

# Efficacy and Safety of PlasmaCap IG, a New 10% Intravenous Immunoglobulin Manufactured Using an Innovative Chromatography Process, In Adults and Children with Primary Immunodeficiency Disorders

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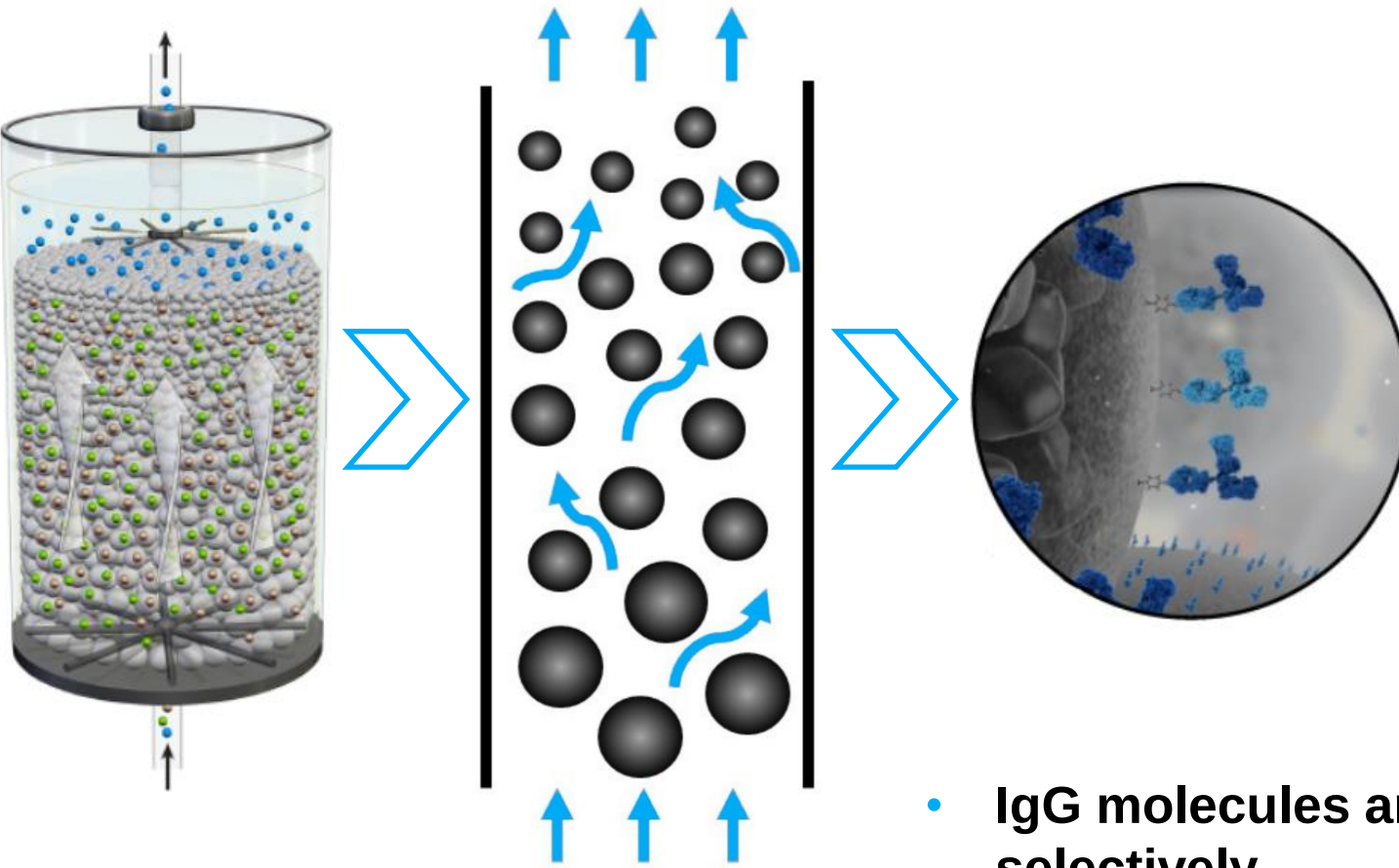
## Background and Rationale

- Primary immunodeficiency disorders (PIDDs) include a heterogenous group of inherited disorders with deficiencies in one or more components of the immune system, increasing susceptibility to infections.<sup>1,2</sup>
- Life expectancy in PIDD patients is reduced, and recurrent infections cause significant morbidity and disability.<sup>3,4</sup>
- For these reasons, patients with PIDD require life-long immunoglobulin (IG) replacement therapy administered intravenously (IVIG or IGIV) or subcutaneously (SCIG) to prevent recurrent infections, notably severe bacterial infections (SBIs) of the respiratory tract.<sup>1,3,5</sup>
- Shortages of IVIG and SCIG continue to be reported globally<sup>6-8</sup>, and the global need for IVIG and SCIG has grown continuously since the 1980s.<sup>9</sup>
- Innovative, new, and improved manufacturing technologies are needed to meet the increasing global demand for plasma-derived therapeutics, especially IG.

