GBT Announces Updated 24-Week Efficacy Data from All Patients Enrolled in Phase 3 HOPE Study Showing Statistically Significant and Sustained Improvements in Hemoglobin with Voxelotor

June 14, 2019

Data Supporting the Potential of Voxelotor as a Disease-Modifying Treatment for Sickle Cell Disease (SCD) Published in The New England Journal of Medicine*and to bePresented During Presidential Symposium at the 24th European Hematology Association (EHA) Congress*

Additional Clinical Data Supporting Voxelotor Program in SCD also Presented at EHA 2019

Company to Host Corporate Update Webcast, Today, Friday, June 14, at 7:00 p.m. CEST/1:00 p.m. ET to Discuss Data and Finalized Details of Planned Confirmatory Transcranial Doppler Study

AMSTERDAM, The Netherlands, June 14, 2019 (GLOBE NEWSWIRE) -- Global Blood Therapeutics, Inc. (GBT) (Nasdaq: GBT) today announced new results from its Phase 3 HOPE Study of voxelotor in patients ages 12 and older with sickle cell disease (SCD). The findings from 274 adolescents and adults treated with voxelotor showed the HOPE Study met its primary endpoint of an improvement in hemoglobin greater than 1 g/dL at 24 weeks with voxelotor 1500 mg compared with placebo, with a favorable safety and tolerability profile. In the study, voxelotor provided a rapid, statistically significant and sustained improvement in hemoglobin levels and reduced the incidence of worsening anemia and hemolysis.

The data were published today in *The New England Journal of Medicine* and featured in the press briefing prior to presentation at 4:15 p.m. CEST as part of the Presidential Symposium at the 24th European Hematology Association (EHA) Congress in Amsterdam.

“These additional data from our multi-national, Phase 3 HOPE Study support and strengthen the 24-week findings from 154 patients that were presented at the American Society of Hematology Annual Meeting in December 2018. These updated results form the basis of the rolling submission of our New Drug Application for voxelotor, which we are on track to complete in the second half of this year for review under an accelerated approval pathway,” said Ted W. Love, M.D., president and chief executive officer of GBT. “We are excited about the potential for voxelotor to improve the major morbid outcomes for people with SCD, given that lower levels of hemoglobin are associated with greater risk of overt stroke, silent infarct and increased mortality. We are also pleased to announce that we have reached final agreement with the FDA on the design of our transcranial doppler post-approval confirmatory study, which we will share more information about during our corporate update webcast later today.”

“These positive data from more than 270 patients enrolled in the HOPE Study provide strong evidence that voxelotor, by significantly improving anemia and hemolysis, has the potential to be a disease-modifying treatment for SCD by preventing chronic organ damage and prolonging survival,” said Jo Howard, MB BChir, MRCP, FRCPath, of Guy’s and St. Thomas’ NHS Foundation Trust and King’s College London and a HOPE Study investigator. “Given the observed ability of voxelotor to reduce anemia, hemolysis and red blood cell sickling, as well as a favorable safety profile, I am confident that voxelotor could potentially become a new standard-of-care for treating adolescents and adults with SCD.”

New HOPE Study Results Show Robust Improvements in Anemia with Voxelotor (Abstract #S147)
The new results from the HOPE Study include 24-week efficacy data from 274 patients ages 12 and older with SCD enrolled in the study from 60 institutions across 12 countries. The data showed that patients treated with once-daily oral voxelotor demonstrated rapid, robust and sustained improvements in anemia, as measured by the increase in hemoglobin from baseline to 24 weeks compared to placebo (see Table 1). The mean increase in hemoglobin levels with voxelotor compared to placebo was similar with or without concurrent hydroxyurea treatment.

These results from the HOPE Study are reported using both intention-to-treat (ITT) and per-protocol (PP) analyses. The PP analysis is based on patients who completed the primary endpoint visit of 24 weeks, whereas the more conservative ITT analysis defines all patients with missing data at 24 weeks as non-responders. Previously, GBT had reported HOPE Study results as assessed only in the PP population. As discussed with the U.S. Food and Drug Administration (FDA), the HOPE Study primary endpoint – hemoglobin response at 24 weeks – is to be assessed in an ITT population for the New Drug Application (NDA). The benefit of voxelotor is highly statistically significant irrespective of ITT or PP analysis, and both analyses are presented below.

