Non-Genotoxic Anti-CD117 Transplant Conditioning in Infants with Newly Diagnosed Severe Combined Immune Deficiency

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Background
Successful hematopoietic stem cell transplantation (HCT) requires vacating recipient hematopoietic stem cell (HSC) niches to permit donor HSC engraftment. Currently, HCT relies on genotoxic modalities to achieve niche clearance. We have pursued a non-genotoxic approach to target and deplete HSC using humanized monoclonal antibody JSP191 that binds CD117 (c-kit). JSP191 acts by inhibiting stem cell factor (SCF) binding to CD117 (c-kit) present on HSC.

Based on safety and successful HSC engraftment in a Phase 1 trial in subjects with severe combined immunodeficiency (SCID), who underwent a second transplant because of HSC engraftment failure and poor immunity (PART A), the study of JSP191 (NCT02963064) was expanded to include additional cohorts (PART B) of newly diagnosed infants with SCID.

This presentation focuses on the two infants in PART B.

JSP191 is a well tolerated conditioning regimen
- No transfusion reactions
- No treatment related toxicities
- No myelosuppression

PART A subjects (re-transplant) may be discharged after 48 hours observation following JSP191 administration

HCT conditioning with JSP191 alone enables engraftment, immune reconstitution, and function in newly diagnosed SCID patients

Baby #1 (Subject 0011) IL2RG (NK-)
- Stem Cell Factor (SCF) / Stem Cell Factor Receptor (CD117) interaction required for stem cell survival
- JSP191 blocks SCF signaling leading to patient stem cell depletion from the bone marrow
- Allows for healthy donor stem cell engraftment

Baby #2 (Subject 0015) RAG2 (NK+)
- No JSP191-related adverse events
- 1 of 2 infants with engraftment at 9 months

Clinical Study Design:
Evaluation of SCID patients in a re-transplant and first transplant setting

JSP191 clearance in newly diagnosed (Cohort B2) and re-transplanted SCID subjects (Cohort A2)

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