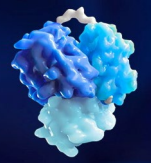
HARPOON
Therapeutics

Spearheading Immunotherapies

CORPORATE PRESENTATION
JANUARY 2024

Forward-looking Statements



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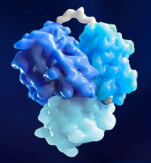
Advancing Next-Generation T Cell Engagers



Program	Indication(s)	Stage of Development: Preclinical	Phase 1	Phase 2	Phase 3
HPN328 (DLL3)	SCLC / NEPC and other Neuroendocrine Tumors				Roche[1]
HPN217 (BCMA)	Multiple Myeloma				
HPN601 (EpCAM)	Multiple Solid Tumors				
Preclinical Candidates					
TriTAC (FLT3, undisclosed)	Oncology				
ProTriTAC (TROP2, Integrin-β6, undisclosed)	Oncology				
TriTAC-XR (Undisclosed)	Oncology / Non-Oncology				
TriTAC, ProTriTAC (Undisclosed)	Oncology				abbvie[2]

TriTAC | ProTriTAC | TriTAC-XR

(1) Roche supply agreement established for the use of atezolizumab in combination with HPN328
(2) Research collaboration with AbbVie to select a fixed number of targets from these platforms

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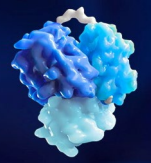
HPN328 Major Value Driver and Additional Opportunity in HPN217/601/Platform



LEAD ASSET HPN328 (DLL3 T-CELL ENGAGER)	• Potential for best-in-class efficacy in small cell lung cancer and neuroendocrine tumors • Confirmed response rate 35% across 1mg priming dose cohorts • Generally well tolerated at 1mg priming and target doses • Large markets with high unmet needs across various tumor types and lines of therapy offer opportunity for multiple products
HPN328 NEAR-TERM CATALYSTS	• Monotherapy dose optimization enrollment completed in October 2023 • RP2D identification YE 2023 • EOP1 meeting 1H 2024 • P1 data update 1H 2024 • Phase 2/3 registrational studies to begin in 2H 2024
ADDITIONAL VALUE DRIVERS	• HPN217 (BCMA) – Clinically active and tolerability profile differentiated • HPN601 (EpCAM) – IND ready, conditionally activated T-cell engager with large market potential • Multiple next-gen T-cell engager platforms – TriTAC®, ProTriTAC™, TriTAC-XR™
WELL FUNDED	• Supported by top-tier investor syndicate • October 2023 financing funds late-stage clinical trials of HPN328 in multiple tumor types

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Unaudited database cutoff as of 9/12/2023, subject to change

