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BE iN DEPENDENT

CASGEVY™ may help people aged 12 years and older with transfusion-dependent beta thalassemia (TDT) live without regular blood transfusions

In a clinical study, 91.4% of people (32 out of 35) were transfusion independent for at least 12 months in a row after receiving CASGEVY.

ARE YOU iN? Talk to a healthcare provider about whether CASGEVY may be right for you.

Josh, living with TDT, and his mom, Alison

People with TDT pictured may or may not have received CASGEVY.

What is CASGEVY?

CASGEVY is a one-time therapy used to treat people aged 12 years and older with beta thalassemia (β-thalassemia) who need regular blood transfusions.

CASGEVY is made specifically for each patient, using the patient's own edited blood stem cells, and increases the production of a special type of hemoglobin called hemoglobin F (fetal hemoglobin or HbF). Having more HbF increases overall hemoglobin levels and has been shown to improve the production and function of red blood cells. This can eliminate the need for regular blood transfusions in people with beta thalassemia.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about CASGEVY?

After treatment with CASGEVY, you will have fewer blood cells for a while until CASGEVY takes hold (engrafts) into your bone marrow. This includes low levels of platelets (cells that usually help the blood to clot) and white blood cells (cells that usually fight infections). Your doctor will monitor this and give you treatment as required. The doctor will tell you when blood cell levels return to safe levels.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

Josh and Luke, living with TDT, and their dad, Fred

People with TDT pictured may or may not have received CASGEVY.

BE iNFORMED

In this brochure, you'll learn about how CASGEVY™ (cas-jeh-vee) works, what it may do for you, what the potential side effects are, and how you will receive it.

Throughout the brochure you will see important words to know. These words are **underlined and bolded** the first time they appear. You can click the word to see its definition in the glossary on page 18.

Read on and get iNformed!

Contents

IMPORTANT SAFETY INFORMATION (continued)

What is the most important information I should know about CASGEVY? (continued)

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of platelet cells:
  - severe headache
  - abnormal bruising
  - prolonged bleeding
  - bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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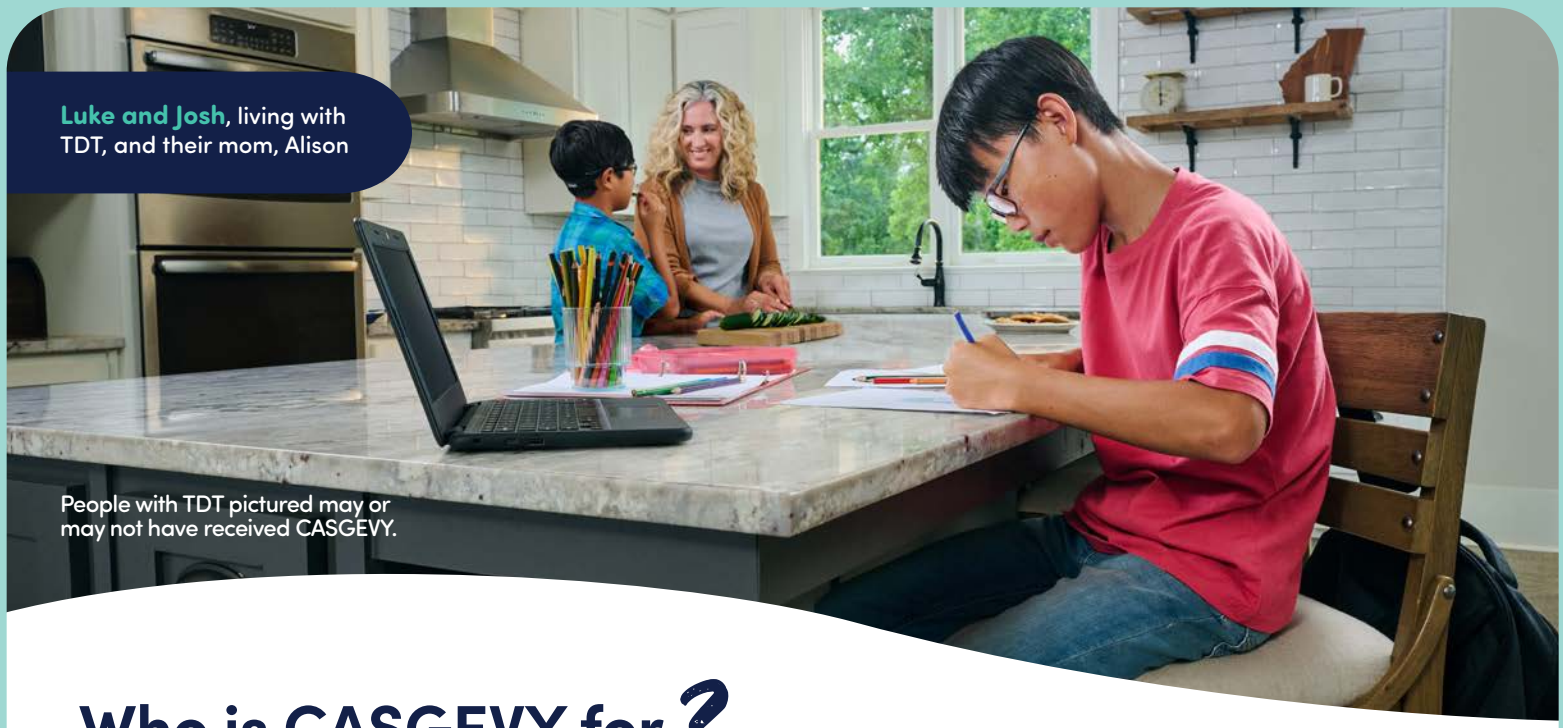

