1 TITLE PAGE

Study title:	Pharmacokinetics, Safety and Efficacy of Recombinant Factor IX Product, IB1001, in Patients with Severe Hemophilia B
Name of investigational product:	IB1001
Indication studied:	Hemophilia B
Sponsor (All regions except EU):	Cangene Corporation (legal name), a subsidiary of Emergent BioSolutions[1]
Sponsor (EU):	Cangene Europe Limited (legal name), a subsidiary of Emergent BioSolutions[1]
Protocol identification number:	IB1001-04
Development phase of study:	Phase 3
Study initiation date (first patient enrolled):	Not applicable (study was not initiated and no patients were enrolled)
Study completion date (last patient completed):	Not applicable
Name and affiliation of principal or coordinating investigator(s) or sponsor's responsible medical officer:	Tim Babinchak, MD Vice President, Clinical Development and Medical Affairs Phone: 484-318-8851 Fax: (484) 318-8841
Name of company/sponsor signatory:	Christine Hall, Ph.D. Director, Clinical Research Tel: (204) 275-4248 Fax: (204) 487-4086
Date of the report:	April 18, 2016

[1] In effect since February 21, 2014, when Cangene Corporation and Cangene Europe Limited became wholly-owned subsidiaries of Emergent BioSolutions, Inc. Cangene Corporation and Cangene Europe Limited continue to exist as distinct legal entities and have retained their corporate legal name, as sponsor of clinical trials.

Sponsor: Cangene Corporation

Authentication: We, the undersigned, declare that we have thoroughly reviewed this report for completeness, accuracy, compliance with the protocol, SOPs and GCP; that we have documented any significant deviations from the requirements; that we have critically evaluated the report for internal consistency; and that to the best of our knowledge this report is scientifically valid.

Bojan Drobic, PhD — 18-APR-2016 (Date)

Senior Scientist, Clinical Research

Medical Review: I, the undersigned, declare that I have thoroughly reviewed this report for medical impact, and to the best of my knowledge the report is internally consistent and medically accurate and scientifically valid.

Tim Babinchak, MD — 19 Apr 2016 (Date)

Vice President, Clinical and Medical Affairs

Approval: I, the undersigned, declare that I have thoroughly reviewed this report for anomalies and compliance with the protocol, and critically evaluated the scientific validity of statements and conclusions of the report; that to the best of my knowledge there are no anomalies that require further comment; and that to the best of my knowledge and judgement this report is scientifically valid.

Christine Hall, PhD — 2016-APR-18 (Date)

Director, Clinical Research

2 SYNOPSIS

Name of Sponsor/Company: Cangene Corporation (a subsidiary of Emergent BioSolutions Inc.) – all regions except EU Cangene Europe Limited (a subsidiary of Emergent BioSolutions Inc.) – EU	
Name of Finished Product: IB1001	
Name of Active Ingredient: Recombinant factor IX (rFIX)	
Title of Study:	Pharmacokinetics, Safety and Efficacy of Recombinant Factor IX Product, IB1001, in Patients with Severe Hemophilia B
Investigators:	Not applicable; no investigators participated in the study
Study Centre(s):	Not applicable; no study centers participated in the study
Studied Period (years): Not applicable	**Phase of Development:** Phase 3

Objectives:

Primary objectives:

- To evaluate safety of IB1001 within the first 50 exposure days,
- To determine IB1001 pharmacokinetics (PK), and
- To assess efficacy of IB1001 prophylaxis with respect to breakthrough bleeding and with respect to control of hemorrhaging in subjects with severe hemophilia B within the first 50 exposure days.

Secondary objectives:

- To evaluate long-term safety of IB1001, and
- To evaluate long-term efficacy of IB1001.

Exploratory objectives:

- To evaluate markers of thrombogenicity during the first 24 hours post-infusion [thrombogenicity markers will include at a minimum D-dimer test; however should there be a clinical reason (e.g., three consecutive elevations in D-dimer levels, a possible clinical thrombogenic episode), sufficient samples will be collected to also evaluate levels of fragment 1+2 (F1+2) and thrombin-antithrombin III complex (TAT)], and
- To evaluate IB1001 immunogenicity response (development of inhibitory and non-

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inhibitory factor IX binding antibodies and antibodies to host cell proteins).
Methodology: Study Design: Phase 3, single arm, open-label study with three defined phases: PK Phase • Initial PK evaluation – single dose of IB1001 • Repeat PK evaluation (after 3 to 6 months of IB1001 prophylaxis) – single dose of IB1001 Treatment Phase • IB1001 prophylaxis treatment for 6 months [50 exposure days (ED)] Continuation Phase • IB1001 prophylaxis treatment for at least an additional 6 months after completion of Treatment Phase (to reach ≥ 100 ED) • IB1001 Recovery to be performed every 6 months Treatment with IB1001 to support a surgical procedure (if required) is permitted for subjects who have completed initial PK evaluation.
Number of patients (planned and analysed): Up to 18 subjects in order to have at least 12 subjects complete all phases of the study.
Diagnosis and main criteria for inclusion: Inclusion Criteria: 1. Males only, age of at least 12 years 2. Body Mass Index of ≤ 29, with a minimum body weight of 40 kg 3. Written Institutional Review Board (IRB)/Ethics Committee (EC)-approved informed consent (ICF) 4. Willingness to make the required study visits, and follow instructions while enrolled in the study (for at least 12 months)

