Compose

# COMPOSE Clinical Trial: Interim Results Summary

## Study: Pegtibatinase Treatment for Patients With Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency (classical homocystinuria [HCU])

**COMPOSE is a clinical trial (first study in humans) to examine the safety and drug effects of pegtibatinase in patients with classical HCU**


Travere Therapeutics, the Sponsor of this clinical trial, would like to thank all the study participants.

Travere is committed to sharing the results of its research efforts, and this summary reports the initial study results from COMPOSE.

Pegtibatinase is currently being studied in this Phase 1/2 clinical trial for treatment of patients with classical HCU and is not yet approved by any health authority. Whether pegtibatinase is safe for use in patients and whether it is effective for the treatment of classical HCU is still not proven.

This summary reports the initial results of this one clinical study that is still in progress. Results from multiple and different types of studies must be reviewed to fully understand if and how a study drug works and if it is safe to give to study participants. These results may be different than those from other studies that will still need to be reviewed.

**NOTE: If you are a participant, please contact the doctor or staff at your study site if you have any questions about the study itself or the results.**

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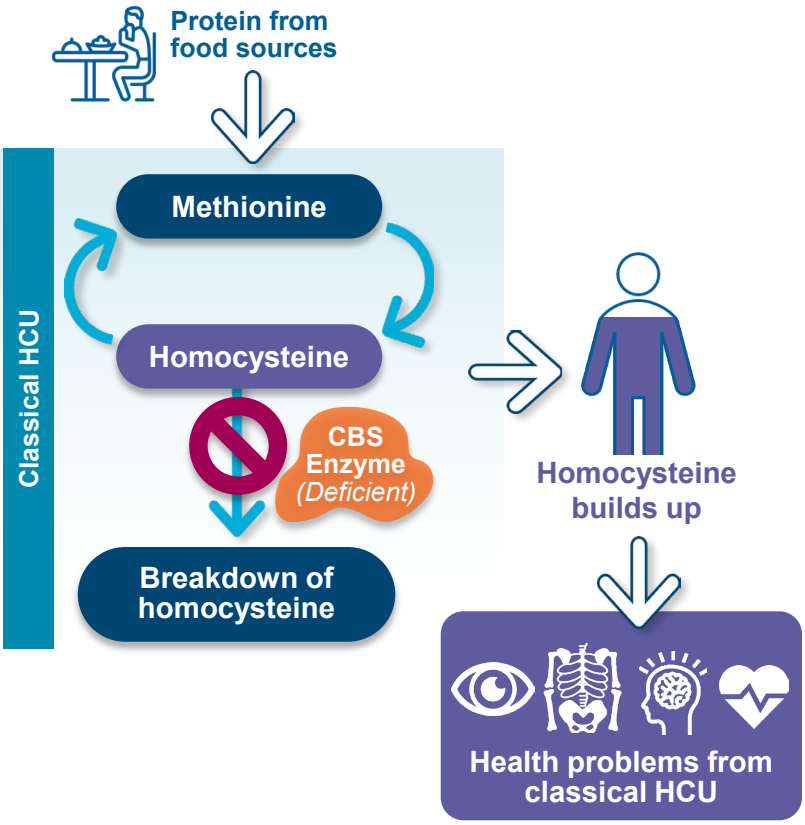
BACKGROUND

## What is Classical Homocystinuria (HCU) and How is it Treated?

- Classical HCU is a slowly progressive genetic disease[1]
  - Caused by problems with the cystathionine β-synthase (CBS) enzyme that breaks down homocysteine (a byproduct of processing methionine, which is a building block that comes from protein in our diet)
  - Causes higher levels of homocysteine in the body that can lead to problems in the eyes, skeleton, brain, and blood vessels[1]
- Current treatment may include a low protein diet (typically with metabolic formula), Cystadane® (betaine), and/or vitamin B6[2]
- Even with treatment, for many patients *it is difficult to keep total homocysteine levels below 100 µM* as recommended[2]
- Pegtibatinase, a modified version of the *human* CBS enzyme,[3] is being studied for the potential treatment of classical HCU




STUDY METHODS & PATIENTS

## The goals of COMPOSE are to determine:

- How safe is pegtibatinase in adults and children with classical HCU aged 12 and over?
- How does pegtibatinase behave in the human body?
- What happens to homocysteine levels after treatment with pegtibatinase?
- What are the effects of pegtibatinase on health problems caused by classical HCU?

