# FREQUENTLY ASKED QUESTIONS (FAQ)

## ZS801 (rAAV5-F9-Shanghai) gene therapy for Hemophilia B

| # | Questions | Answer |
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| 1. | What is this new gene therapy ZS801 for Hemophilia B? | ZS801 consists of rAAV viral vector to deliver a normal copy of the F9 gene (rAAV5-F9- Shanghai) to treat Hemophilia B, just like AdV the viral vector in the AstraZeneca or CanSino vaccines which deliver the SARS-Cov2 spike protein gene to induce an immune response (vaccination).<br>Just like AdV vaccine, several manufacturers can produce the same therapy (or vaccine) using the same technology, which is NOT exclusive to any company.<br><br>rAAV5-F9-Shanghai is manufactured by Real & Best Biotech Co., Ltd China. Other similar AAV based gene therapies are Etranocogene dezparovec (Hemgenix, CSL Behring), Fidanacogene elaparvovec (Beqvez, Pfizer), Dalnacogene ponparvovec (Belief BioMed) and scAAV2/8-LP1-hFIXco (St. Jude Children's Research Hospital). |
| 2. | How effective is it? | We have completed pre-clinical studies in mice & Cynomolgus monkey, which showed that the treatment works.<br><br>ZS801 is currently undergoing clinical trial on patients with Hemophilia B. To date, 13 adult female patients aged 18 to 56 years have been treated. These patients have Factor IX activity of less than 2%, and all had 3 or more bleeding episodes in the past year prior to receiving our gene therapy. Early preliminary data suggest the treatment works. All patients achieved elevated FIX activity after treatment. At 1.5-2 years post treatment (available data to date) mean Factor IX activity level was 20.08% to 32.2%. This had translated into reduced bleeding rate (annualized bleeding rate reduced from 10.6-19.0 before treatment, to 0.63-1.58 after treatment (results in range, depending on low or high dose group). |
| 3. | What about the long-term result? How durable is the treatment efficacy? | Data from the ongoing trial of ZS801 are available up to only 2 years to date. So no long-term results are available yet. ZS801 is similar to other AAV based gene therapies mentioned above, so the longer-term efficacy is also expected to be the same.<br><br>scAAV2/8-LP1-hFIXco has reported 13 years post-treatment follow-up data for patients treated in its trial. The data showed a single administration of the gene therapy resulted in durable factor IX expression and sustained clinical benefit [https://pubmed.ncbi.nlm.nih.gov/40499172/ ] |
| 4. | How safe is it? | The most common adverse effect observed in our trial is elevated liver enzymes, which resolved spontaneously in all patients. |

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| | | Of note no patient had ***acute or chronic serious liver*** injury, nor any patient had Factor IX inhibitor and thrombosis.<br><br>Other side effects observed to date are listed below.<br>• Decreased fibrinogen<br>• Elevated creatine kinase (CK) and creatine kinase isoenzyme<br>• Elevated lactate dehydrogenase (LDH),<br>• Elevated α -hydroxybutyrate dehydrogenase(α-HBDH),<br>• Elevated cytokines<br>• Sinus tachycardia<br>• Elevated uric acid<br>• Elevated lymphocyte count.<br>These were all isolated events without associated signs/symptoms and the events resolved spontaneously in all patients |
| 5. | What happens when there is serious adverse reaction? | The healthcare provider who administers the treatment will manage all adverse reactions and other health related issues.<br>For patients treated under the clinical trial, the manufacturer will agree to support the cost of healthcare required to manage any adverse reactions. |
| 6. | Who is eligible to receive treatment? | All patients aged>= 18 years who have Hemophilia B with Factor IX activity ≤ 2%. and<br>1. Currently use Factor IX prophylaxis therapy and yet have frequent spontaneous bleeding events, which had resulted in chronic arthropathy or which were potentially life-threatening hemorrhages, or<br>2. Currently lacking access to Factor IX, whether on demand or prophylaxis. ***These patients should be treated as early as possible.***<br><br>Patients will also require testing for the presence of (1) AAV antibody, and (2) Factor IX inhibitor, in the blood sample. They will not be eligible to receive treatment if they are tested positive for either. |
| 7. | What is the cost? | ZS801 is undergoing clinical trial. The treatment is therefore free for patients enrolled in the trial.<br><br>For patients who receive the treatment under expanded access program, your healthcare providers who administer the therapy and care for you will charge for their professional services. The manufacturer may also require you to share the manufacturing and logistic costs. |
| 8. | Anything I should prepare prior to undergoing treatment? | Intravenous injection of ZS801 is a simple and safe procedure. No special preparation is required.<br>You should continue your usual Factor IX prophylaxis if you are on it. If you had purchased the Factor IX, you may re-sell remaining doses to other patients. |

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| | | The following examination, test and procedure will be performed prior to administering the gene therapy:<br>• Blood tests consisting of liver function, which may increase after treatment.<br>• One day prior to treatment, oral tacrolimus (0.3 mg/kg per day) and corticosteroids (prednisolone 1 mg/kg of body weight per day) will be given for a total of 30 days, which will then be stopped gradually if the liver function is normal. |
| 9. | What to do after treatment? | For the first month after treatment, please adhere to the following:<br>• Regular blood test to check on **liver enzyme levels (**liver function) which could increase after gene therapy. Consult your healthcare provider immediately if your skin and/or whites of the eyes appear yellowish.<br>• Regular testing of **plasma FIX activity**. It is expected to increase after treatment. FIX activity levels rising above 150% may pose a risk of thrombosis. If the levels were to failed to rise above 2%, or if there is spontaneous bleeding, you will need to resume FIX replacement therapy.<br>• **Temporary shedding of the virus vector** (rAAV5-GLA) can occur up to one month after gene therapy administration. Shedding occurs primarily through body waste. Observe proper procedure in disposing the patient's feces (sealing disposable diapers in disposable trash bags and then discarding into regular trash). Observe good hand hygiene when coming into direct contact with the patient body waste. |
| 10 | Where can I find information about ZS801? | ZS801 is undergoing clinical trial. You can find out more about the trials below<br>https://clinicaltrials.gov/study/NCT05641610?term=ZS801&rank=2 |