

# WHAT IF YOU COULD LET GO OF YOUR TRANSFUSIONS?

ZYNTEGLO® HAS THE POTENTIAL TO FREE  
PEOPLE WITH BETA-THALASSEMIA FROM  
REGULAR TRANSFUSIONS

  
**zynteglo**®  
(betibeglogene autotemcel)  
suspension for IV infusion

## WHAT IS ZYNTEGLO?

ZYNTEGLO is a one-time gene therapy to treat beta-thalassemia (also known as beta-thalassemia major or Cooley's Anemia) in patients who require regular transfusions. Beta-thalassemia is caused by a change in the beta-globin gene, which causes the body to produce reduced or no beta-globin. ZYNTEGLO is made specifically for each patient, using the patient's own blood stem cells and adds functional copies of the beta-globin gene to your cells. This may allow you to produce sufficient hemoglobin to stop receiving regular transfusions.

## IMPORTANT SAFETY INFORMATION

**What is the most important information I should know about ZYNTEGLO?**

**The most common side effects on the day of treatment with ZYNTEGLO are:** increased heart rate and abdominal pain.

**Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.**

ACTOR PORTRAYALS THROUGHOUT.



# HOW TO USE THIS RESOURCE

This resource is designed specifically for people who are living with or caring for someone who has beta-thalassemia and is receiving regular red blood cell transfusions **(which we will refer to as just "transfusions" throughout this resource)**, and are interested in learning about ZYNTEGLO. ZYNTEGLO is for people who have beta-thalassemia and require regular transfusions.

The information presented here can help you think about your needs, concerns, and treatment goals, preparing you to talk to your doctor when considering ZYNTEGLO.

Clinical data reflects information about ZYNTEGLO as of March 2021.

This resource is not intended to make a diagnosis or treatment recommendation or provide medical advice. You should discuss any questions with your healthcare team.



Throughout this resource, there are words that may be new to you, which are underlined at first mention. You can find definitions of these words in the glossary on page 36.

## CAREGIVER PERSPECTIVES



*The majority of this resource is written for people living with beta-thalassemia, but throughout, you will see insights for people who care for those living with beta-thalassemia.*

*These insights are in the purple boxes labeled **"caregiver perspectives."***

## IMPORTANT SAFETY INFORMATION (cont'd)

### What is the most important information I should know about ZYNTEGLO? (cont'd)

**The most common side effects of ZYNTEGLO following treatment for up to 6 months are:** low level of platelets (which may reduce the ability of blood to clot and may cause bleeding), low level of white blood cells (which may make you more susceptible to infection), and pain in arms or legs.

Call your healthcare provider right away if you have new or unusual bleeding which may include any of these signs or symptoms: severe headache, abnormal bruising, nose bleed, blood in your urine, stool, or vomit, coughing up blood, or unusual stomach or back pain.

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## IMPORTANT SAFETY INFORMATION (cont'd)

### What is the most important information I should know about ZYNTEGLO? (cont'd)

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

It is important for you to be monitored at least yearly for at least 15 years for any changes to your blood. There is a potential risk of blood cancer associated with this treatment; however, no cases have been seen in studies of ZYNTEGLO. If you are diagnosed with a cancer, have your treating physician contact bluebird bio at 1-833-999-6378.

**Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.**

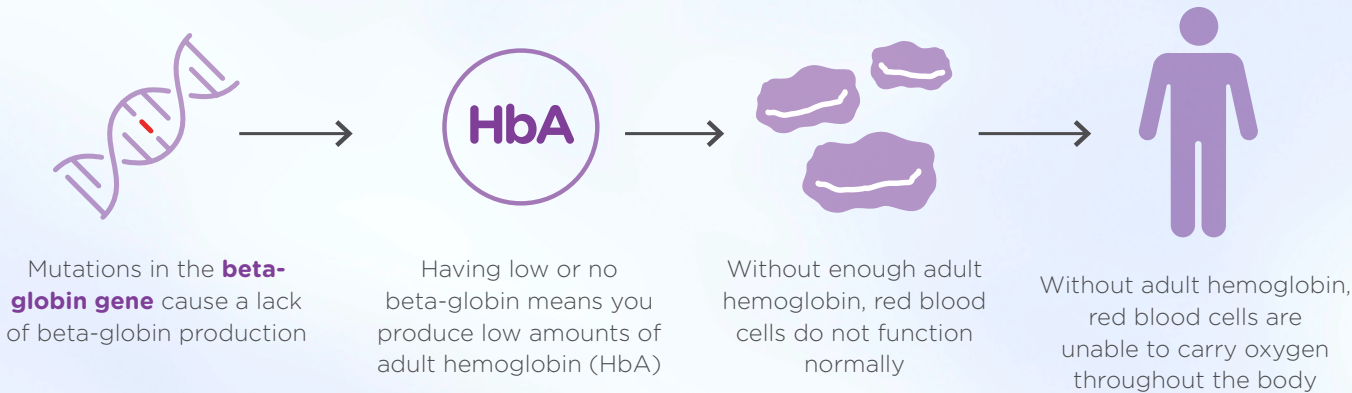


# THE GENETICS BEHIND BETA-THALASSEMIA

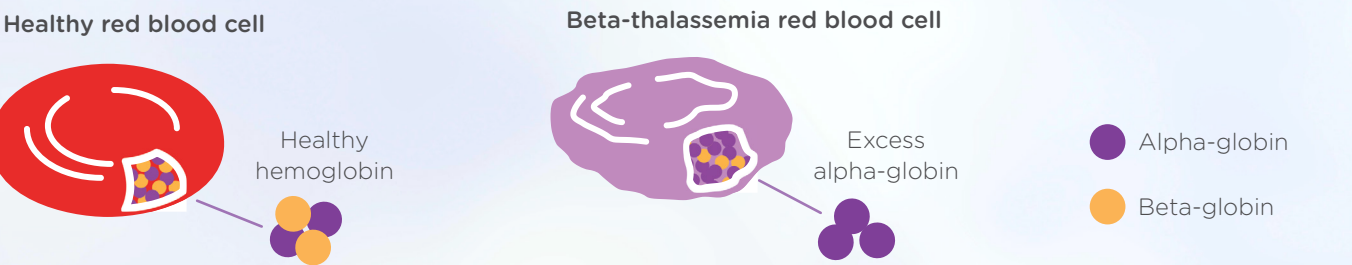
## WHAT IS BETA-THALASSEMIA?

Beta-thalassemia is a genetic disease that's caused by a change (or mutation) in the beta-globin gene. This mutation means your body cannot make enough of the beta-globin protein, which is a part of hemoglobin.

Having low or no beta-globin means you produce low amounts of adult hemoglobin.  
Not having enough hemoglobin in your red blood cells is why you might depend on transfusions.



## THE NEED FOR INCREASING ADULT HEMOGLOBIN



Red blood cells will have a shorter life span without hemoglobin, and will carry less oxygen throughout the body causing anemia.

If you're not able to produce sufficient hemoglobin, you may need regular transfusions.

**Regular transfusions address the symptoms of beta-thalassemia, but do not treat it at the genetic level.**

## THE SWITCH FROM FETAL HEMOGLOBIN TO ADULT HEMOGLOBIN

You may have previously heard of fetal hemoglobin. This is a type of hemoglobin that makes up most of the total hemoglobin while a body is developing as a fetus. Shortly after birth, your body will naturally switch to producing mostly (over 90%) adult hemoglobin as a part of typical normal development.

