



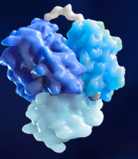
HARPOON
Therapeutics

Spearheading Immunotherapies

CORPORATE PRESENTATION
MAY 16, 2023

Nasdaq: HARP

Forward-looking Statements

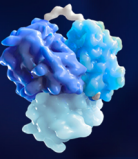


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Clinical-Stage Immuno-Oncology Company

Directing T Cells to Kill Tumors



Advancing a Portfolio of Novel T Cell Engagers (TCEs)

Clinical Pipeline

Addressing broad patient populations

- Clinical-stage T cell engagers across multiple indications
- Clinical benefit seen in hematological and solid tumor settings:
 - Confirmed responses, tumor lesion reductions deepening over time
- Emerging clinical data validate TriTAC platform designed to maximize the therapeutic window

Novel TCE Platforms

Solid and hematological tumors

- Platform technologies allowing for “off-the-shelf” T cell therapies
- Treating broad patient populations with unmet needs
- Addressing solid and hematologic malignancies
- Each platform designed to maximize the therapeutic window

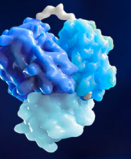
Strong Capabilities

Industry veterans developing novel TCEs

- Deep expertise in oncology, T cell engagement, and protein engineering
- Cash runway expected to fund operations into the second half of 2024
 - \$61.4M in cash, cash equivalents & short-term marketable securities,* including:
 - \$25M preferred equity financing closed in March 2023
- Strong patent protection across platforms and programs

Broad Pipeline of Immuno-Oncology Programs

Advancing Next-Generation T Cell Engagers



Program	Indication(s)	Stage of Development				Partner
		Preclinical	Phase 1	Phase 2	Phase 3	
HPN217 (BCMA)	Multiple Myeloma	<div></div>				abbvie ¹
HPN328 (DLL3)	Small Cell Lung Cancer / Other Solid Tumors	<div></div>				<div>Roche</div> atezolizumab Supply Agreement ²
HPN536 (Mesothelin)	Ovarian, Pancreatic / Other Solid Tumors	<div></div>				
HPN601 (EpCAM)	Multiple Solid Tumors	<div></div>				
Preclinical Candidates						
TriTAC (undisclosed)	Oncology	<div></div>				abbvie ³
ProTriTAC (EGFR, TROP2, Integrin-β6, undisclosed)	Oncology	<div></div>				abbvie ³
TriTAC-XR (FLT3, B Cell Targeting, undisclosed)	Oncology / Non-Oncology	<div></div>				

(1) AbbVie retains an option to worldwide exclusive rights (HPN217)

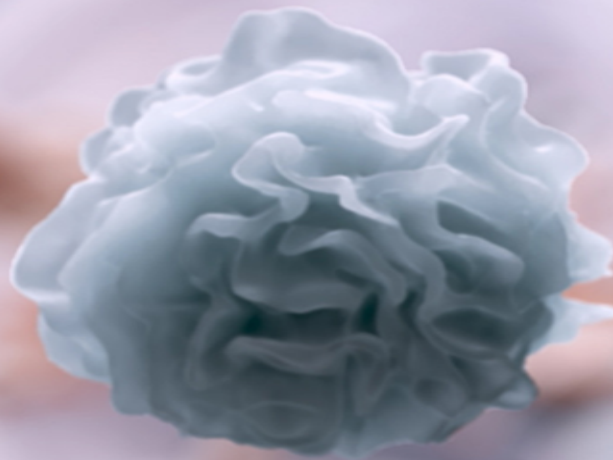
(2) Roche supply agreement established for the use of atezolizumab in combination with HPN328

(3) AbbVie entered in a discovery platform collaboration to select a fixed number of targets from these platforms