## Innovative Manufacturing Technology

- PlasmaCap IG 10% IVIG is prepared from large pools of human donor plasma using expanded bed adsorption (EBA) chromatography (PlasmaCap EBA®) (Figure 1), with no precipitation, that can enable higher yields of certain plasma proteins, including IgG, compared to traditional cold ethanol plasma fractionation.

Figure 1: PlasmaCap EBA® Technology



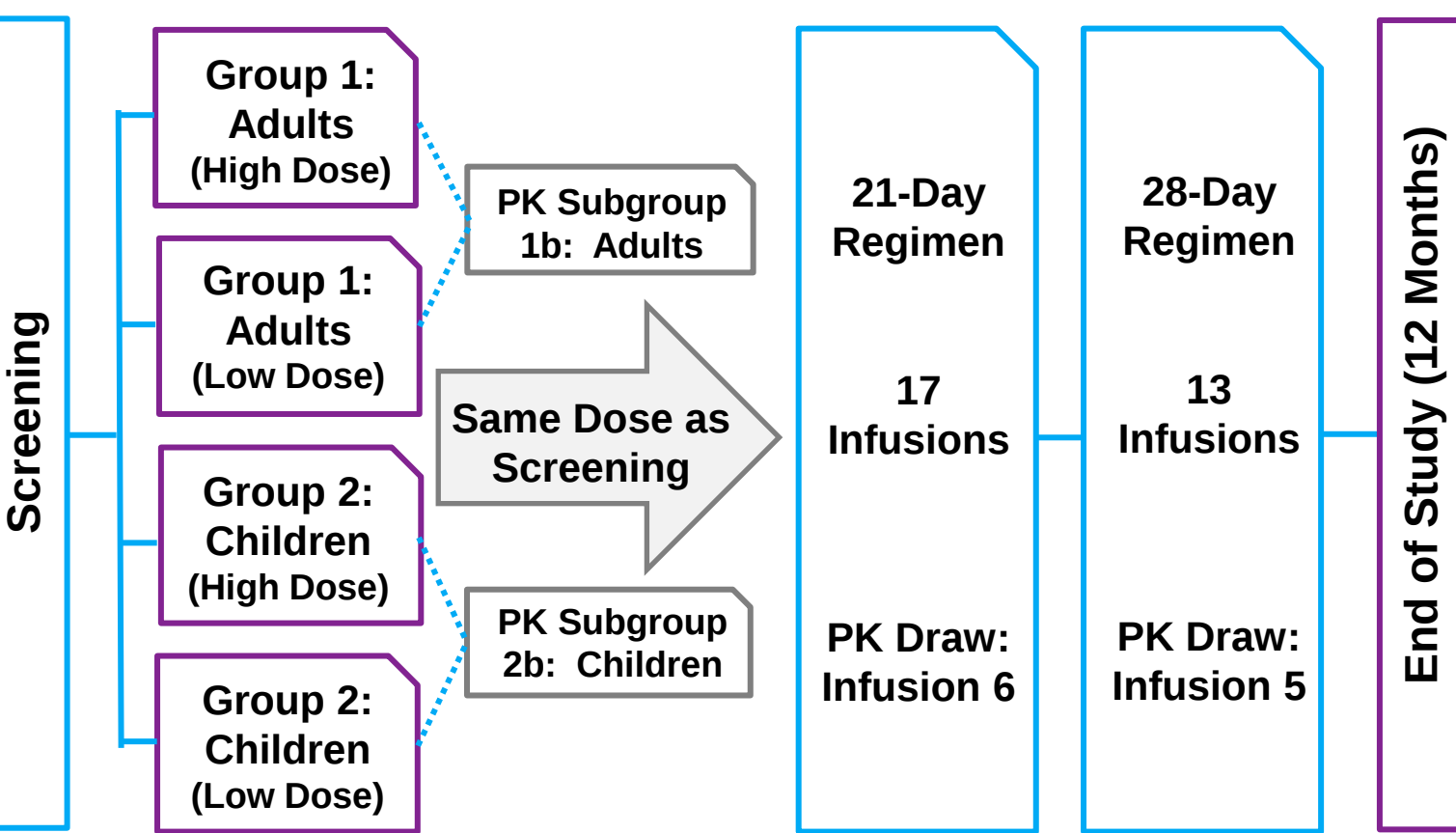
- Expanded Bed Adsorption (EBA) columns are loaded by flowing plasma upward, exposing the ligand to the plasma proteins.
- The EBA resin used to capture IgG contains high- density tungsten carbide imbedded in a microporous agarose bead.
- IgG molecules are selectively captured and eluted.
- Other plasma proteins can be captured using beads with different ligands.

