UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 13, 2021

Global Blood Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-37539**	**27-4825712**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification Number)**

181 Oyster Point Blvd.
South San Francisco, CA 94080
(Address of principal executive offices, including zip code)

(650) 741-7700
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d- 2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	**GBT**	**The NASDAQ Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

In this report, “GBT,” “Company,” “we,” “our,” and “us” means Global Blood Therapeutics, Inc., and/or one or more of our subsidiaries, unless the context otherwise provides.

Item 8.01. Other Events.

On December 13, 2021, we presented at the 63rd American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta, Georgia, a poster titled “GBT021601, a Next-Generation HbS Polymerization Inhibitor: Results of Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Adults Living with Sickle Cell Disease and Healthy Volunteers.” A copy of the poster is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Poster titled “GBT021601, a Next-Generation HbS Polymerization Inhibitor: Results of Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Adults Living with Sickle Cell Disease and Healthy Volunteers.”
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Global Blood Therapeutics, Inc.

Date: December 13, 2021

By: /s/ Jeffrey Farrow
Jeffrey Farrow
Chief Financial Officer

GBT021601, a Next-Generation HbS Polymerization Inhibitor: Results of Safety, Tolerability, Pharmacokinetics and Pharmacodynamics in Adults Living with Sickle Cell Disease and Healthy Volunteers

Clark Brown, MD, PhD[1]; Andrew Redfern, MBChB[2]; Eleanor Lisbon, MD, MPH[3]; Carla Washington, PhD[3]; Irene Agodoa, MD[3]; Kim Smith-Whitley, MD[3]

[1]Aflac Cancer and Blood Disorder Center of Children's Healthcare of Atlanta and Department of Pediatrics, Emory School of Medicine, Atlanta, GA, USA; [2]Linear Clinical Research, Nedlands, Western Australia; [3]Global Blood Therapeutics, South San Francisco, CA, USA

INTRODUCTION

Here we explore the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of GBT021601 in healthy volunteers and adults living with sickle cell disease (SCD).

- SCD is an inherited, lifelong disorder characterized by sickle hemoglobin (HbS) polymerization, resulting in red blood cell (RBC) sickling, RBC destruction, vaso-occlusion, and end-organ damage[1]
- Voxelotor is a first-in-class HbS polymerization inhibitor indicated in the United States for adult and adolescent patients (aged ≥12 years) with SCD. In the pivotal HOPE study, treatment with voxelotor resulted in rapid, robust, and sustained improvements in hemoglobin and hemolysis[2-5]
- GBT021601 is a potent, next-generation HbS polymerization inhibitor that has the potential to achieve higher hemoglobin (Hb) occupancies at lower doses than voxelotor. In an in vivo SCD mouse model, GBT021601 treatment led to substantial improvements in hematological parameters[6]

REFERENCES

1. Kato GJ, Piel FB, Reid CD, et al. Sickle cell disease. Nat Rev Dis Primers. 2018;4:18010.
2. Estepp JH. Voxelotor (GBT440), a first-in-class hemoglobin oxygen-affinity modulator, has promising and reassuring preclinical and clinical data. Am J Hematol. 2018;93(3):326-329.
3. Vichinsky E, Hoppe CC, Ataga KI, et al. A phase 3 randomized trial of voxelotor in sickle cell disease. N Engl J Med. 2019;381(6):509-519.
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5. Oxbryta. Prescribing information. Global Blood Therapeutics; January 2021.
6. Dufu K, Alt C, Strutt S, et al. GBT021601 improves the pathophysiology of sickle cell disease in a murine model. Poster presented at: 26th European Hematology Association Congress; June 9-17, 2021; Virtual. Poster EP1198.
7. Data on file. Global Blood Therapeutics, South San Francisco, CA.
8. Hutchaleelaha A, Patel M, Washington C, et al. Pharmacokinetics and pharmacodynamics of voxelotor (GBT440) in healthy adults and patients with sickle cell disease. Br J Clin Pharmacol. 2019;85(6):1290-1302.

DISCLOSURES

Clark Brown
- Consultant: Global Blood Therapeutics, Imara, Novartis, Novo Nordisk
- Research support: Global Blood Therapeutics, Forma Therapeutics, Imara, Novartis, Pfizer

Andrew Redfern
- Employee: Linear Clinical Research
  Advisory board member: Novartis, Pfizer, Roche, Eisai, AstraZeneca

Eleanor Lisbon
- Employee, equity ownership: Global Blood Therapeutics

Carla Washington
- Clinical consultant
- Shareholder: Global Blood Therapeutics

Irene Agodoa
- Employee, equity ownership: Global Blood Therapeutics

Kim Smith-Whitley
- Employee, equity ownership: Global Blood Therapeutics

ACKNOWLEDGMENTS

- Thank you to all the patients with sickle cell disease, families, caregivers, research nurses, study coordinators, and support staff who contributed to this study.
- This study was supported by Global Blood Therapeutics.

The authors thank Jessica Chen, MD (Healthcare Consultancy Group), with funding from Global Blood Therapeutics, for editorial assistance in the preparation of this report.

RESULTS

Healthy Volunteers Study – Single Ascending Dose

Design for Healthy Volunteers Study – Single Ascending Dose

Phase 1, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the safety and tolerability of single ascending doses of GBT021601 in healthy volunteers

Patient population
- Healthy volunteers aged 18 to 55 years

Primary endpoint
- Safety and tolerability

Key secondary endpoints
- PK
- Effect of food

PK, pharmacokinetics.