Luke and Josh, living with TDT, and their mom, Alison

People with TDT pictured may or may not have received CASGEVY.

Who is CASGEVY for?

CASGEVY is approved for people aged 12 years and older with beta thalassemia who need regular blood transfusions.

You may have heard some other words or phrases used to refer to your condition. Beta thalassemia with a need for regular blood transfusions is also called:

- **Transfusion-dependent beta thalassemia** (abbreviated as "TDT")
- Beta thalassemia major

IMPORTANT SAFETY INFORMATION (continued)

What is the most important information I should know about CASGEVY? (continued)

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of white blood cells:
  - fever
  - chills
  - infections

You may experience side effects associated with other medicines administered as part of the treatment regimen with CASGEVY. Talk to your physician regarding those possible side effects. Your healthcare provider may give you other medicines to treat your side effects.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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Important Safety Information

What is CASGEVY™?

CASGEVY is a one-time therapy used to treat people aged 12 years and older with beta thalassemia (β-thalassemia) who need regular blood transfusions.

CASGEVY is made specifically for each patient, using the patient's own edited blood stem cells, and increases the production of a special type of hemoglobin called hemoglobin F (fetal hemoglobin or HbF). Having more HbF increases overall hemoglobin levels and has been shown to improve the production and function of red blood cells. This can eliminate the need for regular blood transfusions in people with beta thalassemia.

What is the most important information I should know about CASGEVY?

After treatment with CASGEVY, you will have fewer blood cells for a while until CASGEVY takes hold (engrafts) into your bone marrow. This includes low levels of platelets (cells that usually help the blood to clot) and white blood cells (cells that usually fight infections). Your doctor will monitor this and give you treatment as required. The doctor will tell you when blood cell levels return to safe levels.

- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of platelet cells:
  - severe headache
  - abnormal bruising
  - prolonged bleeding
  - bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood
- **Tell your healthcare provider right away** if you experience any of the following, which could be signs of low levels of white blood cells:
  - fever
  - chills
  - infections

You may experience side effects associated with other medicines administered as part of the treatment regimen with CASGEVY. Talk to your physician regarding those possible side effects. Your healthcare provider may give you other medicines to treat your side effects.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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Important Safety Information (continued)

How will I receive CASGEVY™?

Your healthcare provider will give you other medicines, including a conditioning medicine, as part of your treatment with CASGEVY. It's important to talk to your healthcare provider about the risks and benefits of all medicines involved in your treatment.

After receiving the conditioning medicine, it may not be possible for you to become pregnant or father a child. You should discuss options for fertility preservation with your healthcare provider before treatment.