TriTAC **ProTriTAC** **TriTAC-XR**

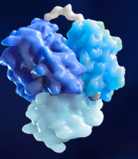
TriTAC®
HPN217
Targeting BCMA

**Interim Data
Presented at
ASH 2022**

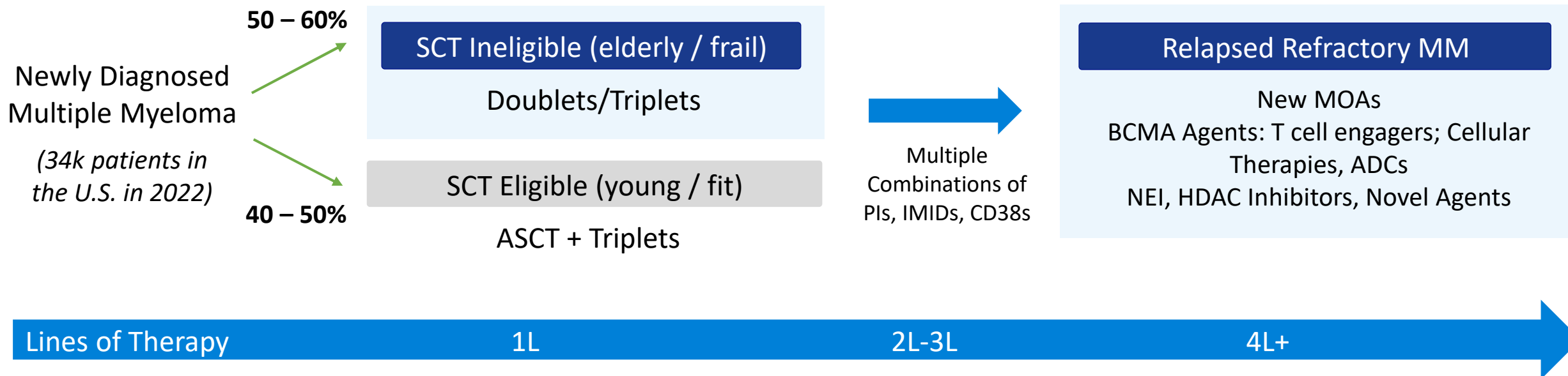


Multiple Myeloma: High Unmet Need Remains

Multiple Development Opportunities in a Rapidly Evolving Landscape



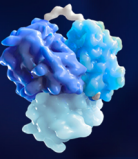
- 58% overall 5-year survival rate in U.S. increasing over time¹, creating **need for multiple lines of therapy**
- BCMA agents beginning to redefine RRMM treatment, with **opportunities to improve upon tolerability, efficacy, and accessibility**
- BCMA agents with improved tolerability have future potential to be **developed in the early line setting**



¹ Over time period 2012 and 2018 Cancer stats Facts: Myeloma <https://seer.cancer.gov/statfacts/html/mulmy.html>