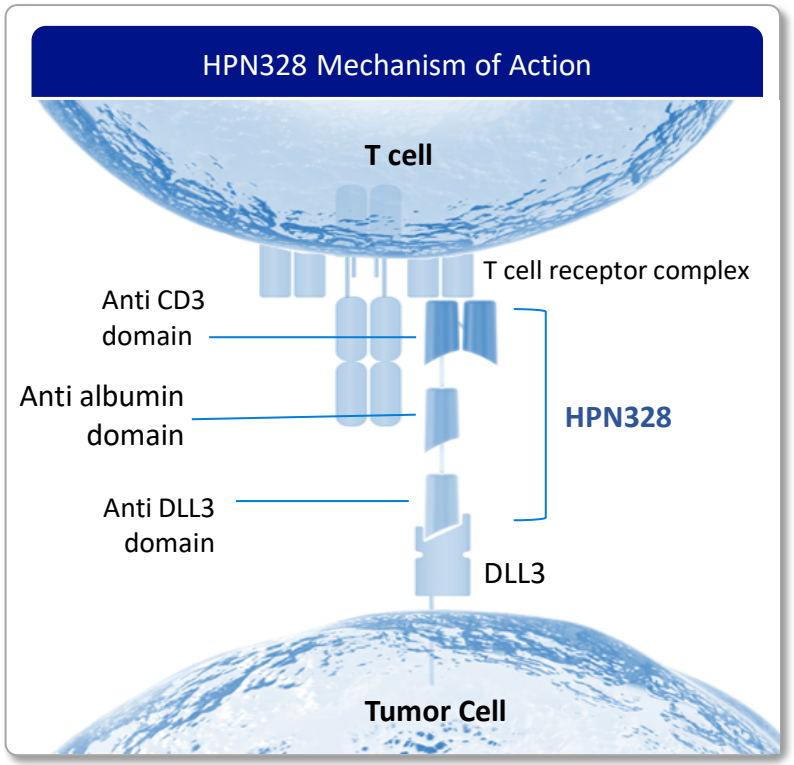
HPN328 Phase 1 Interim Update

Unaudited database as of 9/12/2023

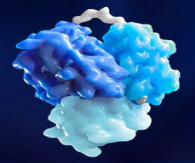
HPN328: A DLL3-TARGETED T CELL ENGAGER

- DLL3 is significantly expressed in SCLC and other neuroendocrine tumor types
- HPN328 is a DLL3-targeting T cell engager built on the TriTAC platform
  - Redirects T cells to kill DLL3-expressing cancer cells
  - Small protein (~50kDa) to potentially enable efficient solid tumor penetration with prolonged half-life
  - Designed to minimize non-specific T cell activation and Fc receptor engagement, intended to increase therapeutic window

HPN328 Mechanism of Action



HPN328 Phase 1 Trial



Target Population

- Extensive stage SCLC relapsed after platinum chemotherapy
- Neuroendocrine prostate cancer and other DLL3 expressing tumors with high grade neuroendocrine features relapsed/refractory to standard therapy

Trial Design

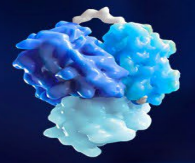
- Assess safety and tolerability at increasing dose levels
- PK and pharmacodynamic data
- Evaluate preliminary anti-tumor activity

Dosing & Administration

- IV infusion with weekly and Q2W administration schedules
- Monotherapy cohorts for all tumor types, and combination cohorts with atezolizumab for SCLC
- Premedication and step dosing to manage cytokine release syndrome (CRS)

Dose Escalation and Optimization Enrollment Nearing Completion

Monotherapy Cohorts - Q423; Combination Cohorts - 1H24



Dose Escalation 3+3 Design Including Fixed & Step Dose Cohorts and Dose Optimization (N=71)

Ongoing 1 mg priming Step-dose Escalation and Optimization Cohorts

	Monotherapy		Combination
	Q1W	Q2W	HPN328: Q2W + Atezo Q4W
1→6 mg N = 16			
1→12 mg	N = 8‡	N = 6‡	†
1→12→24 mg*	N = 8‡	N = 9‡	

* 1 mg to 24 mg cohorts use a 12 mg intermediate step up prior to moving to 24 mg target
† Atezo combination cohorts recently opened; data to be presented at later date
‡ Still enrolling: protocol allows for cohorts of up to 17 patients, depending on cohort

Early Fixed Dose & Step dose Escalation Cohorts

De-escalation to 1 mg prime

- 0.015-3.6 mg, N = 11
- 3.6→ 7.2 mg, N = 4
- 2→ 12 mg, N = 5
- 2→ 24 mg, N = 4

Early Step-dose Escalation Cohorts

Fixed-dose Escalation

Current 1mg Priming Cohorts

Planned Cohorts

Early Dose Escalation Cohorts

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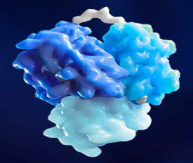
Phase 1 Population Includes Heavily Pre-treated Refractory Patients



Baseline Characteristics (N=71)

Age (Years)	
Median	64
Range	41-81
Sex	
Female	29 (40.8%)
Male	42 (59.2%)
Race	**n (%)**
White	65 (91.5%)
Asian	3 (4.2%)
American Indian or Alaska Native	1 (1.4%)
Multiple	1 (1.4%)
Unknown	1 (1.4%)

Diagnosis	
SCLC	46 (64.8%)
NEPC	11 (15.5%)
Other NENs	14 (19.7%)

Sites of Metastases	
Brain	29 (40.8%)
Liver	37 (52.1%)

ECOG	n (%)
0	29 (40.8%)
1	42 (59.2%)

# Prior Therapies	n (%)
Median	2.5
Range	1-8
PD(L)-1 Inhibitors	56 (78.9%)

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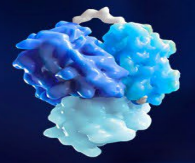
Adverse Events Manageable with No DLTs at Target Doses

No Grade 3 CRS with 1 mg Priming Regimens



Treatment-Related Adverse Events (TRAEs) Incidence ≥10% Patients by Grade [a] (N=71)

