Spark Therapeutics Presents Updated Preliminary Data from Hemophilia B Phase 1/2 Trial Suggesting Consistent and Sustained Levels of Factor IX Activity at the Hemostasis and Thrombosis Research Society (HTRS) 2017 Scientific Symposium

As of data cutoff, the annualized bleeding rate (ABR) has been reduced by 96 percent and the annualized infusion rate (AIR) reduced by 99 percent

Both participants who began a tapering course of steroids have completed their regimen

PHILADELPHIA, April 6, 2017 (GLOBE NEWSWIRE) — Spark Therapeutics (NASDAQ:ONCE) announced updated preliminary data today from 10 infused participants in the ongoing Phase 1/2 clinical trial of investigational *SPK-9001* for hemophilia B. All participants have experienced consistent and sustained increases in factor IX activity following administration of the investigational therapy. These data will be presented at the Hemostasis and Thrombosis Research Society (HTRS) 2017 Scientific Symposium in Scottsdale, Arizona on Friday, April 7, by Adam Cuker, M.D., assistant professor of medicine at the Perelman School of Medicine of the University of Pennsylvania and a clinical investigator at Children's Hospital of Philadelphia.

Data as of March 24, 2017 will be presented on 10 participants in the study, who were dosed with a single administration of 5×10^{11} vector genomes (vg)/kg body weight. All participants have discontinued routine infusions of factor IX concentrates. Based on individual patient history prior to the study, ABR was reduced by 96 percent to a mean of 0.39 annual bleeds, compared with 9.2 bleeds before *SPK-9001* administration. AIR was reduced 99 percent to a mean of 0.98 annual infusions, compared with 68.5 infusions before *SPK-9001* administration.

As of the data cutoff, 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. The mean steady-state factor IX activity level post 12 weeks treatment for the 10 participants was a sustained 33 percent (range as of the data cutoff: 14 to 81 percent). In the study to date, no serious adverse events have been reported, including no factor IX inhibitors and no thrombotic events. These data represent more than 2,400 cumulative patient days of exposure from the start of the trial.

Two of the 10 participants experienced an asymptomatic, transient elevation in liver enzymes, or decline in FIX activity, potentially indicative of an immune response to the Spark100 vector capsid, that occurred

several weeks post infusion. Both participants received a tapering dose of oral corticosteroids, after which their alanine aminotransferase (ALT) levels returned to baseline. The activity level of one of these participants has stabilized at approximately 15 percent for more than nine weeks post corticosteroid use. The other participant had a factor IX activity level between 70 to 80 percent at completion of steroid use.

“The additional preliminary data continue to support our initial observations that a single intravenous administration of *SPK-9001* has resulted in consistent and sustained levels of factor IX activity for trial participants,” said Katherine A. High, M.D., president and chief scientific officer at Spark Therapeutics. “Notably, all participants to date have consistently achieved our targeted therapeutic range of FIX activity. As we continue to glean more insights from these preliminary data, our analysis suggests that a tapering course of oral corticosteroids has been well-tolerated and may help control potential capsid immune responses following *SPK-9001* infusion.”

These data from the Phase 1/2 clinical trial of *SPK-9001* will be presented during a poster session on Friday, April 7, from 5:15-6:15 p.m. MST.

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 *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 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, *SPK-9001*, 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.

Investor Contact:
Ryan Asay
Ryan.asay@sparktx.com
(215) 239-6424

Media Contact:
Monique da Silva
Monique.dasilva@sparktx.com
(215) 282-7470

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