STEP 1: Before CASGEVY treatment, a doctor will give you mobilization medicine(s). This medicine moves blood stem cells from your bone marrow into the blood stream. The blood stem cells are then collected in a machine that separates the different blood cells (this is called apheresis). This entire process may happen more than once. Each time, it can take up to one week.

During this step, rescue cells are also collected and stored at the hospital. These are your existing blood stem cells and are kept untreated just in case there is a problem in the treatment process. If CASGEVY cannot be given after the conditioning medicine, or if the modified blood stem cells do not take hold (engraft) in the body, these rescue cells will be given back to you. If you are given rescue cells, you will not have any treatment benefit from CASGEVY.

STEP 2: After they are collected, your blood stem cells will be sent to the manufacturing site where they are used to make CASGEVY. It may take up to 6 months from the time your cells are collected to manufacture and test CASGEVY before it is sent back to your healthcare provider.

STEP 3: Shortly before your stem cell transplant, your healthcare provider will give you a conditioning medicine for a few days in hospital. This will prepare you for treatment by clearing cells from the bone marrow, so they can be replaced with the modified cells in CASGEVY. After you are given this medicine, your blood cell levels will fall to very low levels. You will stay in the hospital for this step and remain in the hospital until after the infusion with CASGEVY.

STEP 4: One or more vials of CASGEVY will be given into a vein (intravenous infusion) over a short period of time.

After the CASGEVY infusion, you will stay in hospital so that your healthcare provider can closely monitor your recovery. This can take 4-6 weeks, but times can vary. Your healthcare provider will decide when you can go home.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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Important Safety Information (continued)

What should I avoid after receiving CASGEVY™?

- Do not donate blood, organs, tissues, or cells at any time in the future

What are the possible or reasonably likely side effects of CASGEVY?

The most common side effects of CASGEVY include:

- Low levels of platelet cells, which may reduce the ability of blood to clot and may cause bleeding
- Low levels of white blood cells, which may make you more susceptible to infection

Your healthcare provider will test your blood to check for low levels of blood cells (including platelets and white blood cells). Tell your healthcare provider right away if you get any of the following symptoms:

- fever
- chills
- infections
- severe headache
- abnormal bruising
- prolonged bleeding
- bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

These are not all the possible side effects of CASGEVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of CASGEVY

Talk to your healthcare provider about any health concerns.

Please see additional **Important Safety Information** on pages 4-6 and full **Prescribing Information**, including **Patient Information**, for CASGEVY.

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The role of fetal hemoglobin in beta thalassemia

1

FETAL HEMOGLOBIN

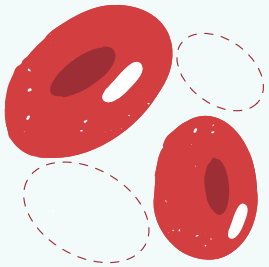
Fetal hemoglobin is a type of **hemoglobin** that carries oxygen while you're growing in the womb.

2

SHIFT TO ADULT HEMOGLOBIN

Shortly after people are born, fetal hemoglobin starts to be replaced by adult hemoglobin. ***BCL11A*** is a **gene** that tells the body to make less fetal and more adult hemoglobin.

3



BETA THALASSEMIA AND HEMOGLOBIN

For people with beta thalassemia, their bodies are not able to make enough working adult hemoglobin. They have fewer, smaller red blood cells (RBCs) that are not as good at carrying oxygen.

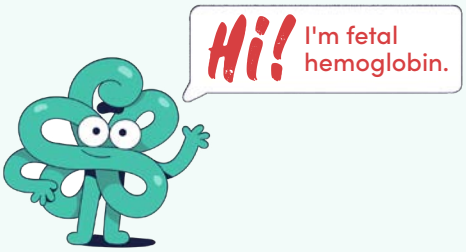
4

SYMPTOMS START

When the body makes less fetal hemoglobin, beta thalassemia symptoms tend to start.