## Methods

### Study Design

- A Phase 3 prospective, open-label, multicenter, study of the efficacy, safety, tolerability, and pharmacokinetics (PK) of PlasmaCap IG in adults and children with PIDD was conducted at 12 sites in the United States (US) and Canada.
- Following screening procedures, eligible adults (Group 1) and pediatric subjects (Group 2) received 300-900 mg/kg of PlasmaCap IG administered either every 21 or 28 days for a period of 1 year (Figure 2).
- Previous dosing was used to determine placement in low-dose or high-dose subgroups.
- A subgroup of adult and pediatric participants were also enrolled in the PK substudy.

Figure 2: Study Design



### Study Endpoints

- Primary Endpoint:**
  - The mean annual acute SBI rate (must be significantly less than 1/subject/year).
- Secondary Efficacy Endpoints:**
  - Number of infection episodes (serious and non-serious).
  - Days of work/school/daycare missed, or days unable to perform normal daily activities due to infections.
  - Days of hospitalization due to infections, episodes of fever, and use of antibiotics to treat infections or for short-term prophylaxes.
  - Evaluation of IgG trough levels and ability to maintain stable, therapeutic IgG levels.
- Secondary Safety Endpoints:**
  - Adverse events (AEs), viral safety, and incidence of hemolytic and thromboembolic events.
- Secondary Pharmacokinetic Endpoints:**
  - Determination and evaluation of the PK profile plasma concentrations for each phase of the PK curve.

## Results\*

### Study Population

- The study population (N=63) was comprised of adults (n=48 [76%]) and children (n=15 [24%]) with a confirmed diagnosis of PIDD (Figure 3, Table 1).