Adverse Events	All Grades, n (%)	Grade ≥3, n (%)
Any treatment-emergent AE	70 (98.6%)	33 (46.5%)
Any treatment-related AE	67 (94.4%)	18 (25.4%)
Treatment-Related AEs in ≥10% of patients		
Cytokine release syndrome (CRS)	42 (59.2%)	2 [c] (2.8%)
Dysgeusia	24 (33.8%)	0
Fatigue	24 (33.8%)	1 (1.4%)
Nausea	12 (16.9%)	0
Vomiting	11 (15.5%)	0
Diarrhea	10 (14.1%)	1 (1.4%)
Decreased appetite	8 (11.3%)	0
Neutropenia [b]	7 (9.9%)	4 (5.6%)
Pruritus	7 (9.9%)	0
Pyrexia	7 (9.9%)	0

Note: Post 9/12/2023 data cut-off, 1 Gr5 SAE (pneumonitis)

Adverse Events	Grade 1	Grade 2	Grade 3
CRS	21 (29.6%)	19 (26.8%)	2 [c] (2.8%)
ICANS [d]	4 (5.6%)	1 (1.4%)	0

No DLTs Observed at Target Doses; Target dose MTD Not Reached

ICANS=Immune effector cell-associated neurotoxicity syndrome

[a] Grading per CTCAE v5.0, except cytokine release syndrome (grading per ASTCT 2019)

[b] Includes both neutropenia and neutrophil count decreased

[c] Two Grade 3 CRS events were DLTs at 2 mg priming dose (above current priming dose)

[d] Immune effector cell encephalopathy (ICE) score for ICANS assessment performed at Screening and 6 times during Cycle 1; All events of ICANS were transient; none resulted in dose reduction

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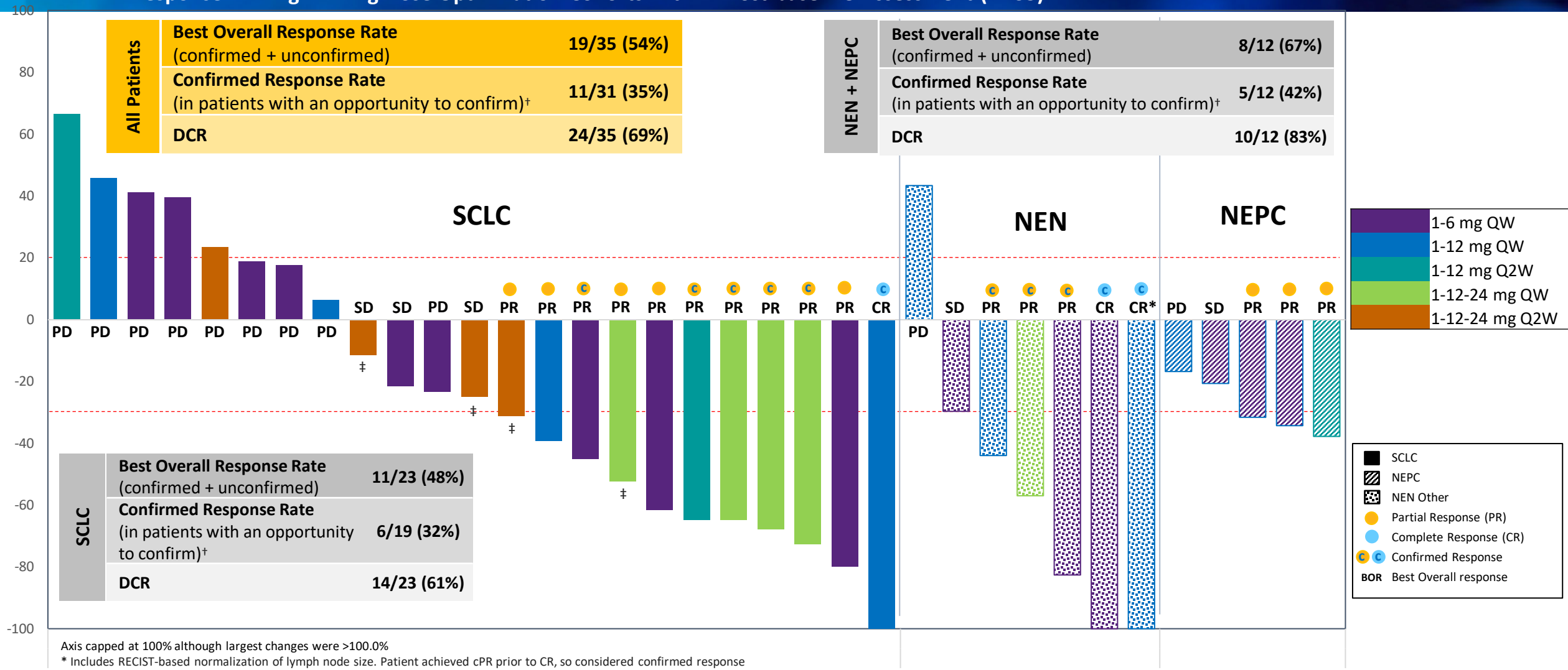
1 mg Priming Dose Regimens: Responses Across Tumor-Types