CASGEVY™ is designed to treat TDT by increasing how much fetal hemoglobin the body makes

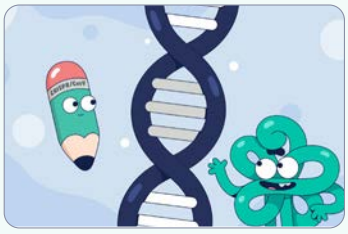
CASGEVY is a gene therapy that is made by editing the *BCL11A* gene. CASGEVY is made with your body's own blood stem cells that are collected and sent for editing.
So no donor is needed.



As you remember, *BCL11A* is a gene that tells the body to make less fetal hemoglobin and more adult hemoglobin.

CRISPR/Cas9 is a precise **gene-editing** technology. It can find and edit parts of **DNA**.

CRISPR/Cas9 is used to edit the DNA and reduce the activity of the *BCL11A* gene.



When *BCL11A* is edited, the body can make more fetal hemoglobin. This can help the body make more working RBCs.

Editing outside of the targeted gene was not observed in the modified blood stem cells of people living with TDT and healthy volunteers. The risk of editing outside of the targeted gene cannot be ruled out, due to differences in people's DNA. The impact of editing outside of the targeted gene is unknown.

Click here to learn more about how CASGEVY works.

IMPORTANT SAFETY INFORMATION (continued)

How will I receive CASGEVY?

Your healthcare provider will give you other medicines, including a conditioning medicine, as part of your treatment with CASGEVY. It's important to talk to your healthcare provider about the risks and benefits of all medicines involved in your treatment.

After receiving the conditioning medicine, it may not be possible for you to become pregnant or father a child. You should discuss options for fertility preservation with your healthcare provider before treatment.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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CASGEVY™ was studied to determine the possible benefits and risks

THE STUDY INCLUDES 52 PEOPLE WITH TDT AGED 12 TO 35 YEARS WHO RECEIVED CASGEVY

The study is open label, which means everyone who is in it knew they were receiving CASGEVY. There was no **placebo**.

PEOPLE RECEIVED CASGEVY AT DIFFERENT TIMES

AT THE TIME THE DATA WERE REVIEWED

35 people were measured for efficacy, or how well CASGEVY worked.

Safety was measured for all 52 people after CASGEVY infusion.

This study is ongoing until all people reach 24 months after receiving CASGEVY.

IMPORTANT SAFETY INFORMATION (continued)

How will I receive CASGEVY? (continued)

STEP 1: Before CASGEVY treatment, a doctor will give you mobilization medicine(s). This medicine moves blood stem cells from your bone marrow into the blood stream. The blood stem cells are then collected in a machine that separates the different blood cells (this is called apheresis). This entire process may happen more than once. Each time, it can take up to one week.

During this step, rescue cells are also collected and stored at the hospital. These are your existing blood stem cells and are kept untreated just in case there is a problem in the treatment process. If CASGEVY cannot be given after the conditioning medicine, or if the modified blood stem cells do not take hold (engraft) in the body, these rescue cells will be given back to you. If you are given rescue cells, you will not have any treatment benefit from CASGEVY.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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Transfusion independence may be possible with CASGEVY™

91.4%

32 OUT OF 35 PEOPLE

did not need a transfusion for at least 12 months in a row after receiving CASGEVY.

20.8 MONTHS

of transfusion independence were reached, measured as a median*

The 32 people who were transfusion independent for 12 months in a row stayed transfusion independent for 20.8 months, measured as a median amount.

*A median amount is the middle value of a group of numbers; half of the numbers are less than the median and half are higher.

IMPORTANT SAFETY INFORMATION (continued)

How will I receive CASGEVY? (continued)

STEP 2: After they are collected, your blood stem cells will be sent to the manufacturing site where they are used to make CASGEVY. It may take up to 6 months from the time your cells are collected to manufacture and test CASGEVY before it is sent back to your healthcare provider.

