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Spark Therapeutics Presents Updated Interim Hemophilia B Data Supporting Consistent and Sustained Response at the International Society on Thrombosis and Haemostasis (ISTH) 2017 Congress

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Data demonstrate a 99-percent reduction in annualized infusion rate (AIR) and a 96-percent reduction in annualized bleeding rate (ABR) in 10 participants as of June 5, 2017

Five trial participants are now at least one-year post investigational SPK-9001 administration, including one participant out approximately 18 months; all have discontinued routine factor IX concentrate infusions and have sustained increases in factor IX activity levels

PHILADELPHIA, July 10, 2017 -- Spark Therapeutics (NASDAQ: ONCE), a fully integrated gene therapy company dedicated to challenging the inevitability of genetic disease, announced today that 10 participants in its ongoing Phase 1/2 clinical trial of SPK-9001 for hemophilia B, as of the June 5, 2017 data cut off, had their AIR reduced approximately 99 percent to a mean of 1.0 annual infusion as of the data cut-off date, compared with 67.5 annual infusions before SPK-9001 administration. Nine of the 10 participants have not experienced a bleed since vector infusion; overall ABR was reduced by approximately 96 percent to a mean of 0.4 annual bleeds, compared with 11.1 bleeds before a single administration of 5 x 1011 vector genomes (vg)/kg body weight of SPK-9001. These data represent approximately 9.63 cumulative patient years of SPK-9001 exposure from the start of the trial, with one participant out approximately 18 months post-infusion and four additional participants out at least one year post-infusion. All 10 trial participants have shown consistent and sustained increases in factor IX activity level and a discontinuation of routine infusions of factor IX concentrates. Their mean steadystate factor IX activity level, or the average of each participant's average activity level after 12 weeks, was 33 percent.

The interim data will be presented today by Lindsey George, M.D., an attending physician in the Division of Hematology at Children's Hospital of Philadelphia and investigator in the ongoing Phase 1/2 clinical trial of SPK-9001 for hemophilia B, at ISTH 2017 Congress in Berlin.

"We continue to be encouraged by the SPK-9001 clinical trial results observed to date, with all participants having discontinued routine infusions of factor IX concentrates," said Katherine A. High, M.D., president and chief scientific officer at Spark Therapeutics. "The growing body of data showing a sustained response is a promising sign for this investigational hemophilia B gene therapy program."

The first participant enrolled in the trial, who, as of June 22, 2017, had been followed for approximately 18 months post-infusion of SPK-9001, reduced to zero his number of intravenous factor IX infusions without having any bleeds. In the 12 months before SPK-9001 administration, he infused factor IX concentrates a total of 98 times and still experienced four breakthrough bleeds. His mean steady-state factor IX activity level after SPK-9001 administration was 33 percent of normal at the 18-month mark post-infusion.

As of the June 5, 2017 data cut-off date, nine of the 10 infused participants have not taken factor IX concentrates to prevent or control bleeding events since vector administration. As previously reported, one participant with severe joint disease has self-administered precautionary infusions for persistent knee pain. In the clinical trial to date, no serious adverse events (SAEs) have been reported, including no factor IX inhibitors and no thrombotic events.

As reported in December 2016, two of the 10 participants experienced an asymptomatic, transient elevation in liver enzymes, associated with a decline in factor IX activity in one of those participants, potentially indicative of an immune response to the Spark100 vector capsid. Elevations in alanine aminotransferase (ALT) occurred several weeks post infusion, and rapidly returned to baseline with a tapered course of oral corticosteroids. Both participants have continued to demonstrate stable factor IX activity levels, now 18 and 12 weeks' post-cessation of steroids, respectively. Neither of these participants has experienced a bleed nor taken factor concentrates.

Improvements in Health-Related Quality of Life in Adults with Hemophilia B

A separate prospective interim data analysis suggests a one-time infusion of SPK-9001 results in meaningful health-related quality of life (HRQoL) improvements in several measures, according to a poster that will be presented by Sylvia von Mackensen, Ph.D., senior scientist at the Institute of Medical Psychology, University Medical Centre Hamburg-Eppendorf, Germany, on Tuesday, July 11, from 12 to 1:15 p.m. CET.

All participants were considered HRQoL responders based on the hemophilia-specific Haem-A-QoL Total Score, with the most marked statistically significant changes after vector infusion in responses related to "being dependent on factor concentrate" ($p < 0.0001$); "feeling different from others because of their hemophilia" ($p < 0.001$); and "worrying that their condition is worsening" ($p < 0.003$). Other measures, including, but not limited to, fear of complications, dependency on physician and not feeling contented about their body, did not reach statistical significance.

Participants on average reported "already good" HRQoL pre-vector infusion in the generic EuroQ-VAS ($M=80.5\pm8.3$), a standardized instrument for measuring HRQoL that comprises a health state classification followed by a health evaluation using a visual analogue scale (VAS), which still improved post-vector infusion ($M=86.1\pm9.1$), but was not statistically significant.

All participants completed generic and hemophilia-specific HRQoL questionnaires prior to vector infusion and four, 12, 26 and 52 weeks after vector infusion.

About Hemophilia B

Hemophilia, a rare genetic bleeding disorder that causes the blood to take a long time to clot because of a deficiency in one of several blood clotting factors, is almost exclusively found 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 also is called congenital factor IX deficiency or Christmas disease. The 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 SPKFIX 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 codon-optimized, 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 a collaboration in December 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.

About Spark Therapeutics
Spark Therapeutics, a fully integrated company, strives to challenge the inevitability of genetic disease by discovering, developing, and delivering gene therapies that address inherited retinal diseases (IRDs), neurodegenerative diseases, as well as diseases that can be addressed by targeting the liver. 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 biallelic 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 (which also has received both breakthrough therapy and orphan product designations by the FDA, and access to the PRIority MEdicines (PRIME) Program by the EMA) in a Phase 1/2 trial for hemophilia B being developed in collaboration with Pfizer, and SPK-8011, in a Phase 1/2 trial 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.

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