Cohorts will Inform Dose Optimization and Selection of RP2D Once Data Matures

Response In 1 mg Priming Dose Optimization Cohorts with ≥1 Post-baseline Assessment (N=35)



Axis capped at 100% although largest changes were >100.0%

* Includes RECIST-based normalization of lymph node size. Patient achieved cPR prior to CR, so considered confirmed response

† In patients with opportunity to have 2 scans or discontinued prior to confirmatory scan due to AE or PD

‡ Patients on study with only 1 imaging assessment to date

- Additional SCLC responses were seen in earlier dose escalation cohorts, including 1 unconfirmed response (0.405 mg), 2 confirmed responses (1.215 escalated to 3.6 mg and 2 mg/12 mg), and 1 additional EC-PR (3.6 mg/7.2 mg)

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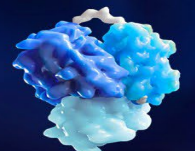
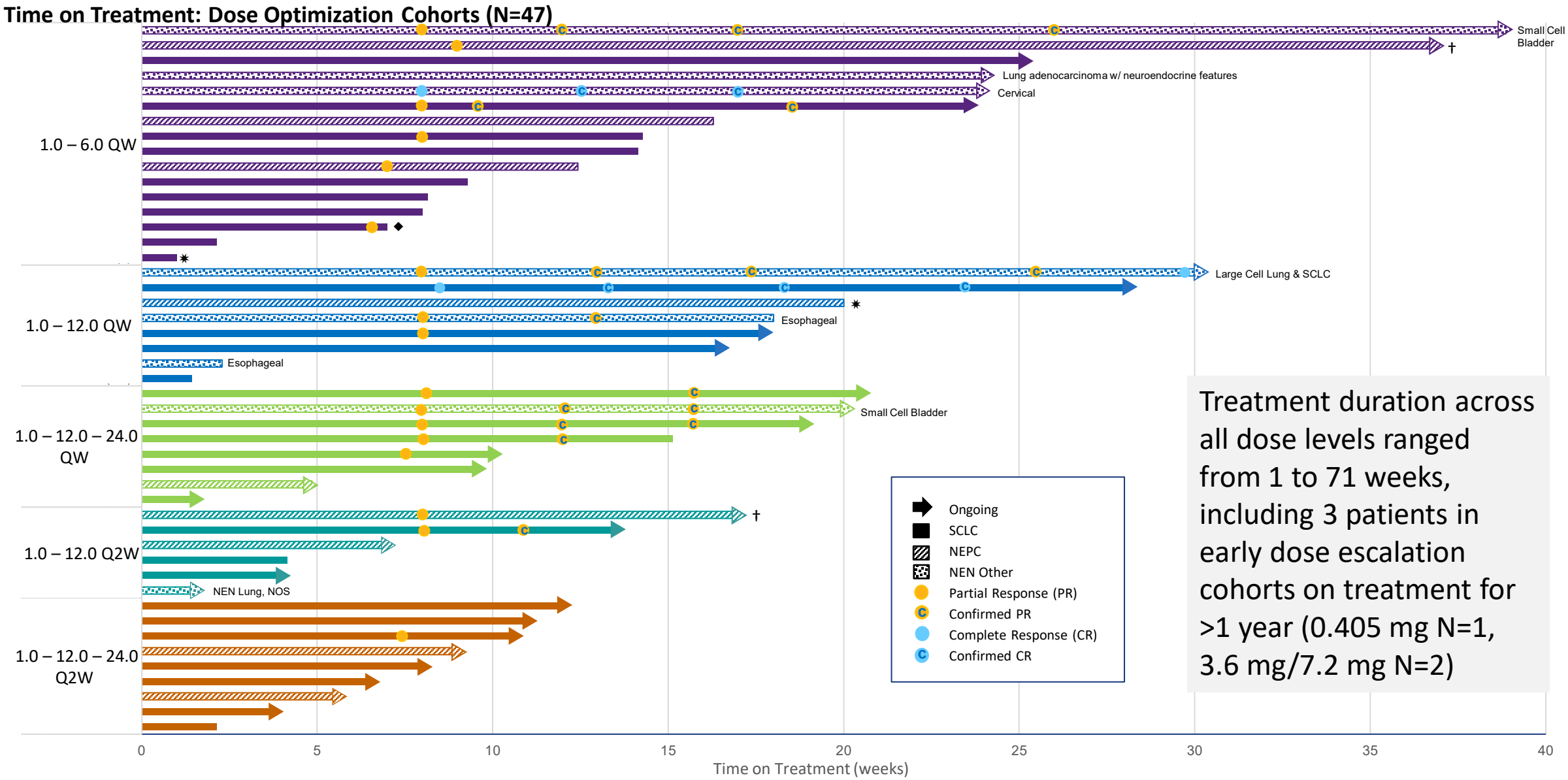
Prolonged Confirmed Responses Ongoing; Durability Data Maturing