STEP 3: Shortly before your stem cell transplant, your healthcare provider will give you a conditioning medicine for a few days in hospital. This will prepare you for treatment by clearing cells from the bone marrow, so they can be replaced with the modified cells in CASGEVY.
After you are given this medicine, your blood cell levels will fall to very low levels. You will stay in the hospital for this step and remain in the hospital until after the infusion with CASGEVY.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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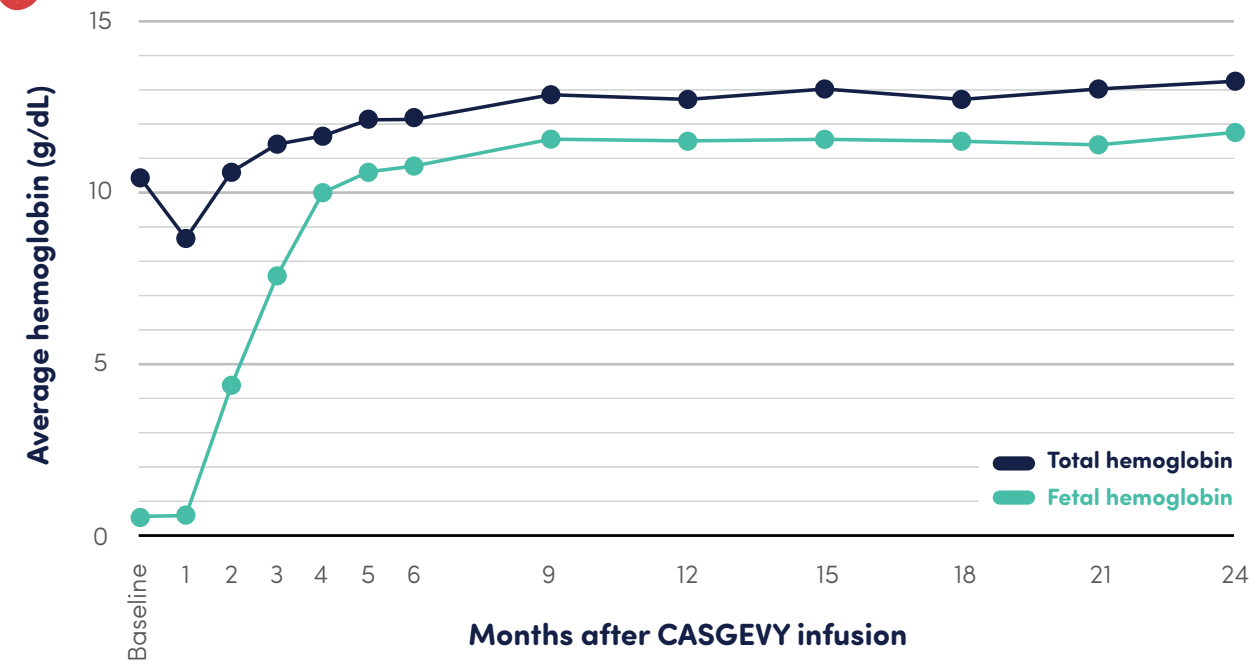
Transfusion independence may be possible with CASGEVY™ (continued)

Average total hemoglobin and fetal hemoglobin levels over time



NUMBER OF PEOPLE													
Total hemoglobin	51	52	50	47	48	45	45	44	43	38	30	24	15
Fetal hemoglobin	51	52	49	46	48	43	45	43	42	35	27	23	15

With CASGEVY, average total hemoglobin and fetal hemoglobin increased and stayed steady over time.

Data were not available for every person at each month.
The study results differed among individuals. Your experience may be different.

IMPORTANT SAFETY INFORMATION (continued)

How will I receive CASGEVY? (continued)

STEP 4: One or more vials of CASGEVY will be given into a vein (intravenous infusion) over a short period of time.

After the CASGEVY infusion, you will stay in hospital so that your healthcare provider can closely monitor your recovery. This can take 4-6 weeks, but times can vary. Your healthcare provider will decide when you can go home.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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Everyone who received CASGEVY™ in the clinical study (52 people) was monitored for safety

After treatment with CASGEVY, you will have fewer blood cells for a while until CASGEVY takes hold (engrafts) into your bone marrow. This includes low levels of platelets (cells that usually help the blood to clot) and white blood cells (cells that usually fight infections).

Your doctor will monitor this and provide treatment as required. The doctor will tell you when blood cell levels return to safe levels.