## CAREGIVER PERSPECTIVES



If you have a child or loved one with beta-thalassemia who requires regular transfusions, have you talked to them about their goals for the future? By encouraging an open dialogue with questions, such as the ones below, you can learn more about how they feel their disease plays a role in their plans.

- **How does beta-thalassemia affect you?**
- **Can you describe a good day and a bad day with beta-thalassemia?**
- **What are your goals for managing your beta-thalassemia?**





# WHAT IS ZYNTEGLO?

## ZYNTEGLO IS A ONE-TIME TREATMENT THAT ADDRESSES BETA-THALASSEMIA AT THE GENETIC LEVEL

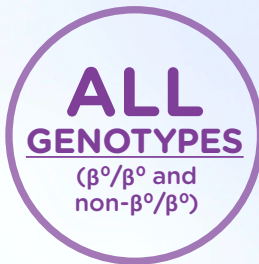
ZYNTEGLO is a gene therapy that uses gene addition to help your body produce functional adult hemoglobin, potentially eliminating the need for regular transfusions.

Specifically made for each person, ZYNTEGLO uses a person’s own blood stem cells and adds working copies of the beta-globin gene (needed to create functional adult hemoglobin) to the person’s cells. This may allow the person to produce sufficient hemoglobin.

Learn more about how ZYNTEGLO works on pages 8–9.

### WHO IS ZYNTEGLO FOR?

ZYNTEGLO is a one-time gene therapy to treat beta-thalassemia in adult and pediatric patients who require regular red blood cell (RBC) transfusions.



- **β°/β°:** no beta-globin is produced
- **Non-β°/β°:** a reduced amount of beta-globin is produced

The safety and efficacy of ZYNTEGLO was studied in clinical trials that enrolled patients between the ages of 4 and 34 years old.



You do not need a donor match for ZYNTEGLO since it uses your own cells.

### IMPORTANT SAFETY INFORMATION (cont’d)

#### How will I get ZYNTEGLO?

Your healthcare providers will give you other medicines, including chemotherapy medicine, as part of your treatment with ZYNTEGLO. It’s important to talk to your healthcare provider about the risks and benefits of all medicines involved in your treatment.

After receiving the chemotherapy it may not be possible for you to become pregnant or father a child. You should consider discussing options for fertility preservation with your doctor before treatment.

### WHERE WILL I RECEIVE ZYNTEGLO?

You will receive ZYNTEGLO at a select specialized hospital called a Qualified Treatment Center (QTC).

Each ZYNTEGLO QTC has been carefully selected based on their expertise in areas such as transplant, cell, and gene therapy and are trained to administer ZYNTEGLO.

Learn more about the ZYNTEGLO treatment process on pages 16–21.

### HOW TO LOCATE A QTC?

As we mentioned above, you will receive ZYNTEGLO at a QTC. These specialized hospitals are located throughout the country. As you and your doctor discuss ZYNTEGLO, **my bluebird support** is here to help you determine which QTC may be right for you.\*

Learn more about **my bluebird support** on pages 34–35.

\*ZYNTEGLO will be available at a limited number of QTCs. **my bluebird support** can help locate QTCs that are in network with your insurance provider.



### TALK TO YOUR DOCTOR ABOUT ZYNTEGLO

Your doctor and care team can help determine whether ZYNTEGLO may be an appropriate treatment option for you.

### IMPORTANT SAFETY INFORMATION (cont’d)

#### How will I get ZYNTEGLO? (cont’d)

**STEP 1:** ZYNTEGLO is made specifically for you from your own blood stem cells. Your healthcare provider will collect your blood stem cells through a process called mobilization and apheresis. This process takes approximately one week and may need to be repeated.

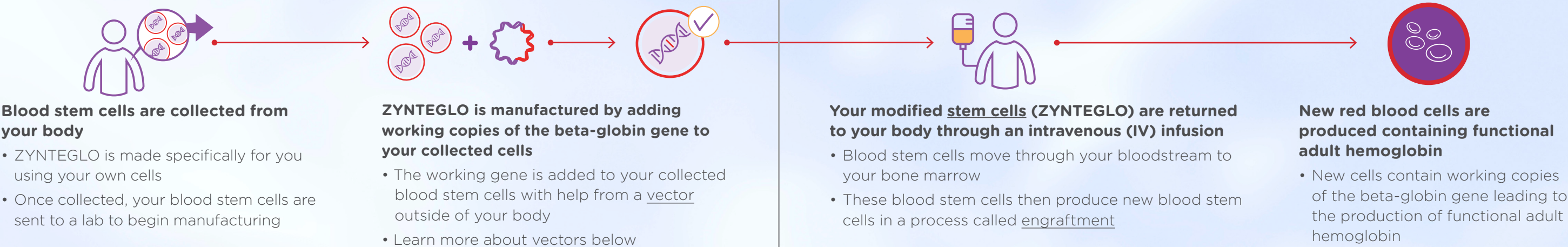
‘Back-up’ stem cells (or ‘rescue cells’) are also collected and stored at the hospital. This is a precaution in case there is a problem in the treatment process. If this happens, your back-up stem cells will be given back to you. If you receive back-up cells, you will have no benefit from ZYNTEGLO.

Please see **Important Safety Information** on pages 22–23 and full **Prescribing Information**, including **Patient Information**.

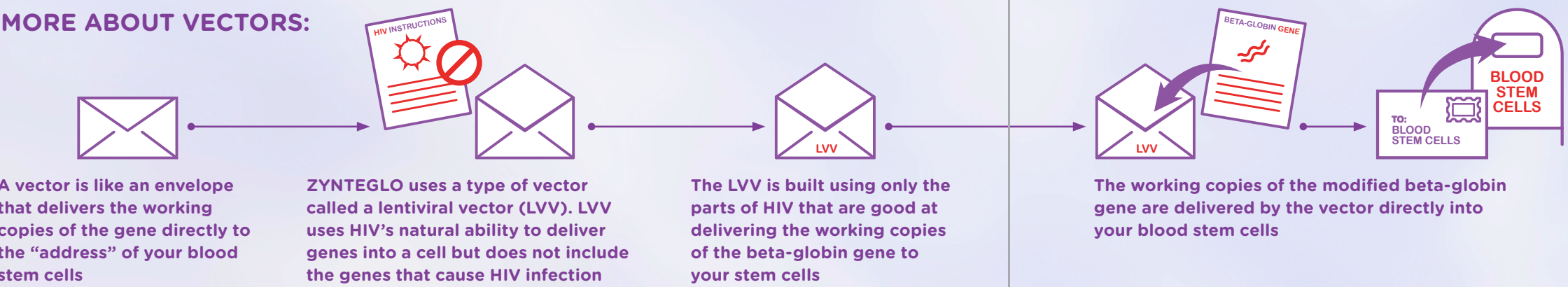


# HOW ZYNTEGLO ADDRESSES BETA-THALASSEMIA AT THE GENETIC LEVEL

## LEARN HOW ZYNTEGLO, A ONE-TIME GENE THERAPY, USES YOUR OWN BLOOD STEM CELLS TO TREAT BETA-THALASSEMIA



### MORE ABOUT VECTORS:



You can learn more about the ZYNTEGLO treatment process on pages 16-21.