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5. Severe (factor IX activity ≤2 IU/dL) hemophilia B subjects with a minimum of 3 bleeding episodes over the preceding 6 months or 6 bleeding episodes over the preceding 12 months or in the event the subject is on prophylaxis, a minimum of 3 bleeding episodes over the preceding 6 months or 6 bleeding episodes over the preceding 12 months prior to being placed on prophylaxis.
6. Subjects must be on prophylaxis or switch to a prophylaxis regimen for the duration of the PK and Treatment/Continuation Phase of the study
7. Previously treated patients with a minimum of 150 exposure days (as documented/determined by the investigator) to a factor IX preparation
8. Willingness to adhere to the 5-day washout period of any factor IX replacement therapy prior to PK evaluations
9. Immunocompetent (CD4 count >400/mm3) and not receiving immune modulating or chemotherapeutic agents
10. Platelet count at least 150,000/mm3
11. Liver function: alanine transaminase (ALT) and aspartate transaminase (AST) ≤2 times the upper limit of the normal range
12. Total bilirubin ≤1.5 times the upper limit of the normal range
13. Renal function: serum creatinine ≤1.25 times the upper limit of the normal range
14. Hemoglobin ≥7 g/dL at the time of the blood draw

Exclusion Criteria:

1. History of factor IX inhibitor ≥0.6 Bethesda Units (BU)
2. Existence of another coagulation disorder
3. Evidence of thrombotic disease, fibrinolysis or disseminated intravascular coagulation (DIC)
4. Use of an investigational drug within 30 days prior to study entry
5. Previous use of IB1001
6. Use of medications that could impact hemostasis, such as aspirin

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7. Hypersensitivity to the active substance or to any of the excipients in the investigational products 8. Known allergic reaction to hamster proteins 9. History of poor compliance, a serious medical or social condition, or any other circumstance that, in the opinion of the investigator, would interfere with participation or compliance with the study protocol 10. History of adverse reaction to either plasma-derived factor IX or recombinant factor IX that interfered with the subject's ability to treat bleeding episodes with a factor IX product
Test product, dose and mode of administration, batch number: IB1001, for intravenous administration only PK Phase: single infusion of 75 ± 5 IU/kg Treatment Phase and Continuation Phase: single infusion of 40 – 75 IU/kg twice weekly (prophylaxis); the dosage and frequency of treatment may be adjusted at discretion of the investigator Recovery Study: single infusion of 75 ± 5 IU/kg Surgery: • Bolus infusion: up to 120 IU/kg 1 hour prior to the start of the procedure, followed by an infusion of 60 IU/kg 12 hours after the first infusion. Continue with 60 IU/kg every 12 hours for a minimum of 3 days post-surgical procedure. The dosage and frequency of treatment may be adjusted at discretion of the investigator • Continuous infusion: target plasma level of factor IX between 70% and 110% for a minimum of 3 days post-surgical procedure. No IB1001 batch numbers are available as the study was not initiated and no subjects were enrolled and dosed with IB1001.
Duration of treatment: for at least 12 months (or 100 exposure days)

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Criteria for evaluation:

Pharmacokinetics: The following pharmacokinetic endpoints will be evaluated for initial and repeat PK:

- Maximum plasma concentration (C_{max})
- Area under the curve ($AUC_{0-\infty}$, AUC_{0-72})
- Area under the moment curve (AUMC)
- Clearance (Cl),
- Rate of elimination for the terminal phase (λz)
- Terminal half-life ($t_{½}$)
- In-vitro recovery (IVR)
- Incremental recovery
- Mean residence time (MRT)
- Volume of distribution at steady state (Vd_{ss})

Efficacy: The following efficacy endpoints will be evaluated for Treatment Phase and Continuation Phase:

- Annualized bleeding rate: (number of bleeding episodes x 12) / (number of months of observation).
- Degree of hemorrhage control: subject's rating of efficacy
- Time from onset of treatment until the bleeding episode stops (as defined by change in pain and change in swelling)
- Number of infusions required to treat the bleeding episode
- Subject's product tolerance (ability to use the product without an AE)

Investigator's rating of efficacy

- Assessment of target joint(s)
- The following efficacy endpoints will be evaluated for surgery:
- Estimated blood loss at time of surgery
- Post-surgery blood loss

Safety: The following assessments will be used to evaluate the safety:

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- Adverse events
- Inhibitory factor IX antibodies
- Non-inhibitory factor IX antibodies
- Anti-CHOP antibodies
- Thrombogenic markers
- Laboratory values
- Vital Signs
- Physical exams

Statistical methods: PK parameters were to be listed and summarized as determined by initial PK and repeat PK. Descriptive statistics of PK parameters were to be provided; no formal statistical test was planned.

Descriptive summaries and listings were to be provided for all efficacy endpoints.

Summary statistics and listings were to be provided for all safety endpoints. Also, incidence of non-inhibitory factor IX antibodies and incidence of anti-CHOP antibodies were to be evaluated.

SUMMARY – CONCLUSIONS

SAFETY RESULTS:

Not applicable.

EFFICACY RESULTS:

Not applicable.

CONCLUSION

This study was planned as supportive of the clinical development of IB1001 after a manufacturing change (i.e., polished IB1001). However, manufacturing comparability data in combination with the data collected in other studies of patients who transitioned to polished IB1001 in ongoing clinical trials (IB1001-01 and IB1001-02) were deemed sufficient to demonstrate reduction of immunogenicity potential of polished IB1001. Hence, study IB1001-04 was not implemented and it was removed from the clinical development plan for IB1001 (i.e., no subjects were recruited into the study).

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