Figure 3: Study Population

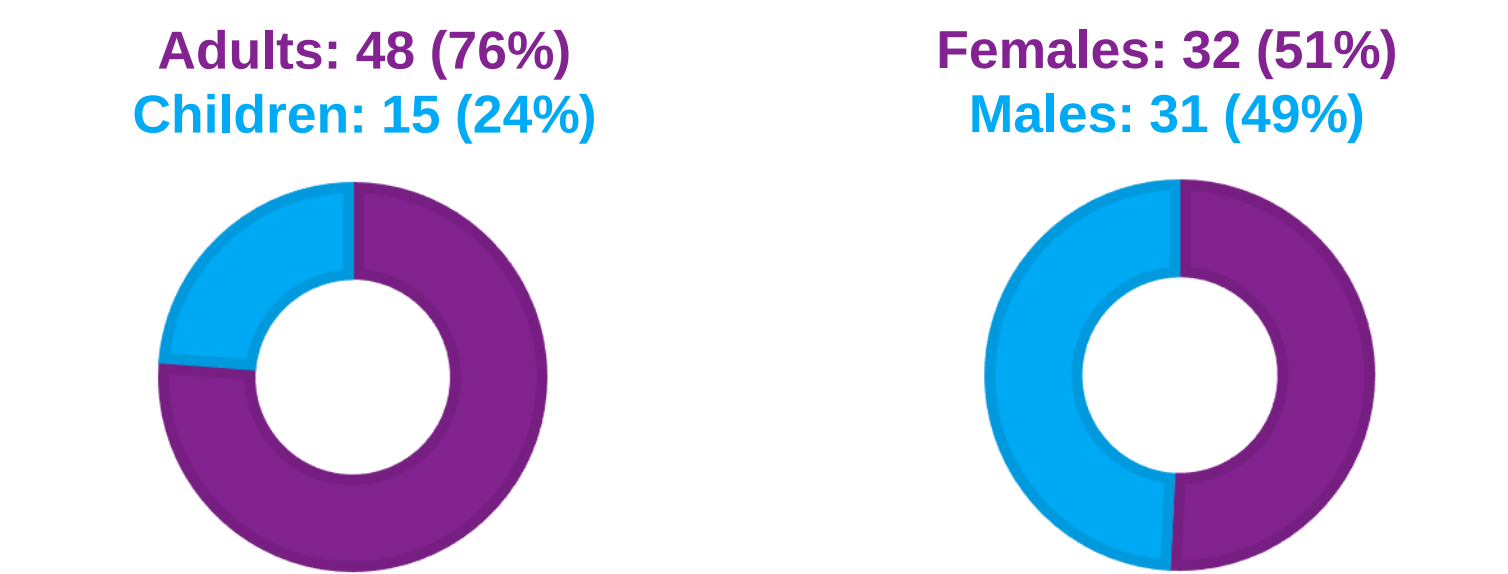


Table 1: Study Population

|                                     | No. of Subjects (%) |
|-------------------------------------|---------------------|
| Adults (≥18 years): Group 1 (All)   | 48 (76%)            |
| Range: 20-70 years                  |                     |
| Adults: Group 1 (High Dose)         | 22 (46%)            |
| Adults: Group 1 (Low Dose)          | 26 (54%)            |
| Adult PK Subgroup (Group 1b)        | 27 (56%)            |
| Children (<17 years): Group 2 (All) | 15 (24%)            |
| Range: 2-14 years                   |                     |
| Children: Group 2 (High Dose)       | 7 (47%)             |
| Children: Group 2 (Low Dose)        | 8 (53%)             |
| Children PK Subgroup (Group 2b)     | 12 (80%)            |
| Females (Groups 1 and 2)            | 32 (51%)            |
| Males (Groups 1 and 2)              | 31 (49%)            |

### Dosing and Infusion Summary

- More than 98% of infusions were completed without interruption, and only 1 infusion was terminated due to an AE; dosing and infusion regimens are summarized in Table 2.

Table 2: Dosing and Infusion Summary

|                               |                     |
|-------------------------------|---------------------|
| Mean Previous Dose:           |                     |
| Adults (Low Dose)             | 445.67±98.11 mg/kg  |
| Adults (High Dose)            | 630.51±121.53 mg/kg |
| Children (Low Dose)           | 333.64±159.47 mg/kg |
| Children (High Dose)          | 566.79±112.47 mg/kg |
| Total Number of Infusions     | 839                 |
| Adults: Number of Infusion    | 613 (73%)           |
| Children: Number of Infusions | 226 (27%)           |

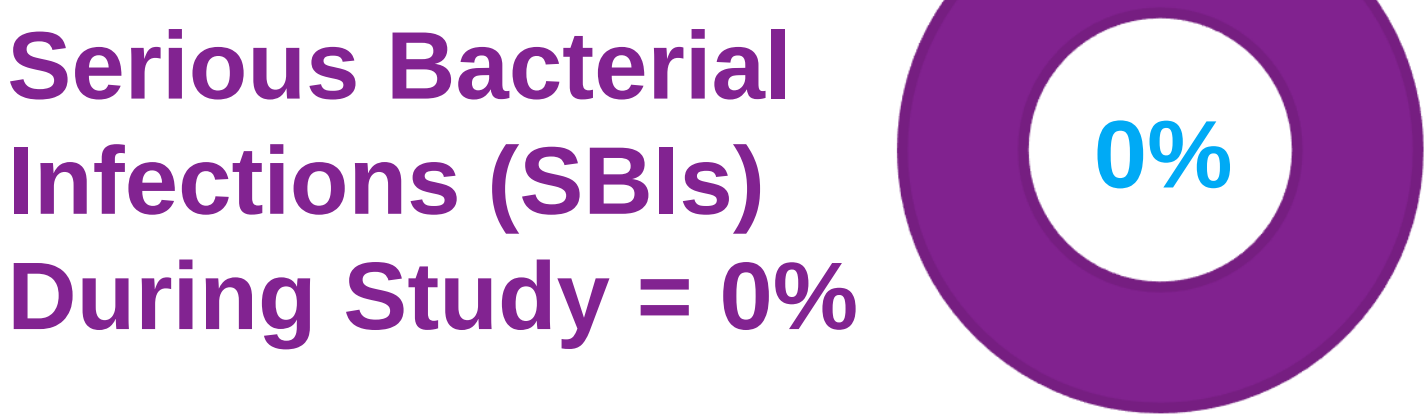
\*Data is still being analyzed and final information may be subject to change prior to regulatory submission.

## Results\*

### Primary Endpoint

- No SBIs occurred in any age group (Figure 4).
- The study met its primary endpoint (SBI rate must be significantly less than 1/subject/year).