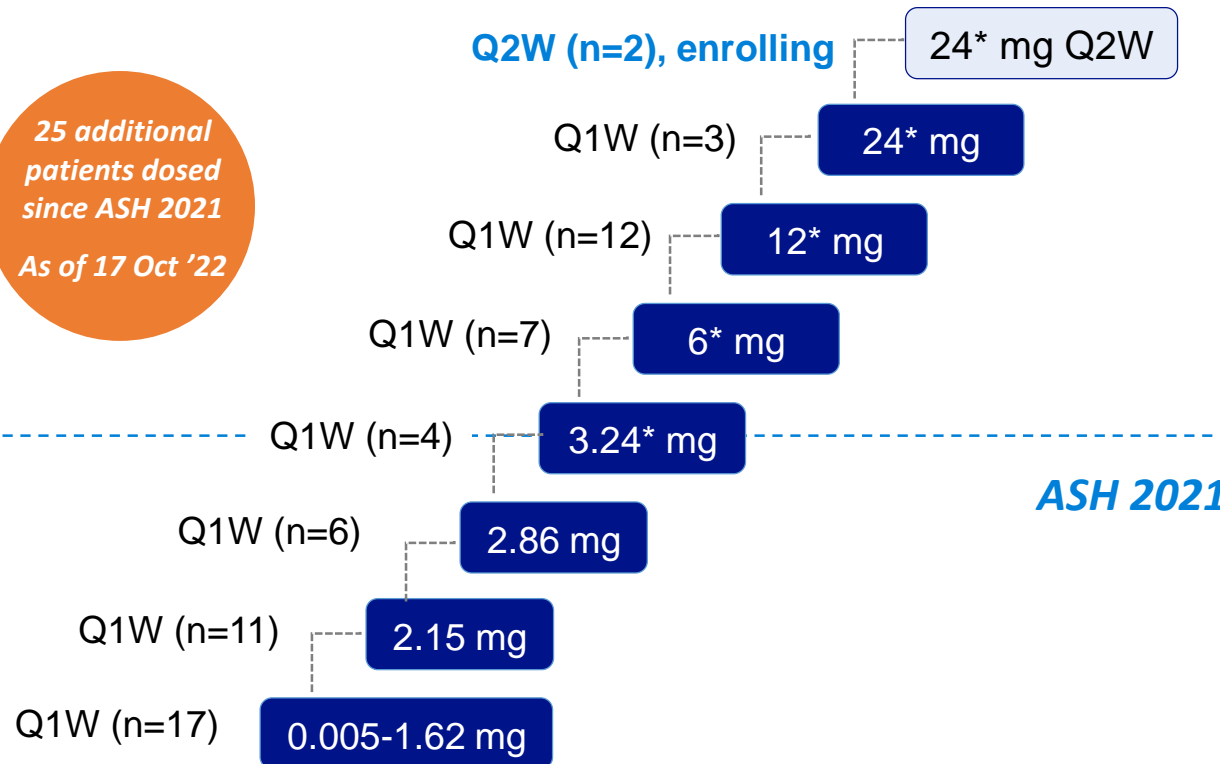
BCMA means B-cell Maturation Antigen; RRMM means Relapsed/Refractory Multiple Myeloma, SCT means Stem Cell Transplant (Accessed Oct 2022); Global Data, 2019; Strassel L; Schreder, M, 2021; KOL Interviews

HPN217-3001 Phase 1 Trial Design Relapsed/Refractory Multiple Myeloma



Dose Escalation 3+3 Design

25 additional
patients dosed
since ASH 2021
As of 17 Oct '22



Fixed- and Step-Dose Escalation Cohorts: 3-6 patients per dose level;
Backfilling permitted; * Step-Dose Regimen

Key Eligibility Criteria

- Relapsed/refractory multiple myeloma
- ≥ 3 prior therapies, including PI, IMiD, and anti-CD38
- Prior BCMA-targeted therapies allowed

Trial Design

- Primary Objectives: Safety, PK, Establish MTD or RP2D
- Secondary Objectives: Clinical Activity per IMWG Criteria

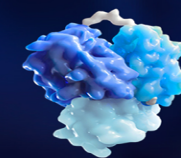
Dosing & Administration

- HPN217 administered by 1-hour IV infusion as flat dose
- Premedication for Cytokine Release Syndrome (CRS) prophylaxis

Next Steps

- Currently enrolling initial bi-weekly dosing cohort
- Dose optimization and backfill ongoing, with final cohort plans to be based upon emerging data

HPN217: Study Patient Population Represents Real-World, Late-Line Population with High-Risk Features



Baseline Characteristics and Demographics

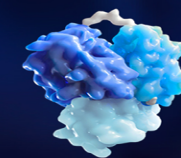
Baseline Characteristics	Total N = 62
Age (yr), Median (range)	70 (38 – 83)
Age ≥ 75 years, n (%)	12 (19%)
Time Since Initial MM Diagnosis (yr), Median (range)	8 (1 – 20)
Baseline sBCMA (ng/mL), Median (range)	240 (27– 2444)
ECOG, n (%)	
0	14 (23%)
1	46 (74%)
Missing	1 (2%)
Revised ISS Stage at Study Entry, n (%)	
I	16 (26%)
II	17 (27%)
III	26 (42%)
Missing	3 (5%)