Treatment duration across all dose levels ranged from 1 to 71 weeks, including 3 patients in early dose escalation cohorts on treatment for >1 year (0.405 mg N=1, 3.6 mg/7.2 mg N=2)

Off treatment for PD unless indicated otherwise; ✷Off treatment for withdrawal of consent. ◆ Withdrawal by Investigator for reasons other than an AE. † Patient continued treatment post PD for clinical benefit.

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HPN328 Patient Case: Relapsed ES-SCLC

Confirmed Complete Response

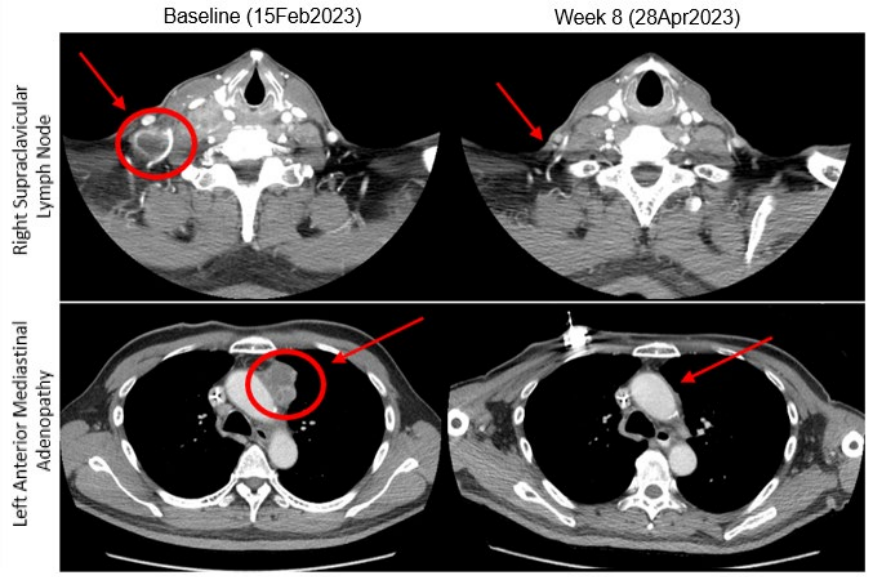
Patient History

- 61-year-old male
- Diagnosed in June 2021 with extensive-stage SCLC
- 60% cells positive for DLL3
- Location of metastases
  - TLs: lymph nodes x2
  - Non-TLs: Lymph nodes x4
- Prior systemic treatment
  - Cisplatin + Etoposide
  - Carboplatin + Etoposide + Atezolizumab
  - Investigational CCR-8 treatment
- Time on most recent prior systemic treatment
  - 4 weeks
- Upon study entry, refractory was best response to most recent prior systemic treatment

Results

- **HPN328: started on 1mg prime and 12 mg target dose/week**
  - Well tolerated
- **Complete Response at week 8, confirmed at week 12**
  - RECIST v1.1: Target Lesions: CR
- **Remains on HPN328 treatment with ongoing response at week 28, as of Sept 11, 2023**

Baseline **Wk 8 On Treatment**



100% reduction at wk 8

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HPN328 Patient Case: Relapsed Cervical Cell Carcinoma