**IMPORTANT CONSIDERATIONS**

Although ZYNTEGLO will not give you HIV infection, treatment with ZYNTEGLO may cause a false-positive HIV test result by some commercial tests. If you need to have an HIV test, talk with your doctor about the appropriate test to use.

HIV = human immunodeficiency virus.

### IMPORTANT SAFETY INFORMATION (cont’d)

#### How will I get ZYNTEGLO? (cont’d)

**STEP 2:** Your blood stem cells will be sent to a manufacturing site where they are used to make ZYNTEGLO. It takes approximately 70-90 days from the time your cells are collected to manufacture and test ZYNTEGLO before it is shipped to your healthcare provider, but the time may vary.

**STEP 3:** Before you receive ZYNTEGLO, your healthcare provider will give you chemotherapy for a few days to make room in the bone marrow. You will be admitted to the hospital for this step and remain in the hospital until after ZYNTEGLO infusion.

### IMPORTANT SAFETY INFORMATION (cont’d)

#### How will I get ZYNTEGLO? (cont’d)

**STEP 4:** ZYNTEGLO is given by an intravenous infusion. You may receive more than one bag of ZYNTEGLO. Each bag is infused in 30 minutes or less.

**Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.**



# ZYNTEGLO WAS STUDIED IN 41 PATIENTS

## EFFICACY AND SAFETY OF ZYNTEGLO STUDIED IN 2 CLINICAL TRIALS

### PURPOSE OF ZYNTEGLO CLINICAL TRIALS

- All studies of ZYNTEGLO were open label, meaning that study participants and their doctors knew they were receiving ZYNTEGLO
- Each study ran for an initial 24-month period to assess transfusion independence

### DESCRIPTION OF THE DIFFERENT CLINICAL TRIALS

STUDY	NAME	DESCRIPTION
Phase 3	STUDY 1 and STUDY 2	Clinical studies used to test efficacy and safety for FDA approval Studies are considered ONGOING as of March 2021
Long-term follow-up	LTF-303	After completing any of these 24-month studies, people could enroll into an ongoing follow-up study for an additional 13 years (15 years total)

All of the clinical trials were designed to measure:

**Transfusion independence**

- The weighted average hemoglobin greater than or equal to 9 g/dL without any blood transfusions for a continuous period greater than or equal to 12 months

**Hb**

- Specifically measured total hemoglobin (Hb) and ZYNTEGLO-derived adult hemoglobin

**Iron**

- Iron reduction (lowering of the amount of iron in the body)

**Safety**

- Evaluate adverse effects that occur

## IMPORTANT SAFETY INFORMATION (cont'd)

### How will I get ZYNTEGLO? (cont'd)

After ZYNTEGLO infusion, you will stay in the hospital for approximately 3-6 weeks so that your healthcare team can closely monitor your recovery. Your healthcare provider will determine when you can go home.

### What should I avoid after receiving ZYNTEGLO?

- Do not donate blood, organs, tissues or cells.

## CLINICAL TRIAL PATIENTS CONTINUE TO BE FOLLOWED LONG TERM, WITH 7 PATIENTS WHO HAVE COMPLETED THEIR 3.5-YEAR FOLLOW-UP VISIT

Those eligible for clinical trials were people with beta-thalassemia (also known as beta-thalassemia major or Cooley's Anemia) requiring regular transfusions categorized as either:

In the 2 years before entering the trial:

- At least 100 mL/kg/year of red blood cells, or
- Eight or more regular transfusions per year

PHASE 3: ONGOING (AS OF MARCH 2021)						
STUDY	TOTAL NUMBER OF PARTICIPANTS	GENOTYPE (See page 6 for more information)	AGE (YEARS)	PRIMARY OUTCOME	ENROLLED IN FOLLOW-UP STUDY	MEDIAN FOLLOW-UP TIME (LTF-303)
STUDY 1	23 (Total) 14 pediatrics 9 adults	23 non-β <sup>0</sup> /β <sup>0</sup>	4 to 34 14 pediatrics 9 adults	Transfusion Independence	19/23 patients*	29.5 months (min, max: 13.0, 48.2)
STUDY 2	18 (Total) 13 pediatrics 5 adults	6 non-β <sup>0</sup> /β <sup>0+</sup> 12 β <sup>0</sup> /β <sup>0</sup>	4 to 33 3 pediatrics 5 adults	Transfusion Independence	10/18 patients*	24.6 months (min, max: 4.1, 35.5)

\*Remaining patients are still in the process of completing their initial clinical trial before they have the option to continue in the follow-up study.

†Non-β<sup>0</sup>/β<sup>0</sup> patients in STUDY 2 included severe genotypes similar to β<sup>0</sup>/β<sup>0</sup>.

### CHARACTERISTICS OF ALL STUDY PARTICIPANTS (N=41)

**GENDER**

49% female 51% male

**LOCATION and ETHNICITY**

44% White/Caucasian 49% Asian

- France
- Germany
- Greece
- Italy
- Thailand
- UK
- US

## IMPORTANT SAFETY INFORMATION (cont'd)

### What are additional possible or reasonably likely side effects of ZYNTEGLO?

ZYNTEGLO will not give you human immunodeficiency virus (HIV) infection. Treatment with ZYNTEGLO may cause a false-positive HIV test result by some commercial tests. If you need a HIV test, talk with your healthcare provider about the appropriate test to use.

Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.



IN TWO PHASE 3 STUDIES  
ABOUT 9 OUT OF 10 (89%) PATIENTS TREATED  
WITH ZYNTEGLO STOPPED TRANSFUSIONS†

THE MAJORITY OF PATIENTS ACHIEVED TRANSFUSION INDEPENDENCE (89%; 32/36 PATIENTS) AND HAD A NORMAL OR NEAR-NORMAL MEDIAN TOTAL HEMOGLOBIN OF 11.5 g/dL\*†



TI: transfusion independence†

The majority of patients treated with ZYNTEGLO achieved transfusion independence  
• 32 of 36 people (88.9%) achieved transfusion independence



STUDY 2 represents patients with severe genotypes, including β<sup>0</sup>/β<sup>0</sup> and non-β<sup>0</sup>/β<sup>0</sup> patients with IVS-I-110 genotypes (similar to β<sup>0</sup>/β<sup>0</sup>)



median total hemoglobin level

Patients who achieved transfusion independence (32/36) had a normal or near-normal median total hemoglobin level driven by ZYNTEGLO-derived adult hemoglobin



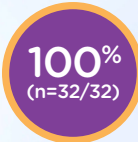
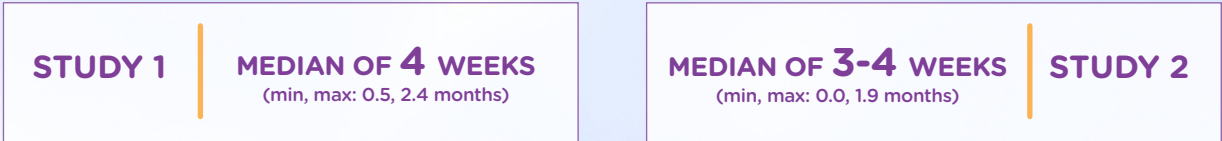
Total hemoglobin levels presented on this page reflect weighted average total hemoglobin during transfusion independence, which is defined as the average across hemoglobin levels taken at each patient visit during the clinical study, factoring in a weighting based on the time duration between study visits

**Results shown are from TI evaluable patients only**  
Results shown are for the 36 out of 41 patients currently evaluable in STUDY 1 and STUDY 2. Patients are evaluable if they have completed 24 months of follow-up in the phase 3 study, or achieved transfusion independence, or won't achieve transfusion independence in the phase 3 study.

