

## **2. REQUEST FOR DEFERRAL OF PEDIATRIC STUDIES**

### **Product name:**

IXINITY<sup>®</sup>, coagulation factor IX (recombinant);

Company code: APVO101 (previously termed IB1001);

International Non-proprietary Name (INN): trenonacog alfa

### **NDA number:**

BLA Number: 125426

IND Number: 013551

### **Applicant:**

Medexus Pharma, Inc.

### **Indication(s):**

- Control and prevention of bleeding episodes in adults and children  $\geq 12$  years of age with hemophilia B.
- Perioperative management in adults and children  $\geq 12$  years of age with hemophilia B.

IXINITY is not indicated for induction of immune tolerance in patients with hemophilia B.

### **2.1. Age Groups Included in Deferral Request**

< 12 Years

### **2.2. Reasons for Requesting Deferral**

The trial experienced enrollment delays due to the COVID-19 pandemic.

### **2.3. Age Groups Not Included in Deferral Request**

Not applicable

### **2.4. Justification for Deferral**

On February 28, 2020, Medexus Pharma, Inc. (Medexus), located In Chicago, IL, acquired all rights to IXINITY<sup>®</sup>, coagulation factor IX (recombinant, code name APVO101) from Aptevo BioTherapeutics LLC, Seattle, WA.

Aptevo BioTherapeutics LLC committed to initiate and projected a study completion date of June 2021 with a final report submission to the Agency by December 14, 2021. Unfortunately, the previous sponsor enrolled the first patient January 2021.

## 1.9 Pediatric Administrative Information

Upon acquisition, Medexus worked diligently with the CRO to drive enrollment, however, the trial experienced enrollment delays due to the COVID-19 pandemic at the investigator sites as follows:

- Georgia: complete lockdown 31 March 2020 - 8 Jun 2020.
- Ukraine- March 2020 - May 2020. Restrictions were then implemented on 8 Jan 2021 – 30 Apr 2021, but patients/CRA could travel with special permission.
- Turkey: Lockdown 16 March 2020 - June 2020; November 2020 - March 2021
- Moldova: Lockdown March 2020 – May 2020
- South Africa: Lockdown 26 Mar 2020 – 30 April 2020. Permits were required to travel freely as long as they had a valid permit. This continued through 1 March 2021.
- Brazil: Lockdown March 2020 – Jul 2020, but there were travel restrictions until Jun 2021. on is to be confirmed by the local team.

## 2.5. Description of Planned or Ongoing Studies

APVO101-903 (formerly IB1001-02B), is a Phase 3/4, single arm, open-label study to evaluate the safety, efficacy and pharmacokinetics (PK) of APVO101 (previously termed IB1001) prophylaxis in severe or moderately severe hemophilia B subjects < 12 years of age. Study APVO101-903 consists of three distinct phases:

- PK Phase – PK evaluation will consist of administration of a single  $75 \pm 5$  IU/kg dose, followed by factor IX activity and safety assessments up to 50 hours post-infusion.
- Treatment Phase – subjects will receive APVO101 prophylaxis for 50 ED (approximately 6 months).
- Continuation Phase – subjects may continue to receive APVO101 prophylaxis for an additional  $\geq 50$  ED.

## 2.6. Projected Date Until Submission Studies Would Be Deferred

Medexus has successfully screened 24 subjects with 21 dosed to date, with 1 early withdrawal. Twenty (20) subjects are in treatment as of the last trial update. The last patient was enrolled in June 2021. To date

- 11 subjects  $\geq 6$  have completed 50 Exposure Days (EDs).
- 7 subjects <6 have completed 50 EDs
  - Two 50 ED visits expected in FEB & MAR 2022
  - Last 50 ED visit expected in JUN 2022

Once the last patient completes the 50 ED visit, Medexus will initiate the final analysis.

## 1.9 Pediatric Administrative Information

An [Interim Analysis Report](#) for 12 subjects that had completed 50 EDs as of May 2021, is provided for the Agency's perusal.

Medexus is committed to fulfilling the PREA requirement inherited as part of the BLA acquisition.

Medexus hereby requests the Agency's approval of the following estimated revised timeline for the APVO101-903 clinical study:

- Study Completion Date: July 31, 2022
- Final Report Submission: January 30, 2023