## Who is able to participate?

**Qualified patients:**

- Must be between 12 and 65 years old with classical HCU and total homocysteine level greater than 80 µM
- Must be willing to maintain stable diet/therapy
- Cannot have known allergic reaction to pegtibatinase or polyethylene glycol (PEG)
- Cannot use injectable drugs containing PEG, other than pegtibatinase or COVID vaccines, within 3 months before study screening and during study
- Cannot have had organ transplantation or chronic immunosuppressive therapy
- Cannot be pregnant or breast-feeding

## How does the COMPOSE study work?

- During the main treatment period (at least 12 weeks) that was "double blind" (doctor and patient were not told if they were receiving pegtibatinase or placebo), 5 different doses were tested
- Some of the key results looked at the occurrence of side effects (safety) and changes in total homocysteine levels (efficacy) at 12 weeks to see how pegtibatinase works

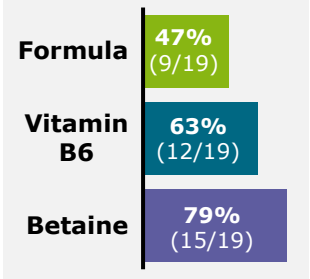
### *Number of Patients*

**19** = **15** + **4**

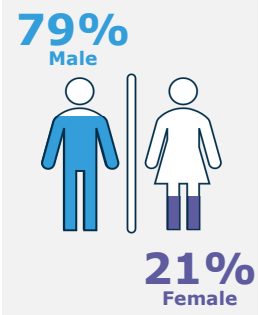
- **19** Total number of patients
- **15** Diagnosed younger than 18
- **4** Diagnosed older than 18

### *Race*


### *Treatment Before Study Start*




### *Gender*




### *Age*

## SAFETY: Pegtibatinase Was Generally Well Tolerated at Doses Up to 1.5 mg/kg Twice a Week

- Patients were on pegtibatinase (or placebo) for about 1.9 years, the longest time being 2.8 years
- No moderate or severe side effects were reported in patients treated with the highest dose (1.5 mg/kg twice a week)

**Most side effects were mild, did not last long, and did not increase with higher doses**

### Most common side effects

- Injection site:
  - reaction (3 people)
  - redness (3 people)
  - pain (3 people)
  - itching (2 people)
  - rash (2 people)
- Hives (3 people)
- Joint pain (2 people)

### Six serious side effects were reported

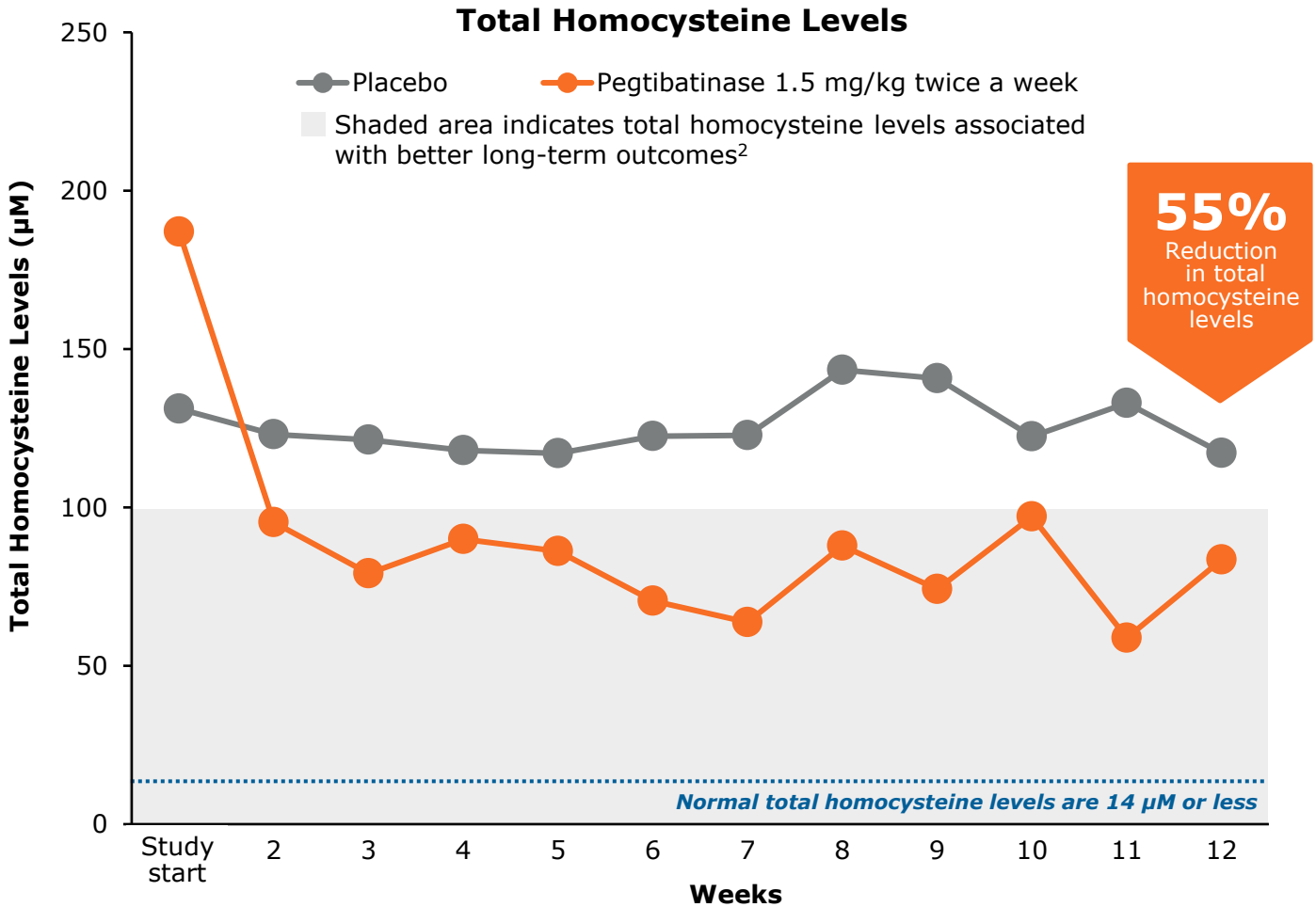
- Only 1 was considered likely related to treatment: a case of acute hives which cleared up in 11 days and did not happen again after treatment restarted
- Other 5 were determined by patients' doctors to be unrelated to study drug