Figure 4: Primary Endpoint



### Key Secondary Endpoints

#### Efficacy

- Measures affecting quality of life such as days absent from work or school due to an infection (mean 6.5 days/patient/year), hospitalization due to infections (mean 0.2 days/patient/year), or with a fever >38.5°C (mean 0.9 days/patient/year) were all low, indicating that treatment with PlasmaCap IG had a positive effect on secondary measures of efficacy.
- Antibiotic use to treat infection and for short-term prophylaxis prior to and following surgical and dental procedures was utilized in 33 subjects (52.4%) including 25 adult (52.1%) and 8 pediatric subjects (53.3%).
- The frequency of pyrexia was low overall (12 subjects [19.0%]; 17 events [2.4%]), with no severe fever recorded.

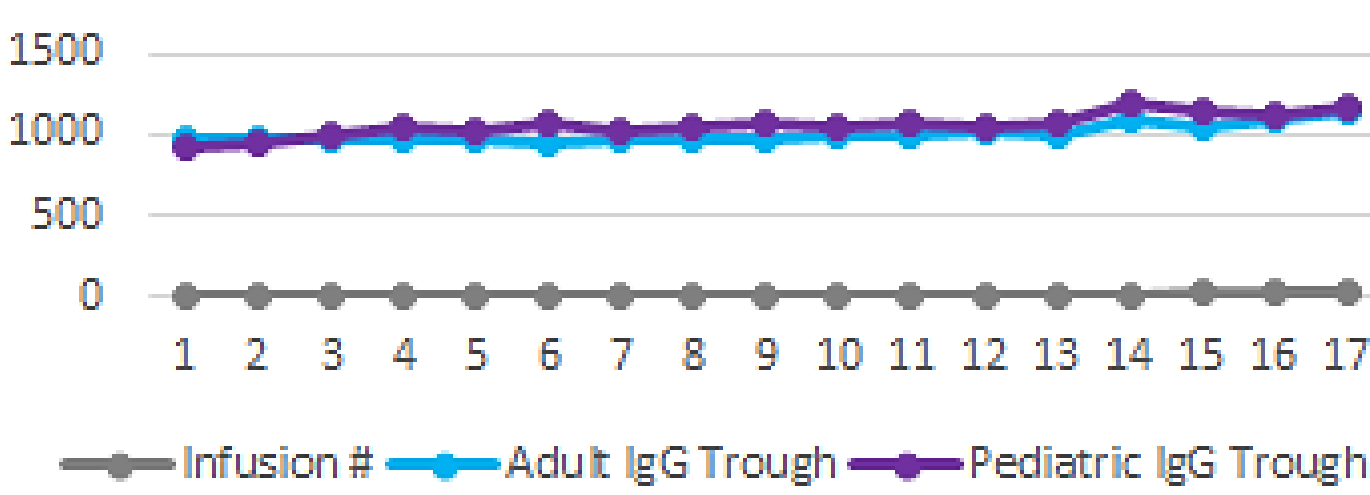
#### Pharmacokinetics

- PK parameters in adults and children were consistent with existing approved IVIG products.
  - IgG trough levels remained above 900 mg/mL for all patients during the study with an increase from baseline at the final treatment visit (Figure 5).
  - No significant difference was observed between total IgG trough concentrations for the 21-day and 28-day regimens.
  - In adults, the mean half-life for total (unadjusted) IgG was 32.6 days in all patients vs. 22.9 days in 21-day patients vs. 34.9 days in 28-day patients.
  - In children, the shorter mean half-life for total (unadjusted) IgG of 22.2 days was attributed to having more patients in the PK subgroup receiving the 21-day dosing regimen.

## Results\*

### Key Secondary Endpoints (continued)

Figure 5: Mean Immunoglobulin G (IgG) Trough Levels



#### Safety

- There were no treatment-related serious adverse events (SAEs) or cases of hemolysis, thromboembolism, or renal failure.
- A total of 127 (17.7%) of AEs were considered related to treatment; 97% were mild or moderate. The most common treatment-related AEs are included in Table 3.

Table 3: Most Common Treatment-Related Adverse Events

| Adverse Event | Number of Subjects (%) |
|---------------|------------------------|
| Headache      | 26 (41.3%)             |
| Fatigue       | 10 (15.9%)             |
| Nausea        | 6 (9.5%)               |

## Conclusions

- This study demonstrates that PlasmaCap IG is effective, safe, and well tolerated in the treatment of adult and pediatric patients with PIDD with no reported SBIs or related SAEs.
- PlasmaCap IG is produced using an innovative manufacturing technology, PlasmaCap EBA®, developed to enable the efficient capture of plasma proteins at high levels of purity and yield from human plasma.

## References

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## Acknowledgments

Evolve Biologics would like to thank all of the investigators and patients who participated in this important study, as well as Shireen Dunwoody of Dunwoody Consulting for assistance with poster design and development.