Table 1

	Intention-To-Treat (ITT) Analysis			**Per-Protocol (PP) Analysis**		
	N	*% with >1 g/dL Increase in Hb*	*Mean* Change in Hb from Baseline to 24 Weeks*	N	*% with >1 g/dL Increase in Hb*	*Mean Change in Hb from Baseline to 24 Weeks*

1500 mg voxelotor	90	51.1% (p<0.001)	1.1 g/dL (p<0.001)	74	59.5% (p<0.001)	1.3 g/dL (p<0.001)
900 mg voxelotor	92	32.6% (p<0.001)	0.6 g/dL (p<0.001)	79	38.0% (p<0.001)	0.7 g/dL (p<0.001)
Placebo	92	6.5%	-0.1 g/dL	76	9.2%	0 g/dL

*Adjusted for baseline stratification factors.
P-value is for comparison versus placebo; not adjusted for multiplicity.

The ITT analysis of all 274 patients at 24 weeks showed:

- Hemoglobin improved rapidly from baseline to the earliest timepoint measured (2 weeks) with voxelotor 1500 mg and was sustained through 24 weeks (p<0.001 vs. placebo). The improvement in hemoglobin was similar in patients with or without background use of hydroxyurea.
- Voxelotor 1500 mg increased hemoglobin levels to a mean of 9.8 g/dL at 24 weeks from a baseline of 8.6 g/dL, consistent with a clinically meaningful improvement in anemia.
- Improvements from baseline in hemoglobin, percent reticulocytes and indirect bilirubin occurred with both voxelotor doses, further demonstrating an improvement in hemolysis consistent with a dose-related inhibition of hemoglobin polymerization.
- There were numerically fewer vaso-occlusive crises (VOCs) and a lower annualized incidence rate (per person-year) of VOCs in both voxelotor dose groups than in the placebo group, despite the significant increases in hemoglobin with voxelotor treatment.
- Voxelotor was generally safe and well tolerated, with both doses having similar safety profiles. Treatment discontinuation rates did not differ substantially among the three trial groups. There was no evidence of impairment of tissue oxygenation at either dose of voxelotor.

Additional data presented in poster sessions at the 2019 EHA Congress further support GBT's voxelotor program in SCD:

- Clinical data from an investigator-initiated ancillary study of three adolescents with SCD enrolled in the HOPE-KIDS 1 Study showed that all participants had unchanged or lower cerebral blood flow as measured by functional MRI with angiography while receiving voxelotor, suggesting that cerebral blood flow was maintained or improved with administration of voxelotor. Lower cerebral blood flow with rising hemoglobin levels suggests improved oxygen delivery to the brain. (Abstract #PF740)
- An *in vitro* study of the mechanism of voxelotor showed that oxygen is released from voxelotor-modified hemoglobin under deoxygenated conditions and that normal physiological compensatory mechanisms to enhance oxygen delivery are not disrupted. This finding suggests that treatment with voxelotor maintains oxygen delivery to tissues and supports the safety of this investigational treatment. (Abstract #PS1522)

Corporate Update Webcast Details
Today, Friday, June 14, 2019, at 7:00 p.m. CEST / 1:00 p.m. ET, members of GBT's management team and Jo Howard, MB BChir, MRCP, FRCPath, Guy's and St. Thomas' NHS Foundation Trust and King's College London, will review the HOPE Study data being presented at the 2019 EHA Congress. Additional presentations by Robert J. Adams, M.D., Medical University of South Carolina, and Jeremie H. Estepp, M.D., St. Jude Children's Research Hospital, will provide an overview on the use of transcranial doppler (TCD) ultrasonography in SCD patients and the final trial design for GBT's post-approval confirmatory TCD study, respectively. The event will be webcast live from GBT's website at www.gbt.com in the Investors section. A replay will be available for 30 days following the event.

