Biogen Enrolls First Patient in Global Phase 3 Study of BIIB093 (IV Glibenclamide) for Large Hemispheric Infarction

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- CHARM study will evaluate IV glibenclamide for the prevention and treatment of severe cerebral edema in LHI, one of the most severe types of ischemic stroke with limited treatment options
- Prior studies demonstrated IV glibenclamide may potentially improve functional outcomes and reduce mortality, supported by imaging measures of brain swelling and biomarkers
- Study initiation advances Biogen's position in its emerging growth area of acute neurology

CAMBRIDGE, Mass., Sept. 04, 2018 (GLOBE NEWSWIRE) -- Biogen (Nasdaq: BIIB) announced today the enrollment of the first patient in the global Phase 3 clinical study CHARM, designed to evaluate BIIB093 (intravenous (IV) glibenclamide) for the prevention and treatment of severe cerebral edema in large hemispheric infarction (LHI), one of the most severe types of ischemic stroke where brain swelling (cerebral edema) often leads to high morbidity and mortality.

"As pioneers in neuroscience, Biogen is dedicated to advancing innovative approaches for investigational drugs in acute neurological conditions with limited or no treatments by leveraging our core expertise," said Michael Ehlers, M.D., Ph.D., executive vice president, research and development at Biogen. "We believe IV glibenclamide could represent a first-in-class therapy with the aim of giving physicians an effective option to improve patient outcomes and reduce mortality risk. LHI is a severe type of ischemic stroke with high mortality (40 percent to 80 percent) and no currently available therapy. BIIB093 has the potential to be the first major innovation in stroke in over 20 years, and we believe the advancement to Phase 3 represents a significant milestone in our stroke clinical program."

The CHARM study is an international, multicenter, randomized, double-blind, placebo-controlled, Phase 3 study that aims to enroll 680 patients with LHI in approximately 20 countries. It will evaluate the efficacy and safety of IV glibenclamide treatment within 10 hours following stroke onset. The primary endpoint is the modified Rankin Scale (mRS), a functional outcome, assessed at 90 days.

Each year approximately 1.7 million ischemic strokes occur in the U.S., Europe and Japan, and approximately 15 percent of these are classified as LHI. In preclinical studies, IV glibenclamide has been shown to inhibit SUR1-TRPM4 channels that mediate stroke-related brain swelling. Phase 2 proof-of-concept studies have demonstrated the potential of IV glibenclamide to reduce brain swelling associated with disability and mortality in individuals with LHI. IV glibenclamide was granted Orphan Drug Designation by the U.S. Food and Drug Administration (FDA) for the treatment of severe cerebral edema in patients with acute ischemic stroke. The FDA has also granted the CHARM study Special Protocol Assessment and IV glibenclamide Fast Track Designation.

For more information about the Phase 3 study, visit www.clinicaltrials.gov (NCT02864953).

About BIIB093 (IV Glibenclamide)
IV glibenclamide is an investigational compound in development for the prevention and treatment of severe cerebral edema due to large hemispheric infarctions (LHI). IV glibenclamide is a high affinity inhibitor of SUR1-TRPM4 channels, which are upregulated following ischemia and trauma. Opening of these channels can lead to cerebral edema, midline shift, increased intracranial pressure and brain herniation, resulting in permanent disability or death. Biogen acquired the IV glibenclamide asset from Remedy Pharmaceuticals following completion of the Phase 2 GAMES-RP study.

IV glibenclamide was previously evaluated in the Phase 2 GAMES-RP study with a primary endpoint measuring the proportion of patients who achieved an mRS score of 0–4 at 90 days without undergoing decompressive craniectomy. Although this study did not meet the primary endpoint, IV glibenclamide demonstrated potential positive effects on functional outcomes and mortality, supported by biomarkers and imaging measures of brain swelling. Mortality at 30 days was reduced from 36 percent in the placebo group to 15 percent in IV glibenclamide-treated patients (p=0.03). In addition, in patients 70 years of age and younger, 90-day functional outcomes were statistically significantly improved (p=0.048) in the IV glibenclamide group versus placebo. These clinical effects correlated with a significant decrease in the concentration of metalloproteinase-9 (MMP-9), a biomarker associated with extracellular matrix breakdown following stroke, in the IV glibenclamide-treated group. The IV glibenclamide-treated group at approximately 72 hours showed a significant reduction in midline shift (p=0.0006), an imaging marker of neurological deterioration and poor outcomes including death.

About Biogen
At Biogen, our mission is clear: we are pioneers in neuroscience. Biogen discovers, develops and delivers worldwide innovative therapies for people living with serious neurological and neurodegenerative diseases. One of the world's first global biotechnology companies, Biogen was founded in 1978 by Charles Weissmann, Heinz Schaller, Kenneth Murray and Nobel Prize winners Walter Gilbert and Phillip Sharp, and today has the leading portfolio of medicines to treat multiple sclerosis; has introduced the first and only approved treatment for spinal muscular atrophy; and is focused on advancing neuroscience research programs in Alzheimer's disease and dementia, multiple sclerosis and neuroimmunology, movement disorders, neuromuscular disorders, pain, ophthalmology, neuropsychiatry and acute neurology. Biogen also manufactures and commercializes biosimilars of advanced biologics.

We routinely post information that may be important to investors on our website at www.biogen.com. To learn more, please visit www.biogen.com and follow us on social media – Twitter, LinkedIn, Facebook, YouTube.

Biogen Safe Harbor Statement
This press release contains forward-looking statements, including statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including statements relating to the potential clinical effects of IV glibenclamide, the potential of Biogen's commercial business and pipeline programs, including IV glibenclamide and risks and uncertainties associated with drug development and commercialization. These forward-looking statements may be accompanied by words such as "aim," "anticipate, "believe," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "potential," "possible," "will" and other words and terms of similar meaning. Drug development and commercialization involve a high degree of risk, and only a small number of research and development programs result in commercialization of a product. Results in early stage

clinical trials may not be indicative of full results or results from later stage or larger scale clinical trials and do not ensure regulatory approval. You should not place undue reliance on these statements or the scientific data presented.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements, including without limitation, uncertainty of success in the development and potential commercialization of IV glibenclamide; the risk that we may not fully enroll our clinical trials or enrollment will take longer than expected; unexpected concerns may arise from additional data, analysis or results obtained during our clinical trials; regulatory authorities may require additional information or further studies, or may fail or refuse to approve or may delay approval of our drug candidates, including IV glibenclamide; the occurrence of adverse safety events; unexpected costs or delays; failure to protect and enforce Biogen's data, intellectual property and other proprietary rights and uncertainties relating to intellectual property claims and challenges; or we may encounter other unexpected hurdles. The foregoing sets forth many, but not all, of the factors that could cause actual results to differ from Biogen's expectations in any forward-looking statement. Investors should consider this cautionary statement, as well as the risk factors identified in Biogen's most recent annual or quarterly report and in other reports Biogen has filed with the Securities and Exchange Commission. These statements are based on Biogen's current beliefs and expectations and speak only as of the date of this press release. Biogen does not undertake any obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

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