Tell your healthcare provider right away if you experience any of the following symptoms:

- fever
- chills
- infections
- severe headache
- abnormal bruising
- prolonged bleeding
- bleeding without injury such as nosebleeds; bleeding from gums; blood in your urine, stool, or vomit; or coughing up blood

The most common side effects of CASGEVY include:

- Low levels of platelet cells, which may reduce the ability of blood to clot and may cause bleeding
- Low levels of white blood cells, which may make you more susceptible to infection

Your healthcare provider will test your blood to check for low levels of blood cells (including platelets and white blood cells).

These are not all the possible side effects of CASGEVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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Everyone who received CASGEVY™ in the clinical study (52 people) was monitored for safety

After receiving the conditioning medicine, which is a form of chemotherapy, it may not be possible for you to become pregnant or father a child.

You should discuss options for fertility preservation with your healthcare provider before treatment.

You may experience side effects associated with other medicines administered as part of the treatment regimen with CASGEVY. Talk to your physician regarding those possible side effects. Your healthcare provider may give you other medicines to treat your side effects.

SAFETY CONSIDERATIONS FROM THE CLINICAL STUDY

There were no cases of **graft-versus-host disease**, graft failure, or graft rejection with CASGEVY.

The side effects were similar to what would be expected from **busulfan** myeloablative conditioning and stem cell transplant.

Please see Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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The CASGEVY™ treatment journey

Treatment with CASGEVY requires a commitment, and it's important to understand what to expect along the way.

TREATMENT OVERVIEW

There are **6 steps** in the CASGEVY treatment journey. The length and timing of certain steps may vary. Location of the steps in this brochure is based on the clinical study. **The entire CASGEVY treatment journey could take up to a year.** Your care team will explain each step in detail and help map out a treatment plan that works for you and your support network.

Your red blood cell transfusions will continue throughout the treatment journey until you have received CASGEVY as determined by your healthcare provider.

STEP 1
DECIDING ON CASGEVY

STEP 2
PREPARING FOR CELL COLLECTION

STEP 3
COLLECTING YOUR BLOOD STEM CELLS

- Location of this step determined by the healthcare provider
- Up to 7 days*
- This may need to be repeated if another collection is needed.

STEP 4
MAKING YOUR CASGEVY

- You'll be at home; CASGEVY is made in a lab
- 5-6 months

STEP 5
CHEMOTHERAPY, RECEIVING CASGEVY, AND RECOVERY

- At your ATC
- Approximately 7 weeks*
- This step includes 4 days of chemotherapy. You should expect to spend the remaining time in the hospital for monitoring and recovery after CASGEVY administration.

STEP 6
AFTER TREATMENT

CASGEVY is only given in authorized treatment centers, or ATCs. The healthcare providers at ATCs are the only ones who can confirm whether CASGEVY is right for you and can help you begin the treatment process.

Click here to learn more about the CASGEVY treatment journey and what to expect at each step.

*Timing of this step is based on the clinical study.

IMPORTANT SAFETY INFORMATION (continued)

What should I avoid after receiving CASGEVY?

- Do not donate blood, organs, tissues, or cells at any time in the future

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IMPORTANT SAFETY INFORMATION (continued)

What are the possible or reasonably likely side effects of CASGEVY?

The most common side effects of CASGEVY include:

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Your healthcare provider will test your blood to check for low levels of blood cells (including platelets and white blood cells). Tell your healthcare provider right away if you get any of the following symptoms:

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Luke, living with TDT, and his mom, Alison

People with TDT pictured may or may not have received CASGEVY.

Getting support during your journey

AN INVESTMENT NOW FOR DIFFERENT POSSIBILITIES

The entire CASGEVY™ treatment journey could take up to a year.

SCHEDULING AND PLANNING

There's a lot to keep track of during your CASGEVY journey. And there is a lot of support available to help you.

Bring a notebook or a smartphone to take notes during your conversations with your healthcare providers. This could help a great deal. So can working with someone in your support network to schedule appointments and plan your treatment.

A COMMITMENT

Your healthcare provider and support network can help you decide if this is the right time to begin the CASGEVY journey.

PREPARING FOR LONG STAYS

It can help to bring things like books, games and familiar items from home during long hospital stays.

TIME OFF FROM SCHOOL OR WORK

You may need to adjust your schedule and routine, including your time at work or school.

