convention Center, Hall AB

Spark Therapeutics Conference Call:
Spark Therapeutics management will also host a conference call on Monday, Dec. 5, 2016, at 8 a.m. ET to discuss the data presented at the meeting. The conference call can be accessed by dialing (855) 851- 4526 (domestic) or (720) 634-2901 (international), and entering passcode 29837698. To access a live audio webcast, please visit the “Investors” section at www.sparktx.com.

A replay of the call will be available for one week following the call and can be accessed by dialing (855) 859-2056 (domestic) or (404) 537-3406 (international), and entering passcode 29837698 or by visiting the "Investors" section at www.sparktx.com.

About Hemophilia B

Hemophilia, a rare genetic bleeding disorder that causes the blood to take a long time to clot as a result of a deficiency in one of several blood clotting factors, is common almost exclusively in males. People with hemophilia are at risk for excessive and recurrent bleeding from modest injuries, which have the potential to be life threatening. People with severe hemophilia often bleed spontaneously into their muscles or joints. The incidence of hemophilia B is one in 25,000 male births. People with hemophilia B have a deficiency in clotting factor IX, a specific protein in the blood. Hemophilia B is also called congenital factor IX deficiency or Christmas disease. Current standard of care requires recurrent intravenous infusions of either plasma-derived or recombinant factor IX to control and prevent bleeding episodes. There exists a significant need for novel therapeutics to treat people living with hemophilia.

About the SPK-FIX Program and SPK-9001

Spark Therapeutics' proprietary technology platform for selecting, designing, manufacturing and formulating gene therapies was applied to developing compounds in the SPK-FIX program. The SPK-FIX program leverages a long history of hemophilia gene therapy research and clinical development conducted by Spark Therapeutics and its founding scientific team over nearly three decades. SPK-9001 is a novel, investigational bio-engineered adeno-associated virus (AAV) capsid expressing a codonoptimized, high-activity human factor IX variant enabling endogenous production of factor IX. SPK-9001 is being developed under a collaboration with Pfizer. Spark Therapeutics and Pfizer entered into a collaboration in 2014 for the SPK-FIX program, including SPK-9001, under which Spark Therapeutics is responsible for conducting all Phase 1/2 studies for any product candidates, while Pfizer will assume responsibility for pivotal studies, any regulatory activities and potential global commercialization of any products that may result from the collaboration. SPK-9001 has received breakthrough therapy and orphan product designations from the U.S. Food and Drug Administration.

About Spark Therapeutics

Spark Therapeutics, a fully integrated company, is challenging the inevitability of genetic disease by discovering, developing, and delivering gene therapies that address inherited retinal diseases (IRDs), liver-mediated diseases such as hemophilia, and neurodegenerative diseases. Our validated platform successfully has delivered proof-of-concept data with investigational gene therapies in the retina and liver. Our most advanced investigational candidate, voretigene neparvovec, in development for the treatment of RPE65-mediated IRD, has received orphan designations in the U.S. and European Union, and breakthrough therapy designation in the U.S. The pipeline also includes SPK-7001, in a Phase 1/2 trial for choroideremia, and two hemophilia development programs: SPK-9001 in a Phase 1/2 trial for hemophilia B being developed in collaboration with Pfizer (which also has received both breakthrough therapy and orphan product designations) and SPK-8011, a preclinical candidate for hemophilia A to which Spark Therapeutics retains global commercialization rights. To learn more about us and our growing pipeline, visit www.sparktx.com.

Spark Cautionary Note on Forward-looking Statements

This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the company's SPK-FIX program. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that: (i) our lead SPK-FIX product candidate, SPK9001, may not produce sufficient data in our Phase 1/2 clinical trial to warrant further development; and (ii) our overall collaboration with Pfizer may not be successful.

For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, as well as discussions of potential risks, uncertainties and other important factors, in our Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and other filings we make with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Spark undertakes no duty to update this information unless required by law.

Pfizer and Rare Diseases
Rare diseases are among the most serious of all illnesses and impact millions of patients worldwide, representing an opportunity to apply our knowledge and expertise to help make a significant impact in addressing unmet medical needs. The Pfizer focus on rare diseases builds on more than two decades of experience, a dedicated research unit focusing on rare diseases, and a global portfolio of more than 20 medicines approved worldwide that treat rare diseases in the areas of hematology, neuroscience, inherited metabolic disorders, pulmonology, and oncology.

Pfizer Inc: Working together for a healthier world®
At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. For more information, please visit us at www.pfizer.com. In addition, to learn more, follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

Pfizer Disclosure Notice:
The information contained in this release is as of Dec. 3, 2016. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about SPK-9001 and the SPK-FIX program, including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet anticipated clinical study commencement and completion dates as well as the possibility of unfavorable study results, including unfavorable new clinical data and additional analyses of existing clinical data; risks associated with initial data, including the risk that the final results of the Phase I/2 study for SPK-9001 and/or additional clinical trials may be different from (including less favorable than) the initial data results and may not support further clinical development; whether and when any applications may be filed with regulatory authorities for SPK-9001; whether and when regulatory authorities may approve any such applications, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of SPK-9001; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2015 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future

Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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