### Other

- No patient stopped treatment due to a side effect related to the drug
- There were no reports of severe allergic or immune reactions due to the drug
- Other general bloodwork and EKG results were as expected

## EFFICACY: How Pegtibatinase Affected Total Homocysteine Levels

- Patients who received the highest dose of pegtibatinase (1.5 mg/kg twice a week) had the largest decrease in total homocysteine level (55%)
- Treatment with pegtibatinase at the highest dose resulted in a rapid reduction in total homocysteine level to less than 100 µM which lasted over the 12-week study period
- Total homocysteine levels under 100 µM is an important clinical threshold for treatment



## CONCLUSIONS

**Pegtibatinase was generally well tolerated at all doses tested and there were no reports of severe allergic or immune reactions due to study drug; no patients stopped treatment due to side effects**

**Patients on higher doses of pegtibatinase showed rapid reduction in total homocysteine levels; patients treated with the highest dose had an average reduction of 55% at 12 weeks**

**Patients treated with the highest dose of pegtibatinase twice a week had a lasting reduction of total homocysteine over 12 weeks and maintained their average total homocysteine level below 100 µM as recommended**

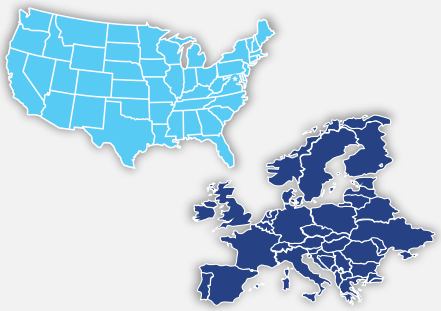
**These results suggest that pegtibatinase may have the potential to be a new treatment for classical HCU**

## FUTURE STEPS

### Future Steps for Pegtibatinase Development

COMPOSE continues to enroll to study a higher dose and new formulation

Discussions with regulatory authorities are taking place to develop the Phase 3 pivotal study (next step to getting a treatment approved for use)



Engagement with health care practitioners, patients, and other interested parties is ongoing to learn more about classical HCU and the potential role of pegtibatinase

## COMPOSE STUDY DETAILS

### *To learn more about the COMPOSE Study:*

**Official Study Title:** A Double Blind, Randomized, Placebo-controlled, Phase 1/2 Study to Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Effects on Clinical Outcomes of Pegtibatinase (TVT-058), Administered Subcutaneously in Patients With Cystathionine Beta-Synthase Deficient Homocystinuria (COMPOSE)

**Sponsor:** Travere Therapeutics, 3611 Valley Centre Drive, Suite 300, San Diego, CA 92130 USA

**Contact:** Travere Medical Information, 1-877-659-5518, medinfo@travere.com

**Medicine Studied:** Pegtibatinase (TVT-058)

**Protocol Number:** CBS-HCY-CT-01

**ClinicalTrials.gov Identifier:** NCT03406611

**Date of Summary:** October 2022

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**REFERENCES**

**1.** Sacharow SJ, et al. 2004 Jan 15 [Updated 2017 May 18]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. **2.** Morris AAM, et al. *J Inherit Metab Dis*. 2017;40:49-74. **3.** Majtan T, et al. *Life Sci*. 2018;200:15-25. **4.** Levy HL, et al. Poster presented at: SIMD 2022; April 10-13, 2022; Orlando, FL. **5.** Greblikas F. "COMPOSE Phase 1/2 Study: Interim Results." GMDI 2022, May 5-7, 2022, Lake Las Vegas, NV. Invited Presentation.


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