IMPORTANT SAFETY INFORMATION (continued)

What are the possible or reasonably likely side effects of CASGEVY? (continued)

These are not all the possible side effects of CASGEVY. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of CASGEVY

Talk to your healthcare provider about any health concerns.

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VERTEX Connects PATIENT SUPPORT™

CONNECTING YOU TO THE JOURNEY AHEAD

Vertex Connects™ is a program for people who have been prescribed a Vertex gene therapy and their loved ones.

SUPPORT IS HERE FOR YOU

From the start of your treatment journey, your Vertex Connects Care Manager will be with you. They understand the CASGEVY™ treatment process and have experience working with patients and families.

AFTER ENROLLING* IN VERTEX CONNECTS, YOUR CARE MANAGER WILL:

- Answer key questions about the treatment process and share useful guides to help you and your loved ones prepare for each step
- Connect in a way that works best for you—whether it's by email or phone
- Keep in touch with your treatment center team to help coordinate the logistics of your treatment journey
- Spend time getting to know you so they can provide meaningful support

*A completed Vertex Connects enrollment form is needed to participate in the program and determine eligibility for certain program offerings. Enrollment in Vertex Connects Patient Support is not required to receive Vertex gene therapy.

Click here to learn more about Vertex Connects.

Please see Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

Glossary

Here is a quick guide to some of the words used in this brochure.

BCL11A	A gene that controls the production of fetal hemoglobin in the body. *BCL11A* normally tells the body to make less fetal hemoglobin in early childhood.
Busulfan	A chemotherapy drug used to prepare the body to receive blood stem cell transplant. Chemotherapy is a treatment, usually given for cancer, that kills cells or stops them from reproducing.
CRISPR/Cas9	Stands for CRISPR (clustered regularly interspaced short palindromic repeats)/ CRISPR-associated protein 9. This tool allows for specific gene editing.
DNA	Stands for deoxyribonucleic acid. It is a part of a cell that carries genetic instructions for how the body works.
Fetal hemoglobin	The main type of hemoglobin found before birth in fetuses and for a few months after birth in newborns.
Gene	Sequence of DNA that tells the body how to make specific proteins.
Gene editing	The process of changing a specific sequence of DNA to change what a gene does.
Graft-versus-host disease	A condition where donated stem cells or bone marrow (the graft) see the healthy tissues in the person's body (the host) as foreign and attack them.
Placebo	An inactive pill or substance that is used in a clinical study to compare against the treatment being studied.
Hemoglobin	A protein in red blood cells that carries oxygen from the lungs to the rest of the body.
Transfusion-dependent beta thalassemia	Also known as beta thalassemia major, the most serious form of beta thalassemia. People require regular, lifelong red blood cell transfusions.

Please see Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

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Josh and Luke, living with TDT, and their parents

People with TDT pictured may or may not have received CASGEVY.

CASGEVY™ is a one-time gene therapy that may help people aged 12 years and older with transfusion-dependent beta thalassemia (TDT) live without regular blood transfusions.

Treatment involves a multi-step process that could take up to a year. This includes the collection and editing of blood stem cells to make your CASGEVY. It also includes preparing you for CASGEVY, administration of CASGEVY, and follow-up monitoring for recovery and potential side effects.

CASGEVY is made with your body's own blood stem cells. **So no donor is needed.**

IN THE CASGEVY CLINICAL STUDY:

91.4% of people (32 out of 35) did not need a transfusion for at least 12 months in a row after CASGEVY infusion.

ARE YOU iN?

Click here to visit CASGEVY.com to learn more.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about CASGEVY?

After treatment with CASGEVY, you will have fewer blood cells for a while until CASGEVY takes hold (engrafts) into your bone marrow. This includes low levels of platelets (cells that usually help the blood to clot) and white blood cells (cells that usually fight infections). Your doctor will monitor this and give you treatment as required. The doctor will tell you when blood cell levels return to safe levels.

Please see additional Important Safety Information on pages 4-6 and full Prescribing Information, including Patient Information, for CASGEVY.

VERTEX | CRISPR THERAPEUTICS

FOR THE COMMUNITY BETA THALASSEMIA WITH THE COMMUNITY

This material was created by Vertex with insight and support from the TDT community.