\*Normal Hb ranges for healthy individuals from the American College of Clinical Pharmacy:  
• 2-9 years: 11.5-14.5 g/dL  
• Males 10-17 years: 12.5-16.1 g/dL  
• Females 10-17 years: 12-15 g/dL  
• Male adults (≥18 years): 13.5-18 g/dL  
• Female adults (≥18 years): 12.5-16 g/dL

†**Transfusion independence** meant that patients achieved a weighted average hemoglobin of ≥9 g/dL without any transfusions for a continuous period of ≥12 months at any time during the study after infusion of ZYNTEGLO.

The patients who achieved transfusion independence had their last transfusion prior to achieving transfusion independence at a median time of about 4 weeks post ZYNTEGLO infusion.



of patients who achieved transfusion independence maintained it with a min, max duration of ongoing transfusion independence of 12.5+ to 39.4+ months. Median duration of transfusion independence was not reached.

No differences in efficacy or clinical safety were observed between **pediatrics†** and adults  
Engraftment times were longer in pediatric patients but not associated with increases in infections or bleeding events

†Pediatric is defined as people under the age of 18

**IMPORTANT SAFETY INFORMATION (cont'd)**  
**What are additional possible or reasonably likely side effects of ZYNTEGLO? (cont'd)**  
These are not all the possible side effects of ZYNTEGLO. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.  
**Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.**





# THE MAJORITY OF PATIENTS WHO ACHIEVED TRANSFUSION INDEPENDENCE WERE NOT RECEIVING CHELATION AS OF LAST FOLLOW-UP

## RESULTS FROM PHASE 3 CLINICAL TRIALS

PATIENTS WHO ACHIEVED TRANSFUSION INDEPENDENCE	STUDY 1 20 patients with non-β <sup>o</sup> /β <sup>o</sup>	STUDY 2 12 patients with β <sup>o</sup> /β <sup>o</sup> and non-β <sup>o</sup> /β <sup>o</sup>
Were not receiving <u>chelation</u> at last follow-up	65% (13/20 patients)	58% (7/12 patients)
Of those who were not on chelation at last follow-up	Did not restart chelation 69% (9/13 patients)	43% (3/7 patients)
	Restarted then stopped chelation 31% (4/13 patients)	57% (4/7 patients)
Received <u>phlebotomy</u> (a method for blood removal) to remove iron	35% (7/20 patients)	8% (1/12 patients)

Iron removal therapy was managed at a doctor’s discretion. Restarting iron chelation after ZYNTEGLO may be necessary.



### CAREGIVER PERSPECTIVES

Understanding the ZYNTEGLO study results can help you and the doctor decide if this treatment may be right for your child or loved one. If you would like more information, their doctor can help.

## IMPORTANT SAFETY INFORMATION (cont’d)

### General Information

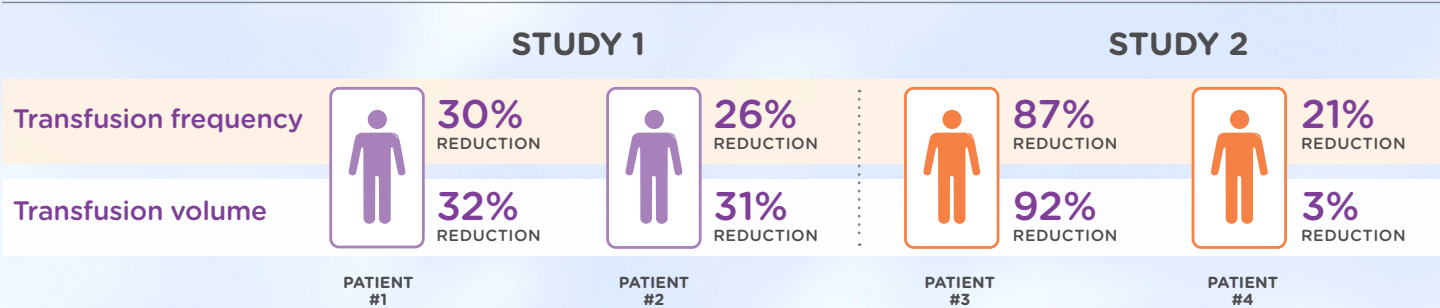
It is important that you have regular check-ups with your healthcare provider, including at least annual blood tests, to detect any adverse effects and to confirm that ZYNTEGLO is still working. Talk to your healthcare provider about any concerns.

# PATIENTS UNABLE TO ACHIEVE TRANSFUSION INDEPENDENCE STILL REDUCED TRANSFUSIONS

In the phase 3 trials, **4 out of 36 patients** who were evaluated for transfusion independence didn’t achieve it, but were able to:

- Reduce red blood cell transfusion frequency
- Reduce red blood cell transfusion volume

## RESULTS FROM PHASE 3 CLINICAL TRIALS



Reductions observed in phase 3 clinical trials from 6 months post-ZYNTEGLO infusion to the patient’s last follow-up visit when compared with their pre-enrollment transfusion requirements.

Some questions you may ask them include:

- How do I know if ZYNTEGLO may be right for them?
- After ZYNTEGLO, will my child still need chelation therapy?

## IMPORTANT SAFETY INFORMATION

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

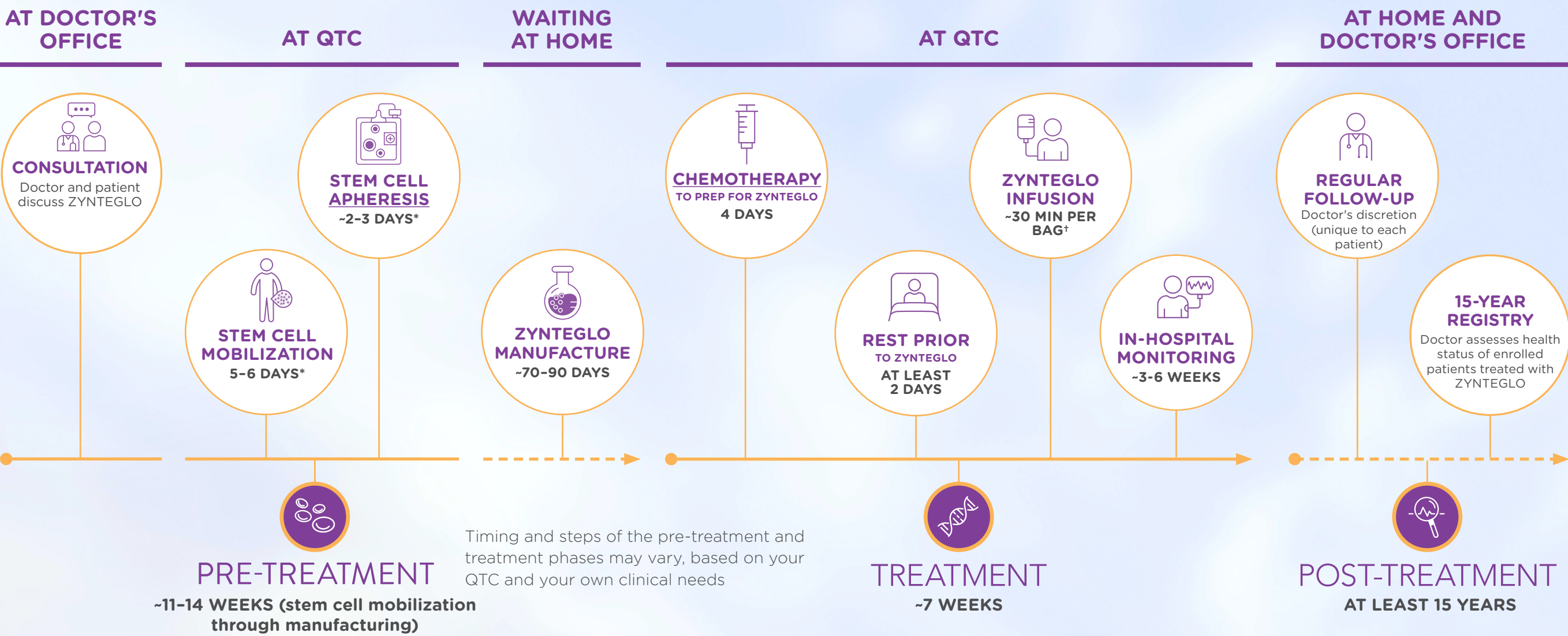
The most common side effects on the day of treatment with ZYNTEGLO are: increased heart rate and abdominal pain.

Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.



# TREATMENT JOURNEY WITH ZYNTEGLO

Here's an overview of what treatment pathway with ZYNTEGLO could look like. It's important to keep in mind that these time frames are meant as **an approximate guideline**. Your journey may look different depending on your circumstances unique to you and your care team at the QTC.



\*These steps may need to be repeated in order to collect enough blood stem cells. Apheresis can start on Day 5.  
†ZYNTEGLO is supplied in up to 4 bags. Number of bags vary by patient.

## IMPORTANT SAFETY INFORMATION (cont'd)

### What is the most important information I should know about ZYNTEGLO? (cont'd)

**The most common side effects of ZYNTEGLO following treatment for up to 6 months are:** low level of platelets (which may reduce the ability of blood to clot and may cause bleeding), low level of white blood cells (which may make you more susceptible to infection), and pain in arms or legs.

## IMPORTANT SAFETY INFORMATION (cont'd)

### What is the most important information I should know about ZYNTEGLO? (cont'd)

Call your healthcare provider right away if you have new or unusual bleeding which may include any of these signs or symptoms: severe headache, abnormal bruising, nose bleed, blood in your urine, stool, or vomit, coughing up blood, or unusual stomach or back pain.

Please see [Important Safety Information](#) on pages 22-23 and full [Prescribing Information](#), including [Patient Information](#).





# PRE-TREATMENT

## CELL COLLECTION

-1 WEEK

- Mobilization takes place over 5-6 days. Apheresis, or cell collection, is done on day 5 and day 6 (day 6 as needed)
- To begin, you go through mobilization, which is where you receive a medication that moves your stem cells into your blood stream
- Once your blood stem cells are in your bloodstream, they will need to be separated from the rest of your blood before being collected
- Collection of your stem cells is called apheresis, a process that uses a machine to collect your blood stem cells and return the rest of your blood to your body; this mobilization and apheresis may be repeated to ensure enough cells are collected
  - Back-up "rescue" cells are collected in case stem cells or ZYNTEGLO is compromised or there's engraftment issues. If engraftment issues occur, your rescue cells will be given back to you, which means you will have no benefit from ZYNTEGLO

Helping to set expectations for the treatment journey can help your child or loved one feel more prepared about starting ZYNTEGLO. While you may be excited about the potential benefits, you may both have some fears or anxiety about side effects and different parts of the journey. Speak to your doctor so that you and your loved one have all the information you need to feel prepared.

## IMPORTANT SAFETY INFORMATION (cont'd)

### What is the most important information I should know about ZYNTEGLO? (cont'd)

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

## MANUFACTURING

-70-90 DAYS, WAITING AT HOME

- Once collected, your blood stem cells are sent to a manufacturing site where all your collected cells are used to make ZYNTEGLO. This process takes about 70-90 days, but the time may vary

### LOOKING FOR A QTC?

Contact [my bluebird support](#) at **1-833-888-NEST (6378)** or visit [zynteglo.com/treatment-center-locator](https://zynteglo.com/treatment-center-locator) to find the QTC options you can discuss with your doctor.

It's important to keep in mind that these time frames are meant as **an approximate guideline**. Your journey may look different depending on circumstances unique to you and your care team at the QTC.



# TREATMENT

## CHEMOTHERAPY

4 DAYS MINIMUM WITH AT LEAST 2 REST DAYS

- At least 6 days before you receive ZYNTEGLO, you will be admitted into the QTC
- Once you are admitted to the QTC, you undergo a 4-day course of conditioning with chemotherapy, which is used to clear out the cells in your bone marrow to make room for ZYNTEGLO cells
- After chemotherapy, you need at least 2 days of rest at the QTC before you receive ZYNTEGLO
- Please note that following chemotherapy, it may not be possible for you to become pregnant or conceive a child. You may wish to consider discussing options for fertility preservation with your doctor before deciding to proceed with ZYNTEGLO

## ZYNTEGLO INFUSION AND RECOVERY

-3-6 WEEKS

- Once your doctor determines that your body is ready, you receive ZYNTEGLO through an IV infusion for ~30 minutes per bag
  - ZYNTEGLO is supplied in up to 4 bags. Number of bags vary by patient
- You stay in the QTC after receiving ZYNTEGLO for about 3 to 6 weeks so that your doctors can monitor your recovery; during this time, your doctors will be:
  - Monitoring your immune system as it recovers
  - Checking that ZYNTEGLO is moving through your bone marrow and begins to multiply and develop into healthy new blood cells (engraftment)
  - Observe neutrophil (white blood cell) and platelet levels
  - Address any side effects that you may experience
- Engraftment may be delayed or may not occur after treatment with ZYNTEGLO

Talk to your healthcare provider about side effects that may occur with mobilization, apheresis, and chemotherapy. It's important to talk to your healthcare provider about the risks and benefits of all medicines involved in your treatment.

## IMPORTANT SAFETY INFORMATION (cont'd)

### What is the most important information I should know about ZYNTEGLO? (cont'd)

It is important for you to be monitored at least yearly for at least 15 years for any changes to your blood. There is a potential risk of blood cancer associated with this treatment; however, no cases have been seen in studies of ZYNTEGLO. If you are diagnosed with a cancer, have your treating physician contact bluebird bio at 1-833-999-6378.

Please see [Important Safety Information](#) on pages 22-23 and full [Prescribing Information](#), including [Patient Information](#).