About Sickle Cell Disease
SCD is a lifelong inherited blood disorder caused by a genetic mutation in the beta-chain of hemoglobin, which leads to the formation of abnormal hemoglobin known as sickle hemoglobin (HbS). In its deoxygenated state, HbS has a propensity to polymerize, or bind together, forming long, rigid rods within a red blood cell (RBC). The polymer rods deform RBCs to assume a sickled shape and to become inflexible, which causes hemolytic anemia (low hemoglobin due to RBC destruction) that can lead to multi-organ damage and early death. This sickling process also causes blockage in capillaries and small blood vessels. Beginning in childhood, SCD patients typically suffer unpredictable and recurrent episodes or crises of severe pain due to blocked blood flow to organs, which often lead to psychosocial and physical disabilities.

About Voxelotor in Sickle Cell Disease
Voxelotor (previously called GBT440) is being developed as an oral, once-daily therapy for patients with SCD. Voxelotor works by increasing hemoglobin's affinity for oxygen. Since oxygenated sickle hemoglobin does not polymerize, GBT believes voxelotor blocks polymerization and the resultant sickling and destruction of red blood cells. With the potential to improve hemolytic anemia and oxygen delivery, GBT believes that voxelotor may potentially modify the course of SCD. In recognition of the critical need for new SCD treatments, the U.S. Food and Drug Administration (FDA) has granted voxelotor Breakthrough Therapy, Fast Track, Orphan Drug and Rare Pediatric Disease designations for the treatment of patients with SCD. The European Medicines Agency (EMA) has included voxelotor in its Priority Medicines (PRIME) program, and the European Commission (EC) has designated voxelotor as an orphan medicinal product for the treatment of patients with SCD.

GBT is currently evaluating voxelotor in the HOPE (Hemoglobin Oxygen Affinity Modulation to Inhibit HbS PolymErization) Study, a Phase 3 clinical study in patients age 12 and older with SCD. Additionally, voxelotor is being studied in the ongoing Phase 2a HOPE-KIDS 1 Study, an open-label, single- and multiple-dose study in pediatric patients (age 4 to 17) with SCD. The HOPE-KIDS 1 Study is assessing the safety, tolerability,

pharmacokinetics and exploratory treatment effect of voxelotor.

About GBT
GBT is a clinical-stage biopharmaceutical company determined to discover, develop and deliver innovative treatments that provide hope to underserved patient communities. GBT is developing its lead product candidate, voxelotor, as an oral, once-daily therapy for sickle cell disease. To learn more, please visit www.gbt.com and follow the company on Twitter @GBT_news.

Forward-Looking Statements
Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995, including statements about GBT's development plans for voxelotor and the potential benefits of voxelotor for SCD patients and other statements containing the words "anticipate," "planned," "believe," "forecast," "estimated," "expected," and "intend," among others. These forward-looking statements are based on GBT's current expectations and actual results could differ materially. Statements we make in this press release may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. We intend these forward-looking statements, including statements regarding our plan to submit an NDA for voxelotor under an accelerated regulatory approval pathway, the availability of, and sufficiency of our data to support, accelerated regulatory approval, the therapeutic potential and safety profile of voxelotor, including the potential to be a disease-modifying therapy for SCD, our plan to initiate a TCD confirmatory study, the potential for TCD flow velocity to serve as an acceptable primary endpoint in a confirmatory study, the potential for voxelotor to become a new standard of care for treating adolescents and adults with SCD, our ability to implement and complete our clinical development plans for voxelotor, the potential for an increase in hemoglobin of 1 g/dL or greater to reduce the risk of stroke and mortality in patients with SCD, our ability to generate and report data from our ongoing and potential future studies of voxelotor (including data from patients enrolled in our Phase 3 HOPE Study, and data from our ongoing Phase 2a HOPE-KIDS 1 Study), regulatory review and actions relating to voxelotor, our potential commercial launch of voxelotor, and the timing of these events, to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Securities Exchange Act and are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. We can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved, and furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control including, without limitation, the risks that our clinical and preclinical development activities may be delayed or terminated for a variety of reasons, that results of clinical trials may be subject to differing interpretations, that regulatory authorities may disagree with our clinical development plans or require additional studies or data to support further clinical investigation of our product candidates, that drug-related adverse events may be observed in clinical development, and that data and results may not meet regulatory requirements or otherwise be sufficient for further development, regulatory review or approval, along with those risks set forth in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, and in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, as well as discussions of potential risks, uncertainties and other important factors in our subsequent filings with the U.S. Securities and Exchange Commission. Except as required by law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

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Source: Global Blood Therapeutics, Inc.