Prior Systemic Therapies

Prior Cancer Therapy	Total N = 62
Prior Systemic Therapies, Median (range)	6 (2-19)
Prior Transplantation, n (%)	46 (74%)
Exposure Status, n (%)	
Triple-class ^a exposed	58 (94%)
Penta-drug ^b exposed	41 (66%)
BCMA exposed	13 (21%)
Relapsed/Refractory Status, n (%)	
Triple-class ^a refractory ^c	47 (76%)
Penta-class ^b refractory ^c	26 (42%)
BCMA refractory ^c	11 (18%)

^aIMiD, PI, and anti-CD38; ^bAt least 2 Pis, at least 2 IMiDs, and at least 1 anti-CD38 antibody; ^cNo response to regimen or discontinued regimen due to progression, adapted from Rajkumar et al (Blood 2011)

HPN217: Safety Summary



Common Treatment-Emergent Adverse Events (Regardless of Relationship), ≥15%

AE Preferred Term	All Grades (N=62) ^a	≥ Grade 3 (N=62) ^a
Anemia	27 (44%)	21 (34%)
Fatigue	20 (32%)	2 (3%)
Cytokine release syndrome ^b	17 (27%)	0 (0%)
Headache	15 (24%)	0 (0%)
Hypokalemia	13 (21%)	2 (3%)
Nausea	13 (21%)	0 (0%)
Back Pain	11 (18%)	1 (2%)
Diarrhea	11 (18%)	1 (2%)
Hypophosphatemia	11 (18%)	4 (7%)
AST increased	11 (18%)	5 (8%)
Cough	11 (18%)	0 (%)
Arthralgia	10 (16%)	1 (2%)
Neutrophil count decreased	10 (16%)	8 (13%)
Dyspnea	10 (16%)	2 (3%)
ALT increased	9 (15%)	4 (7%)
Constipation	9 (15%)	0 (%)
Hypercalcemia	9 (15%)	1 (2%)

• Dose Limiting Toxicity

- Fixed Dose: 2 patients at 2.86 mg/week, reversible transaminitis (Gr 3, n=1; Gr 4, n=1), no clinical sequelae
- Step Dose: No DLTs; MTD not reached

• Neurologic/Psych Events^c

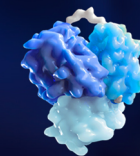
- **Treatment related** events reported in 10 patients
 - All events Grade 1 - 2
 - Most common: Headache (n=6) and Confusion (n=2)