## POST-TREATMENT

### FOLLOW-UP CARE

- Following your treatment with ZYNTÉGLO, make sure to work with your QTC team, along with your regular healthcare provider to establish a long-term follow-up plan and monitoring
- The QTC may require you to return for follow-up care at their center within a certain period of time
- It is important that you have regular check-ups with your healthcare provider, including at least annual blood tests, to detect any adverse effects and to confirm that ZYNTÉGLO is still working
- Treatment with ZYNTÉGLO may cause a false-positive human immunodeficiency virus (HIV) test result by some commercial tests. If you need to have an HIV test, talk with your HCP about the appropriate test to use
- It is important for you to be monitored at least yearly for at least 15 years for any changes to your blood. There is a potential risk of blood cancer associated with this treatment. However, no cases have been seen in studies of ZYNTÉGLO. If you are diagnosed with a cancer, have your treating physician contact bluebird bio at 1-833-999-NEST (6378)

### REGISTRY PARTICIPATION

- In addition, your QTC team will offer you participation in a 15-year registry study. The US FDA recommends long-term follow-up for patients treated with gene therapy
- The ZYNTÉGLO registry is a study that collects health outcome data over time about long-term safety and effectiveness with ZYNTÉGLO
- Your participation in the registry is voluntary. Ongoing research for gene therapy, like the registry study, may benefit future patients who may consider treatment with ZYNTÉGLO and contributes to understanding of the effects of ZYNTÉGLO
- To learn more, speak with your primary doctor at a QTC

## POTENTIAL FREEDOM FROM REGULAR TRANSFUSIONS



### What is ZYNTÉGLO?

ZYNTÉGLO is a one-time gene therapy to treat beta-thalassemia (also known as beta-thalassemia major or Cooley's Anemia) in patients who require regular transfusions. Beta-thalassemia is caused by a change in the beta-globin gene, which causes the body to produce reduced or no beta-globin. ZYNTÉGLO is made specifically for each patient, using the patient's own blood stem cells and adds functional copies of the beta-globin gene to your cells. This may allow you to produce sufficient hemoglobin to stop receiving regular transfusions.

**Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.**



# IMPORTANT SAFETY INFORMATION

## What is the most important information I should know about ZYNTEGLO?

### The most common side effects of ZYNTEGLO are:

- On the day of treatment with ZYNTEGLO
  - Increased heart rate
  - Abdominal pain
- Following treatment for up to 6 months
  - Low level of platelets, which may reduce the ability of blood to clot and may cause bleeding
  - Low level of white blood cells, which may make you more susceptible to infection
  - Pain in arms or legs

Call your healthcare provider right away if you have new or unusual bleeding which may include any of these signs or symptoms:

- Severe headache
- Abnormal bruising
- Nose bleed
- Blood in your urine, stool, or vomit
- Coughing up blood
- Unusual stomach or back pain

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

It is important for you to be monitored at least yearly for at least 15 years for any changes to your blood. There is a potential risk of blood cancer associated with this treatment; however, no cases have been seen in studies of ZYNTEGLO. If you are diagnosed with a cancer, have your treating physician contact bluebird bio at 1-833-999-6378.

### How will I get ZYNTEGLO?

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

After receiving the chemotherapy it may not be possible for you to become pregnant or father a child. You should consider discussing options for fertility preservation with your doctor before treatment.

**STEP 1:** ZYNTEGLO is made specifically for you from your own blood stem cells. Your healthcare provider will collect your blood stem cells through a process called mobilization and apheresis. This process takes approximately one week and may need to be repeated.

'Back-up' stem cells (or 'rescue cells') are also collected and stored at the hospital. This is a precaution in case there is a problem in the treatment process. If this happens, your back-up stem cells will be given back to you. If you receive back-up cells, you will have no benefit from ZYNTEGLO.

**STEP 2:** Your blood stem cells will be sent to a manufacturing site where they are used to make ZYNTEGLO. It takes approximately 70-90 days from the time your cells are collected to manufacture and test ZYNTEGLO before it is shipped to your healthcare provider, but the time may vary.

**STEP 3:** Before you receive ZYNTEGLO, your healthcare provider will give you chemotherapy for a few days to make room in the bone marrow. You will be admitted to the hospital for this step and remain in the hospital until after ZYNTEGLO infusion.

**STEP 4:** ZYNTEGLO is given by an intravenous infusion. You may receive more than one bag of ZYNTEGLO. Each bag is infused in 30 minutes or less.

After ZYNTEGLO infusion, you will stay in the hospital for approximately 3-6 weeks so that your healthcare team can closely monitor your recovery. Your healthcare provider will determine when you can go home.

## What should I avoid after receiving ZYNTEGLO?

- Do not donate blood, organs, tissues or cells.

## What are additional possible or reasonably likely side effects of ZYNTEGLO?

ZYNTEGLO will not give you human immunodeficiency virus (HIV) infection. Treatment with ZYNTEGLO may cause a false-positive HIV test result by some commercial tests. If you need a HIV test, talk with your healthcare provider about the appropriate test to use.

These are not all the possible side effects of ZYNTEGLO. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

## General Information

It is important that you have regular check-ups with your healthcare provider, including at least annual blood tests, to detect any adverse effects and to confirm that ZYNTEGLO is still working. Talk to your healthcare provider about any concerns.

Please see full [Prescribing Information](#), including [Patient Information](#).



# WHAT OTHER INFORMATION SHOULD I KNOW WITH ZYNTEGLO?

## ADDITIONAL INFORMATION

- As of March 2021, all patients treated with ZYNTEGLO in clinical trials remain alive at last follow-up
- It is important for you to be monitored at least yearly for at least 15 years for any changes to your blood. There is a potential risk of blood cancer associated with this treatment. However, no cases have been seen in studies of ZYNTEGLO. If you are diagnosed with a cancer, have your treating physician contact bluebird bio at 1-833-999-NEST (6378)
- Although ZYNTEGLO will not give you human immunodeficiency virus (HIV) infection, treatment with ZYNTEGLO may cause a false-positive HIV test result by some commercial tests. If you need to have an HIV test, talk with your doctor about the appropriate test to use.

**Clinical trial patients in the long-term follow-up study and patients who enroll in the registry will be followed for a total of 15 years after receiving ZYNTEGLO.**

- As of March 2021, all of the patients who completed a 2-year clinical trial of ZYNTEGLO have enrolled in the long-term study, allowing them to be assessed for safety and treatment effects for an additional 13 years
- Other people who are treated with ZYNTEGLO will be encouraged to enroll in a registry to evaluate safety and treatment effects for 15 years

Safety is important to think about, so it will help to have an open conversation with your doctor about the side effects that you could experience with ZYNTEGLO. You may want to ask about potential side effects related to specific parts of treatment (example: chemotherapy). This discussion could help you consider the benefits and risks of ZYNTEGLO. You may also ask about the post-treatment monitoring period and what may happen during that time.

## CAREGIVER PERSPECTIVES



Safety information is important for your child or loved one to know. If they understand that there may be times when they experience side effects during treatment with ZYNTEGLO, they can be better prepared along the way. For you, knowing what to expect during treatment can help you decide if ZYNTEGLO may be right for your loved one.

## GENERAL INFORMATION ABOUT THE SAFE AND EFFECTIVE USE OF ZYNTEGLO

- It is important that you have regular check-ups with your healthcare provider, including at least annual blood tests, to detect any adverse effects and to confirm that ZYNTEGLO is still working
- Talk to your healthcare provider about any concerns

For more information, go to [ZYNTEGLO.com](https://www.zynteglo.com) or call **1-833-888-NEST (6378)**.

Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.





## WHO SHOULD I TALK TO ABOUT ZYNTEGLO?

Before you begin treatment, you and your doctor will work together to discuss whether ZYNTEGLO is right for you.

ZYNTEGLO is only available at select specialized hospitals called QTCs. Each ZYNTEGLO QTC has been carefully selected based on their expertise in areas such as transplant, cell, and gene therapy and is trained to administer ZYNTEGLO. Your hematologist will work with them to coordinate your care.

