**CDX-301: BACKGROUND**

- **FI3 receptor (CD135)** is expressed on hematopoietic stem cells (HSC), early progenitor cells, immature myelocytes, and steady state dendritic cells (DC).
- **Fms-like tyrosine kinase-3 ligand (Flt3L)** uniquely binds CD135 and induces the proliferation, differentiation and mobilization of CD135-bearing cells in the bone marrow, peripheral blood, and lymphoid organs.

- Immunex product.
- CDX-301 is composed of the identical amino acid sequence as rhFlt3L.
- Generally well-tolerated.
- Effectively mobilized large numbers of CD34+ stem cells in humans.
- Studied as monotherapy for cancer immunotherapy.
- Given by daily subcutaneous injection during an inpatient treatment period.
- Post-treatment safety follow-up for at least 28 days.

**STUDY DESIGN**

- **Phase 1 open label, dose escalation study in healthy volunteers**
- **Objectives:**
  - Safety and tolerability
  - Pharmacokinetic profile
  - Immunogenicity
  - Extend biological characterization of rhFlt3L in humans

- **Design:**
  - Sequential cohorts enrolled after 21-day observation for dose-limiting toxicity (DLT) and immunogenicity.
  - CDX-301 given by daily subcutaneous injection during an inpatient treatment period.
  - Post-treatment safety follow-up for at least 28 days.

**ENROLLED SUBJECTS**

- **Demographic Characteristics (n=30)**
  - Age, years [Median (range)]: 34 (19-54)
  - Male [%]: 20 (67%)
  - Black / African American: 12 (40%)
  - White: 10 (33%)
  - Asian: 1 (3%)
  - Other: 7 (23%)

**SAFETY**

- **One possible DLT (temporal association with dosing)**
  - A volunteer in Cohort 5 (75 µg/kg) with a remote history of community acquired pneumonia developed community acquired pneumonia on study day 12; the event responded rapidly to antibiotic treatment and fully recovered within 2 weeks.

**FLOW CYTOMETRY**

- Preliminary peripheral blood flow cytometry results are available for the first five cohorts (5-day dosing).
- No consistent changes observed in CD3+ T cells, CD20+ B cells, or CD33+ NK cells.
- Marked increase in CD14+ monocytes, CD34+ stem cells, type 1 myeloid DCs (BDCA-1+) and type 2 myeloid DCs (BDCA-3+) observed.

**HEMATOLOGIC CELL POPULATIONS**

- Data from this current Phase 1 trial are consistent with previous studies showing that rhFlt3L is well-tolerated and can safely and effectively mobilize hematopoietic cell populations.
- The short term dosing regimen (5 days) showed significant mobilization of dendritic cells (DCs) and stem cells, with the highest levels achieved with the maximum dose of 75 µg/kg/day.
- The longer dosing regimen of 7 and 10 days significantly enhanced the levels of CD34+ cells and DCs.
- Comprehensive analysis on the expansion of stem cells, DCs, and other specific cell populations are pending.
- Investigation of varying dose and duration of treatment with rhFlt3L has not been reported previously and will be valuable for assessing the appropriate regimen for future studies of CDX-301 in allogeneic hematopoietic stem cell transplantation (HSCT) and immunotherapy.

**CONCLUSIONS**

- The study is complete with 30 subjects enrolled.
- All enrolled volunteers completed the expected duration of dosing and safety follow-up.

**Prior Clinical Experience**

- Safety and biologic activity of recombinant human Flt3L (rhFlt3L) were originally demonstrated in clinical studies conducted by Immunex utilizing a 14 day dosing regimen.
- Over 550 individuals treated, including ~150 healthy volunteers and 400 oncology patients.
- Studied as monotherapy for cancer immunotherapy and cancer vaccine adjuvant and in combination with GM-CSF or G-CSF for peripheral blood stem cell (PBSC) mobilization.
- Effectively mobilized large numbers of CD34+ stem cells into peripheral blood, and markedly increased the number of myeloid and plasmacytoid dendritic cells in the circulation.
- Generally well-tolerated – in healthy volunteers, Grade 2 events were limited to injection site reactions/pain.
- The expected pharmacologic effects of the rhFlt3L (increased WBC and monocytes) were observed.
- No neutralizing anti-rhFlt3L antibodies were observed in any tested patients.

CDX-301 is composed of the identical amino acid sequence and has comparable biologic activity as the Immunex product.