Confirmed Complete Response

Patient History

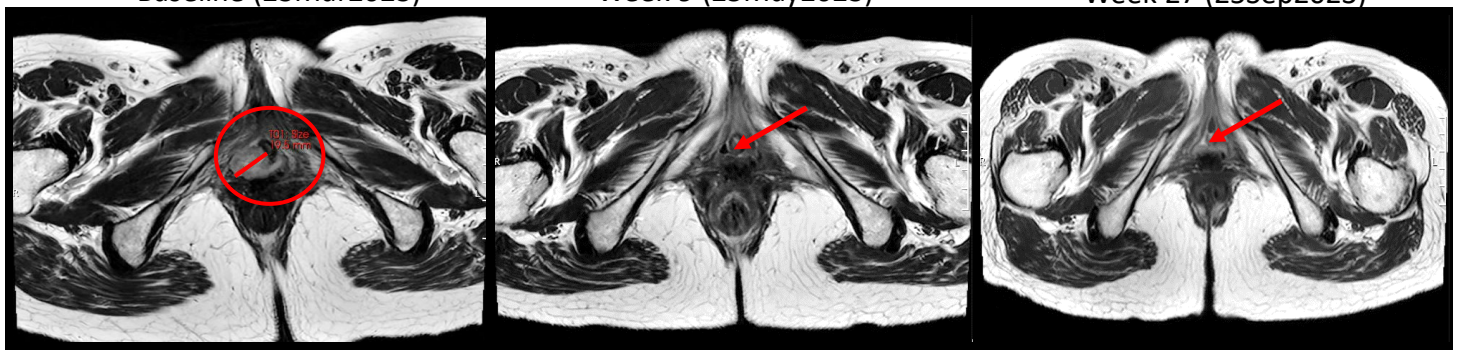
- 44-year-old female diagnosed in October 2021 with stage IV cervical small cell carcinoma
- Location of metastases
  - TL: Pelvis x1
  - Non-TLs: Lung x1
- Prior surgery, external beam radiation, and intracavitary brachytherapy x 3
- Prior systemic treatment
  - Carboplatin + Etoposide + Atezolizumab → Atezolizumab maintenance
- Time on most recent prior systemic treatment
  - 16 weeks
- Upon study entry, refractory was best response to most recent prior systemic treatment

Results

- **HPN328: started on 1mg prime and 6 mg target dose /week**
  - Well tolerated
- **Complete response at week 9, confirmed at week 13**
  - RECIST v1.1: Target Lesion: CR
  - 100% cells positive for DLL3
- **Ongoing response**
- **Remains on HPN328 treatment as of Sept 27, 2023**

Pelvic Recurrence

Pre-Treatment	Wk 9 On Treatment	Wk 27 On Treatment
Baseline (23Mar2023)	Week 9 (25May2023)	Week 27 (25Sep2023)



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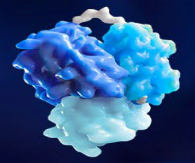
HPN328 - 1mg Priming Dose Cohorts

Clinically Active and Well Tolerated in Ongoing Dose Escalation Study



Potentially Best-in-class Efficacy

Active agent at 1mg priming dose cohorts at interim update

- 54% (19/35) overall response rate across all tumor types (SCLC, NEPC, other NENs)
- 32% (6/19) confirmed response rate in SCLC patients
- 5 of 7 confirmed responders in patients with other NENs
- 69% (24/35) disease control rate across all tumor types

Manageable Tolerability Profiles

Generally well tolerated at 1mg priming cohorts

- CRS events most common with initial priming dose administration
- Only Grade 1 and 2 CRS seen at 1mg priming cohorts
- No Grade 3+ ICANS

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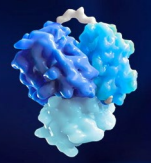
Large Addressable Population in SCLC and Other High Grade NENs with Significant Unmet Need



	7 Major Market Incidence[1]	5-yr Survival	DLL3 Expression (>1%)
Small Cell Lung Cancer	~90,000	7%[2]	82%[3]
Neuroendocrine Prostate Cancer (NEPC)	~20,000[4]	14%[5,6]	77%[7]
NET, High Grade	~11,500	mOS 10 months[8]	Highly expressed
Extrapulmonary NEC, except NEPC	~2,600	Stomach 9%[9] Rectum 11%[9] Colon 15%[9] Pancreas 20%[9] Small Intestine 43%[9] Appendix 65%[9]	Cervix 81%[10] Gastroentero-pancreatic 77%[11] Pancreas 19-50%[12] Bladder 68%[13]
LCNEC, Lung	~1,300	21%[2]	82%[3]

High grade NENs have an estimated annual incidence >120K across 7 major markets, mostly with high DLL3 expression

1. GlobalData Forecast 2023 incidence, 7 major markets (7MM) - US, Japan, France, Germany, Italy, Spain, UK; 2. SEER; 3. Lima et al. *Cancer Res* (2022); 4. Aparicio et al. *Cancer Discov* (2011); 5. Alabi et al. *Pharmacology & Therapeutics* (2022); 6. Bhagirath et al. *Sci Rep* (2021); 7. Puca et al. *Sci. Transl Med.* (2019); 8. Dasari, *JAMA Oncol.* (2017); 9. White, *Lancet* (2018); 10. Cimic, *Appl Immunohistochem Mol Morphol* (2021); 11. Liverani, *Endocr Onc* (2021); 12. Yao, *Oncologist* (2022); 13. Koshin, *Clin Cancer Res* (2019)