As you and your doctor discuss ZYNTEGLO, **my bluebird support** is here to help you determine which QTC may be right for you.\*

### CONNECT WITH **my bluebird support**



In addition to talking to your healthcare provider team, our patient services program, **my bluebird support**, can help you along on your ZYNTEGLO treatment journey, including locating a QTC that may be right for you.\*

For more information on how **my bluebird support** can help you, go to page 34.

\*ZYNTEGLO will be available at a limited number of QTCs. **my bluebird support** can help locate QTCs that are in network with your insurance provider.

Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.



# CONNECTING WITH A QTC



Deciding to move forward with ZYNTEGLO is a big decision. So it's important to make sure you have asked your doctor all of your questions and gathered all the information you need to start your ZYNTEGLO journey with confidence.

It may be helpful to have a list of questions ready when you connect with your doctor and the QTC. Your list may include:

- Where will I need to go for my treatment with ZYNTEGLO?
- Who will be the doctor and care team overseeing my ZYNTEGLO treatment?
- What are the potential side effects I could experience during treatment?
- What kind of support does the QTC for ZYNTEGLO provide? What about for my family?
- Can you explain the ZYNTEGLO treatment timeline to me? How long does treatment take?



For a worksheet on preparing for conversations with your doctor, see page 32 of this resource.

## IMPORTANT SAFETY INFORMATION

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

The most common side effects on the day of treatment with ZYNTEGLO are: increased heart rate and abdominal pain.

Please see [Important Safety Information](#) on pages 22-23 and full [Prescribing Information](#), including [Patient Information](#).





# QUESTIONS FOR YOUR DOCTOR

Throughout this resource, we have included questions to think about asking your doctor as you are talking through the possibility of treatment with ZYNTEGLO. Here, we have included questions in one place for your reference and to help you think about how you would like to start the discussion.

WHERE YOU ARE WITH ZYNTEGLO	QUESTIONS TO CONSIDER ASKING IF YOU HAVE BETA-THALASSEMIA AND REQUIRE REGULAR TRANSFUSIONS	QUESTIONS TO CONSIDER ASKING IF YOU ARE THE CAREGIVER
Thinking about ZYNTEGLO	<div><b>FOR YOUR CONSIDERATION:</b><ul style="list-style-type: none"><li>What would ZYNTEGLO offer me as a treatment?</li><li>What would potentially no longer relying on regular blood transfusions mean to me?</li><li>How long is the ZYNTEGLO treatment journey from start to finish?</li></ul></div> <div><b>FOR YOUR DOCTOR'S CONSIDERATION:</b><ul style="list-style-type: none"><li>What safety considerations should I know about ZYNTEGLO?</li><li>Am I a candidate for ZYNTEGLO?</li><li>How do you think ZYNTEGLO could change my experience with beta-thalassemia?</li><li>What are the possible side effects of treatment with ZYNTEGLO?</li><li>How will I receive ZYNTEGLO?</li><li>What should I avoid after receiving ZYNTEGLO?</li></ul></div>	<div><b>FOR THE PERSON:</b><ul style="list-style-type: none"><li>How do you think ZYNTEGLO could help you reach your treatment goals?</li><li>How do you think ZYNTEGLO could change your relationship with beta-thalassemia?</li><li>What concerns do you have about ZYNTEGLO that we should discuss with the doctor?</li></ul></div>

## IMPORTANT SAFETY INFORMATION (cont'd)

What is the most important information I should know about ZYNTEGLO? (cont'd)

The most common side effects of ZYNTEGLO following treatment for up to 6 months are: low level of platelets (which may reduce the ability of blood to clot and may cause bleeding), low level of white blood cells (which may make you more susceptible to infection), and pain in arms or legs.

Call your healthcare provider right away if you have new or unusual bleeding which may include any of these signs or symptoms: severe headache, abnormal bruising, nose bleed, blood in your urine, stool, or vomit, coughing up blood, or unusual stomach or back pain.

Please see [Important Safety Information](#) on pages 22-23 and full [Prescribing Information](#), including [Patient Information](#).

Learning about how ZYNTEGLO works	<b>FOR YOUR CONSIDERATION:</b> <ul style="list-style-type: none"><li>What does gene therapy with ZYNTEGLO mean for me?</li></ul>	<b>QUESTIONS TO ASK IF YOU ARE THE CAREGIVER</b>
Understanding the ZYNTEGLO results	<b>FOR YOUR CONSIDERATION:</b> <ul style="list-style-type: none"><li>What specific treatment results are most important to me?</li><li>What does the potential efficacy of ZYNTEGLO mean for me?</li></ul> <b>FOR YOUR DOCTOR'S CONSIDERATION:</b> <ul style="list-style-type: none"><li>How will I manage my iron levels after ZYNTEGLO?</li><li>Will I still need chelation therapy after ZYNTEGLO?</li><li>How long will ZYNTEGLO work and who will monitor my follow-up?</li></ul>	<b>FOR YOU:</b> <ul style="list-style-type: none"><li>What may I want to consider before deciding if ZYNTEGLO may be right for my child?</li></ul>
Moving forward with ZYNTEGLO	<b>FOR YOUR DOCTOR'S CONSIDERATION:</b> <ul style="list-style-type: none"><li>Where will I need to go for my treatment with ZYNTEGLO?</li><li>Who will be the doctor and care team overseeing my ZYNTEGLO treatment?</li><li>What kind of support does the QTC provide to people receiving treatment with ZYNTEGLO?</li><li>What might my calendar of events for each step of treatment look like at the QTC?</li><li>Where will I be monitored after ZYNTEGLO, and for how long?</li><li>What travel and logistics will I need to address before I receive care at the QTC?</li><li>What is apheresis like? Mobilization? Chemotherapy?</li><li>What can you tell me about the other medicines that I'll be taking as part of treatment with ZYNTEGLO? What side effects could I expect from these other medicines?</li><li>What does follow-up care look like?</li></ul>	
Considering coverage for ZYNTEGLO	<b>FOR YOUR DOCTOR'S CONSIDERATION:</b> <ul style="list-style-type: none"><li>What will be covered by my insurance provider?</li><li>How much will I be responsible for?</li><li>What other assistance could be available for covering ZYNTEGLO?</li></ul>	



# QUESTIONS FOR YOUR QTC CARE TEAM

The following questions can help you to think about what you would like to discuss with your doctor about ZYNTEGLO for yourself or your child (or loved one).

**What are the most important things to know about receiving treatment at this QTC?**

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**What will I need to consider and plan for in order to move forward with ZYNTEGLO (eg, transportation, social, financial)?**

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**What should I consider when planning the treatment process with my QTC?**

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**What have I read in this resource that I want to know more about?**

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**What specific concerns do I have to think about when considering whether ZYNTEGLO may be right for me?**

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**What else would I like to know about ZYNTEGLO before I start planning for treatment?**

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**What are things I need to know following treatment with ZYNTEGLO?**

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This resource is meant to help you start thinking about conversations to have with yourself, your family, and your doctor about ZYNTEGLO. It is also designed to be a resource that you can return to over time as you think about your treatment for beta-thalassemia. We understand that the decision to move forward with ZYNTEGLO is a big step. You will probably have a lot of questions and things to think about. This resource, your doctor, and members of your care team are available to support you at every step.

