**RATIONAL**

HPN328 is a DLL3-Targeting TriTAC

- uCD3: anti-CD3 moiety engages T cells
- uALB: single domain antibody binds albumin to extend serum half-life
- uDLL3: single domain antibody targets cancer cells expressing DLL3

**HPN328 is a tri-specific single chain molecule of ~50 kDa**

**PHARMACOLOGY**

- HPN328 Has a Half-Life of 2.8 to 3.3 days in Cynomolgus Monkeys
- Has a terminal half-life of 72 hours in cynomolgus monkeys
- More than 15 half-lives in cynomolgus monkey blood
- Dosing Retains TDCC Activity

**IN VITRO PHARMACOLOGY**

- HPN328 Exhibits Potent Cytotoxicity against SCLC Cells
- In vitro MTT assay
- CD3 and DLL3 single domain antibodies
- DLL3 expression
- HPN328 exhibits significant cytotoxicity against SCLC cells

**IN VIVO PHARMACOLOGY**

- Anti-DLL3 TriTACs Potently Inhibit Growth of NCI-H82 Xenografts
- Kaplan-Meier survival curves
- Significant growth inhibition
- Increased median survival

**HARPOON Therapeutics**

- South San Francisco, CA

**INTRODUCTION**

- HPN328 is an Anti-DLL3 T Cell Engager for Treatment of Small Cell Lung Cancer
- T cell killing
- DLL3 expression

**BIOPHYSICAL CHARACTERIZATION**

- Process: Depth filtration
- Purity & Stability: SDS-PAGE
- Analytical SDS
- Intrinsic Fluorescence
- Dynamic Light Scattering
- Particle Size
- **Diameter (nm)**

**ABSTRACT**

**C033 AACR-NCI-EORTC 2019**

**HPN328**

**Rationale**

- Each year more than 30,000 patients in the US are diagnosed with small cell lung cancer (SCLC).
- Median progression-free survival is 3–6 months and median overall survival 8–12 months with a 2-year OS rate of ~25%.
- Standard of care (SOC) for patients with extensive stage SCLC is radiation, etoposide, cisplatin or carboplatin, and prophylactic cranial irradiation. Although SCLC is often responsive to the SOC, treatment refractory, is common.
- DLL3 in a notch inhibitory ligand and is expressed in more than 70% of SCLC.
- DLL3 has little or no surface expression in normal adult tissues outside of the DVS.
- HPN328 is engineered to direct T cells to kill small cell lung cancer cells expressing DLL3.

**HPN328**

- Projected to enter a first-in-human clinical trial in the second half of 2020.

- Has a half-life of 2.8 to 3.3 days in Cynomolgus Monkeys.
- More than 15 half-lives in cynomolgus monkey blood.
- Dosing retains TDCC activity.

**HPN328**

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- Dosing retains TDCC activity.

**HPN328**

- A TriTAC that binds to human and cynomolgus DLL3, CD3e, and albumin.
- Directs T cells to kill DLL3 expressing cells in vivo.
- Inhibits tumor growth in models of small cell lung cancer.
- Has a terminal half-life in cynomolgus monkeys of 67–79 hours, stability of 1 week in circulation in cynomolgus monkeys.
- Anticipated to be an efficacious, safe, and convenient therapeutic for patients with DLL3 expressing malignancies.
- Projected to enter a first-in-human clinical trial in the second half of 2020.