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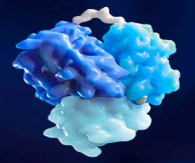
HPN217
Interim Update

IMS Poster Summary
September 28, 2023

HPN217 (BCMA)
Clinically Active and Differentiated Tolerability Profile at 12mg QW



Compelling Efficacy Data

Active Agent at 12mg target dose QW regimen

- 63% ORR, 53% with VGPR or better
- Durable response
- Median responder time on treatment 21.8 months (10.4-27.5+) in 2.15-6mg cohorts
- 12mg cohort response ongoing, current median responder time on treatment 8.3 months

Superior Tolerability

Low CRS and Serious Adverse Events

- 16% CRS and no ≥ grade 3 at 12mg target dose; 30% CRS in all patients
- No ICANS at 12mg target dose
- No DLT across all step dose regimens

Achievements & Milestones

- Full data presented at ASH in December 2023
- RP2D selection YE 2023
- Seek partner to support development plan in R/R MM

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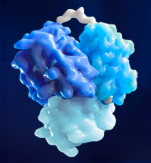
HPN601 (EpCAM)

HPN601 (EpCAM)

First IND from Harpoon's ProTriTAC Platform Targeting EpCAM



- EpCAM is overexpressed in many tumor types, expression is also found on normal tissues
- HPN601 is engineered to preferentially target tumors and spare normal tissues
- Large addressable population with high unmet need
- No actively marketed systemic therapies targeting EpCAM
- Next steps
  - IND filing to enable a Phase 1 dose exploration study dependent on available resources

Tumor	EpCAM Expression[1] (% mod./high expression by IHC)	HPN601 Population[2,3] (est. annual incidence in USA)
Prostate	89	171,000
NSCLC	74	147,000
Breast	46	128,000
Colon	94	99,000
Endometrial	88	58,000
Thyroid	87	46,000
SCLC	75	22,000
Gastric	74	21,000
Ovarian	73	16,000
Esophageal	65	12,000
Neuroendocrine	88	11,000
Gallbladder	66	8,000
Total		**729,000**

[1]Based on Spizzo et al., J Clin Pathol, 2011. [2]Estimated annual incidence in US, rounded to the nearest 1,000, based on the American Cancer Society's (ACS) publication, Cancer Facts & Figures 2020, multiplied by the percentage of moderate and high EpCAM expression. [3] The neuroendocrine tumor annual incidence taken from ASCO Cancer.net. Exemplary IHC figures adapted from proteinatlas.org.

T Cell Engager	Route of Admin.	Clinical Results
Solitomab / AMG110 (Amgen)	Systemic	Program stopped due to on-target tox[1] MTD: 24 µg/day Anti-tumor activity noted at 2 - 4x MTD
Catumaxomab (Fresenius)	Intraperitoneal	Approved in 2009 for malignant ascites in EU[2] Not tolerated as systemic therapy[3]

1. Kebenko, OncoImmunol 2018. 2. Parsons, ASCO 2008. 3. Mau-Sorensen, Cancer Chemother Pharmacol 2015.

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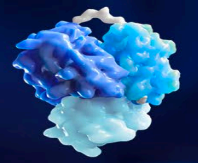
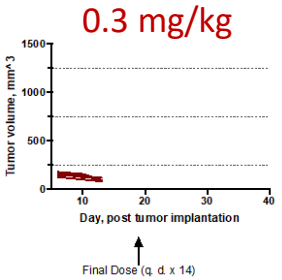
EpCAM ProTriTAC: 10x Therapeutic Index Expansion in an Established Tumor Model



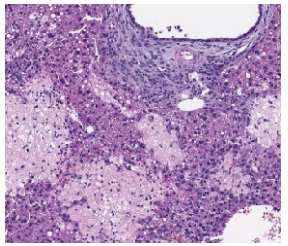
	Minimum Efficacious Dose (LoVo)	Maximum Tolerated Dose	Therapeutic Index (TI)
TriTAC	0.03 mg/kg	0.03 mg/kg	1
ProTriTAC	0.1 mg/kg	1 mg/kg	10
		ProTriTAC Advantage	**10x**

Conventional T Cell Engager:

Efficacy (Tumor growth)

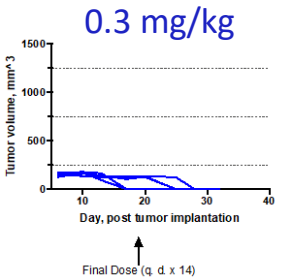


Safety (Liver H&E Stain)

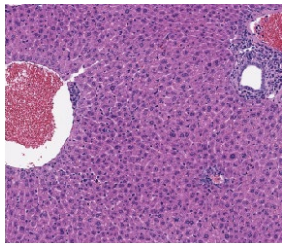


ProTriTAC:

Efficacy (Tumor growth)



Safety (Liver H&E Stain)



- **Therapeutic index expansion demonstrated:** efficacy + tox in the **same** animal
  => Identical drug exposure for efficacy and safety assessment
- **Preclinical model validated:** similar on-target tissue tox in mouse and in human[1]
- **Robust in vivo performance:** TI expansion demonstrated across different targets

1. Kebenko, OncoImmunol 2018. A multicenter phase 1 study of solitomab (MT110, AMG110), a bispecific EpCAM/CD3 T-cell engager (BiTE®) antibody construct in patients with refractory solid tumors
2. Lin et al., AACR 2021 poster presentation available on Harpoon's website

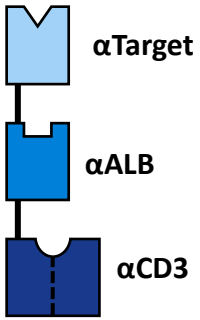
HARPOON Therapeutics

Harpoon's T Cell Engager Platforms Designed to Address Broad Number of Targets and Tumor Types

TriTAC®

Tri-specific T cell activating construct platform

Active

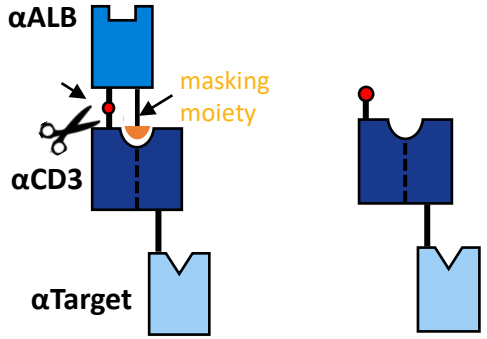


- Designed to minimize off-target toxicities by reducing nonspecific T cell activation
- Best suited for targets with restricted normal tissue expression
- Multiple active clinical-stage programs

ProTriTAC™

Prodrug activation in tumor micro-environment

Prodrug Long-lived → ***Activation in tumor micro-environment*** → **Active** Short-lived

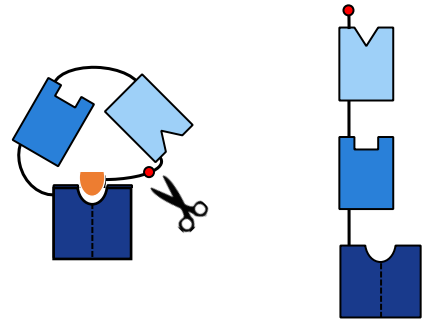


- Designed to minimize toxicities by preferential activation within tumor
- Best suited for targets expressed in both tumor and normal tissue
- Lead program in IND-enabling studies

TriTAC-XR™

Prodrug activation in systemic circulation

Prodrug → ***Slow activation in circulation*** → **Active**



- Designed to maximize systemic exposure while minimizing CRS
- Heme malignancies and solid tumors with potential expansion to non-oncology
- Finalizing platform validation

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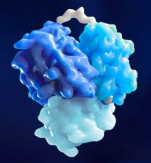
Focus on Execution: Accomplishments and Upcoming Milestones



HPN328 (DLL3)
SCLC, NEPC and other neuroendocrine tumors

- ✓ Positive interim results from P1/2 trial presented at ESMO 2023
- ✓ Completed monotherapy dose optimization enrollment
- Monotherapy P2 dose selection YE 2023
- Combination dose escalation cohorts with atezolizumab enrolling
- Discuss RP2D and late-stage development plans with regulators in 1H 2024
- P1 data update 1H 2024
- Expect to begin P2/3 registrational trial(s) in 2H 2024

HPN217 (BCMA)
Multiple myeloma

- ✓ Demonstrated early and durable responses in P1 trial for RRMM at IMS 2023
- ✓ P1 study results oral presentation at ASH 2023
- ✓ RP2 regimen(s) identified by YE 2023

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Nasdaq: HARP