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Because you have lived with beta-thalassemia your whole life, you know your experience with beta-thalassemia better than anyone.

- **What should I plan to discuss with my doctor about ZYNTEGLO?**
- **What are my goals of therapy?**
- **What does my doctor think?**

Learning more about ZYNTEGLO and asking questions can help you decide together whether ZYNTEGLO may be right for you.

 To learn more about ZYNTEGLO, please talk to your doctor and visit [ZYNTEGLO.com](https://www.zynteglo.com).

**IMPORTANT SAFETY INFORMATION (cont'd)**

**What is the most important information I should know about ZYNTEGLO? (cont'd)**

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

It is important for you to be monitored at least yearly for at least 15 years for any changes to your blood. There is a potential risk of blood cancer associated with this treatment; however, no cases have been seen in studies of ZYNTEGLO. If you are diagnosed with a cancer, have your treating physician contact bluebird bio at 1-833-999-6378.

**Please see Important Safety Information on pages 22-23 and full [Prescribing Information](#), including [Patient Information](#).**



# COMMITTED TO SUPPORT COMMITTED TO EDUCATION COMMITTED TO WHAT'S AHEAD

If you're considering ZYNTEGLO, we want to make sure you're supported. That's why we've created **my bluebird support**—a collection of educational resources aimed at helping you or someone you care for stay informed for any decision-making process with your doctor.

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As you are thinking about ZYNTEGLO and your health insurance:

- What will be covered by my insurance?
- How much will I need to pay?
- What other support could be available regarding access to ZYNTEGLO?

Visit [mybluebirdsupport.com](https://mybluebirdsupport.com) for more information



To start accessing the benefits of **my bluebird support**, you'll need to contact your Patient Navigator. This person is knowledgeable about bluebird bio gene therapies and will be your main point of contact for **my bluebird support** throughout your treatment journey. You can rely on your Patient Navigator to help you in a variety of ways, including:



### NAVIGATING EDUCATION

Providing you with educational materials as well as a list of patient advocacy organizations relevant to beta-thalassemia.



### NAVIGATING INSURANCE

Collaborating with your health insurance provider and your doctor's office staff by offering guidance and answers to coverage questions. They may also be able to work to provide information related to treatment cost and the specific benefits available through your insurance if available.



### NAVIGATING TREATMENT

Guiding you through each step of your treatment journey, with support that ranges from helping you locate a QTC (a specialized hospital qualified to administer a bluebird bio gene therapy) to addressing nonclinical barriers to treatment access.

Please note that your doctor will always be your primary source for information about your care. You should always talk to your doctor about your treatment journey.



**Call today and learn how **my bluebird support** can help you**

Call 1-833-888-NEST (6378) Monday–Friday, 8 AM–8 PM ET  
Visit [mybluebirdsupport.com](https://mybluebirdsupport.com)

Please see **Important Safety Information** on pages 22–23 and full Prescribing Information, including Patient Information.



# GLOSSARY

**Apheresis:** the process of separating blood stem cells from blood cells using a machine

**Beta-thalassemia:** a genetic blood disorder that reduces or eliminates the production of fully functional beta-globin (due to a change/defect in the beta-globin gene)

**Blood stem cell:** an immature cell that has the potential to develop into any of the types of blood cells, including white blood cells, red blood cells, and platelets

**Chelation:** Iron Chelators are a type of medicine that helps to reduce the amount of iron in your body

**Chemotherapy:** a medicine that's typically used to get rid of cancer cells. During treatment with ZYNTEGLO, chemotherapy is used to make room in the bone marrow for ZYNTEGLO

**Clinical trials:** studies that evaluate the safety and efficacy of a medication in humans

## IMPORTANT SAFETY INFORMATION (cont'd)

### How will I get ZYNTEGLO?

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

After receiving the chemotherapy it may not be possible for you to become pregnant or father a child. You should consider discussing options for fertility preservation with your doctor before treatment.

**Please see Important Safety Information on pages 22-23 and full Prescribing Information, including Patient Information.**

**Donor match:** a person who has specific proteins on the surface of their white blood cells (called human leukocyte antigens, HLAs) that match yours. When these matched cells are used in a bone marrow transplant, they are less likely to cause certain side effects

**Engrafting (or engraftment):** the process by which transplanted stem cells travel through the blood to the bone marrow, where they begin to make new white blood cells, red blood cells, and platelets

**False positive:** a test result that indicates that a person has a specific disease or condition when the person actually does not have the disease or condition

**Gene:** a sequence of DNA responsible for controlling inherited traits

**Gene addition:** adds functioning genetic material to do the work of a faulty gene

**Gene therapy:** a method of treating genetic diseases at the genetic level (the source) with the goal of changing the course of a disease

**Genetic disease:** a disease that is caused by a genetic change

**Genotype:** your genetic makeup for any trait, which may be labeled with a pair of letters, each representing the copy of a gene inherited from one of your parents

**Hemoglobin:** a protein in your red blood cells that helps to carry oxygen throughout your body; the switch from fetal to adult hemoglobin typically occurs at ~6 months after birth

- Adult hemoglobin contains iron and a balanced amount of beta-globin and alpha-globin
- Fetal hemoglobin contains iron and a balanced amount of gamma-globin and alpha-globin

**Insertional oncogenesis:** blood cancer that is driven by a change (mutation) in a gene caused by adding new genetic material into an existing gene

**Mobilization:** a process in which a medicine is used to get blood stem cells to move out of the bone marrow and into the circulating blood

**Normal or near normal hemoglobin levels:** hemoglobin levels that are close to the normal range for a person, based on their age and birth gender.

Normal Hb ranges for pediatric and adult patients are:

- 2-9 years: 11.5-14.5 g/dL
- Males 10-17 years: 12.5-16.1 g/dL
- Females 10-17 years: 12-15 g/dL
- Male adults (≥18 years): 13.5-18 g/dL
- Female adults (≥18 years): 12.5-16 g/dL

**Patient Navigator:** a patient support specialist who is knowledgeable about bluebird bio gene therapies and is equipped with resources to help patients and hospital office staff navigate challenges that range from nonclinical barriers to treatment access to understanding what a patient's journey may look like

**Phlebotomy:** a blood draw process that can be used for iron reduction and is only possible for patients who have sufficient hemoglobin levels without red blood cell transfusions

**Qualified Treatment Center (QTC):** a hospital that has been carefully selected based on their expertise in areas such as transplant, cell, and gene therapy, and are trained to administer ZYNTEGLO

**Red blood cell (RBC):** a hemoglobin-containing cell that carries oxygen throughout your body

**Stem cell:** cells in the body which can form all the different cell types with specific functions, such as blood cells, brain cells, muscle cells, or bone cells

**Transfusion independence:** in ZYNTEGLO trials, this was defined specifically as an average hemoglobin level greater than or equal to 9 g/dL without red blood cell transfusions for 12 months or more

**Vector:** a delivery system used to introduce genetic material into the nucleus



# WHAT COULD ZYNTEGLO MEAN FOR YOU?

TALK TO YOUR DOCTOR  
ABOUT WHETHER ZYNTGLO  
MAY BE RIGHT FOR YOU.

Visit [ZYNTGLO.com](https://www.zynteglo.com) for more  
information about ZYNTGLO,  
[my bluebird support](#), and how to  
locate a QTC where you can learn  
about your treatment journey.

**Please see Important Safety  
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Information, including  
Patient Information.**

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