Healthy Volunteers SAD Cohorts: Demographics and Baseline Characteristics Were Similar Across Groups

	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Mean age, years (SD)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Male, n (%)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Race, n (%)								
White	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Asian	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Black or African American	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Other	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

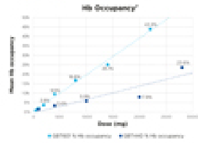
Healthy Volunteers SAD Cohorts: Most TEAEs Were Grade 1 or 2

Overview of TEAEs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Number of TEAEs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Number of participants with at least 1 TEAE, n (%)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Number of TEAEs grade ≥3	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Number of drug-related TEAEs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Number of participants with at least 1 drug-related TEAE, n (%)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Number of TEAEs leading to study drug discontinuation	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Number of SAEs	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Favorable Whole Blood PK Parameters and Hemoglobin Occupancy after Single Ascending Dose per Cohort

Parameter, mean	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
% Hb occupancy	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Single Doses of GBT021601 Showed a Dose-Dependent Increase in Percent Hb Occupancy in Healthy Volunteers



- There was no observable difference in Hb occupancy between fasting and fed states (200 mg)
- These Hb occupancies exceed those reported in healthy volunteers receiving single doses of voxelotor over a similar range

Healthy Volunteers Study – Multiple Ascending Dose

Design for Healthy Volunteers Study – Multiple Ascending Dose

Ongoing phase 1, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the safety and pharmacological effects of multiple ascending doses of GBT021601 in healthy volunteers

Patient population
- Healthy volunteers aged 18 to 55 years

Primary endpoint
- Safety and tolerability

One dose cohort to date
- LD: 300 mg × 3 days
  MD: 15 mg × 11 days

Key secondary endpoints
- PK
- Effect on ECG parameters

Healthy Volunteers 15 mg MAD Cohort: Demographics and TEAEs

Demographics	15 mg maintenance (n=10)
Mean age, years (SD)	40.7 (8.9)
Male, n (%)	8 (80.0)
Race, n (%)	
White	7 (70.0)
Black or African American	3 (30.0)

Overview of TEAEs	15 mg maintenance (n=10)
Number of TEAEs	5
Number of participants with at least 1 TEAE, n (%)	4 (40.0)
Number of TEAEs grade ≥3	0
Number of drug-related TEAEs	1
Number of participants with at least 1 drug-related TEAE, n (%)	1 (10.0)
Number of TEAEs leading to study drug discontinuation	0
Number of SAEs	0

Preliminary Whole Blood PK Parameters and Hemoglobin Occupancy in Healthy Volunteers 15 mg MAD Cohort

Parameter, mean	Day 14 (15 mg)
C_{max} µg/mL (CV%)	130.7 (14.3)
t_{max} h (range)	6 (0.5-24)
AUC_{0-24} µg·h/mL (CV%)	2865 (13.7)
B:P ratio	162.4
% Hb occupancy (CV%)	16.0 (14.3)

Adults Living with SCD Study

Design for Adults Living with SCD Study

Ongoing phase 1, single-arm, intrapatient single-dose and multiple-ascending-dose trial to evaluate the safety and efficacy of GBT021601 in adults with SCD

Patient population
- Patients with HbSS, aged 18 to 60 years
- Baseline Hb ≥6.5 g/dL and ≤10.5 g/dL
- No VOCs or transfusions within 30 days of screening

Primary endpoint
- Safety and tolerability

Key secondary endpoints
- PK
- Relationship between time-matched GBT021601 concentrations and the changes in clinical measures of anemia and hemolysis from baseline

SCD Cohort: Demographics and Baseline Characteristics

	SCD (N=6)
Mean age, years (SD)	20.2 (2.25)
Male, n (%)	4 (66.7)
Race, n (%)	
Black or African American	5 (83.3)
Other	1 (16.7)
HbSS genotype, n (%)	6 (100)
Current hydroxyurea use, n (%)	6 (100)
Number of VOCs within 12 months of screening	
0	2 (33.3)
1	1 (16.7)
2	3 (50.0)
Number of transfusions within 12 months of screening	
0	4 (66.7)
1	2 (33.3)

SCD SAD Cohort: All TEAEs Were Grade 1 or 2

Overview of TEAEs	SAD (N=6)
Number of TEAEs	7
Number of participants with at least 1 TEAE, n (%)	5 (83.3)
Number of TEAEs grade ≥3	0
Number of drug-related TEAEs	1
Number of participants with at least 1 drug-related TEAE, n (%)	1 (16.7)
Number of TEAEs leading to study drug discontinuation	0
Number of SAEs	0

CONCLUSIONS

Single doses and multiple daily doses of GBT021601 are well tolerated in healthy volunteers and adults living with SCD, with studies currently ongoing. Preliminary single-dose data of GBT021601 showed a linear dose-dependent increase in percent Hb occupancy up to the highest dose evaluated, 2200 mg.

GBT021601 has the potential to achieve a targeted Hb occupancy and attain desired hematological effects at lower doses than voxelotor, therefore reducing pill burden and improving clinical outcomes for individuals living with SCD.

Further multiple-dose data will help evaluate GBT021601's potential as a best-in-class, oral, disease-modifying therapy for SCD.

Presented at: American Society of Hematology Annual Meeting & Exposition 2021; December 11-14, 2021