• Infections^d

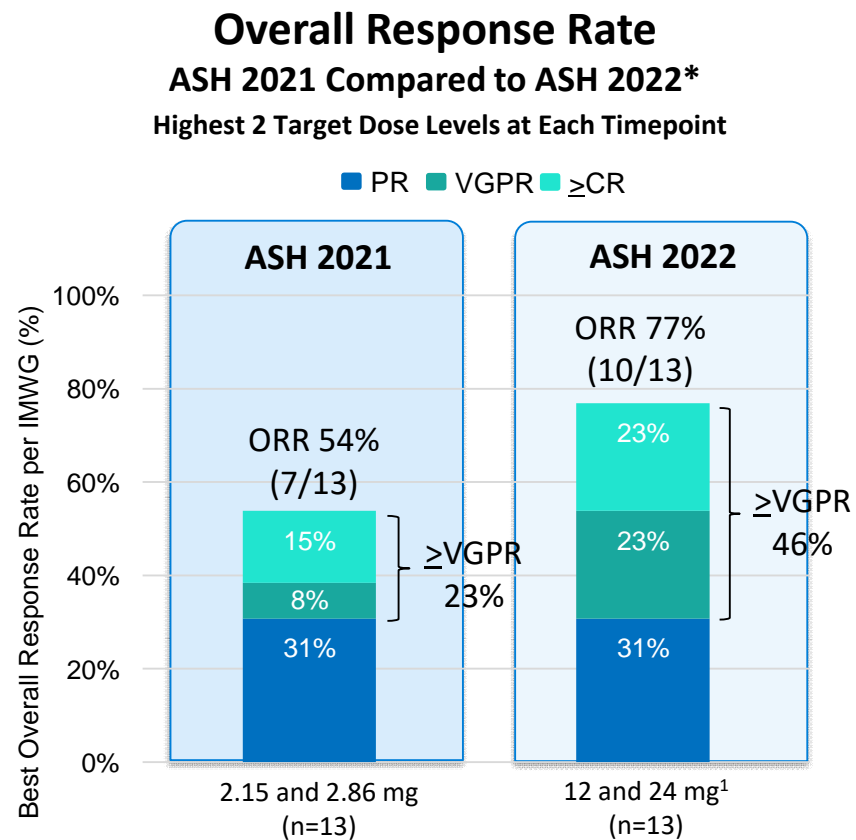
- Reported in 28 (45%) patients (Gr 3/4, 16%)
- Most common: Pneumonia (n=6), upper respiratory tract infection (n=5) and urinary tract infection (n=5)

^a Grading per CTCAE v5.0; ^b Grading per ASTCT 2019 Criteria; ^c SOC nervous system disorders and psychiatric disorders; ^d SOC infections and infestations

HPN217: ORR and CRS Rates Suggest Potentially Differentiated Profile with Widened Therapeutic Index

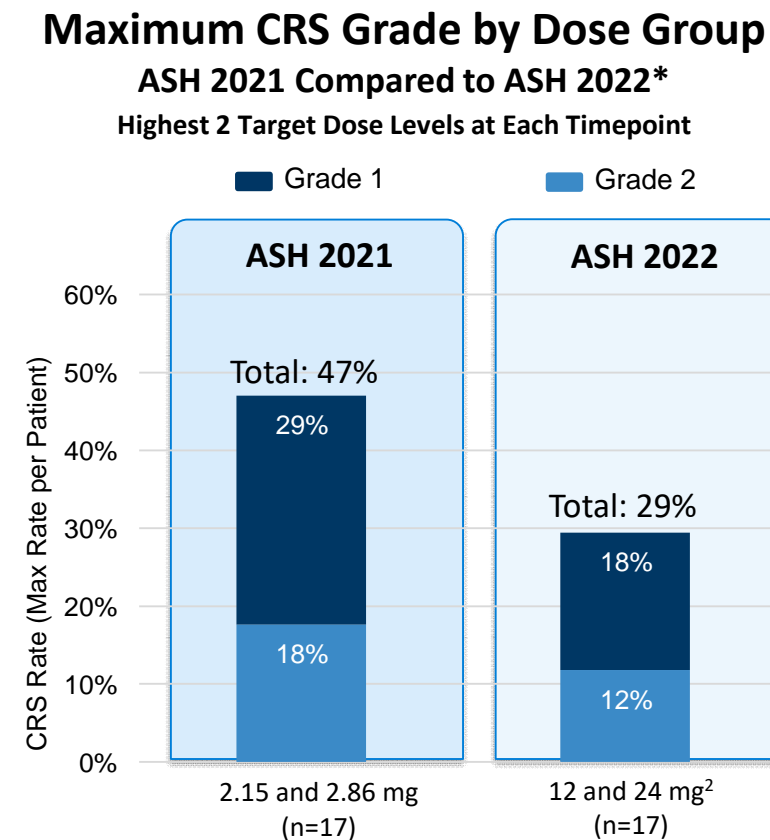


ORR



Confirmed and Unconfirmed Responses per Investigator Assessment
Disease-evaluable patients shown with at least 1 post-baseline assessment

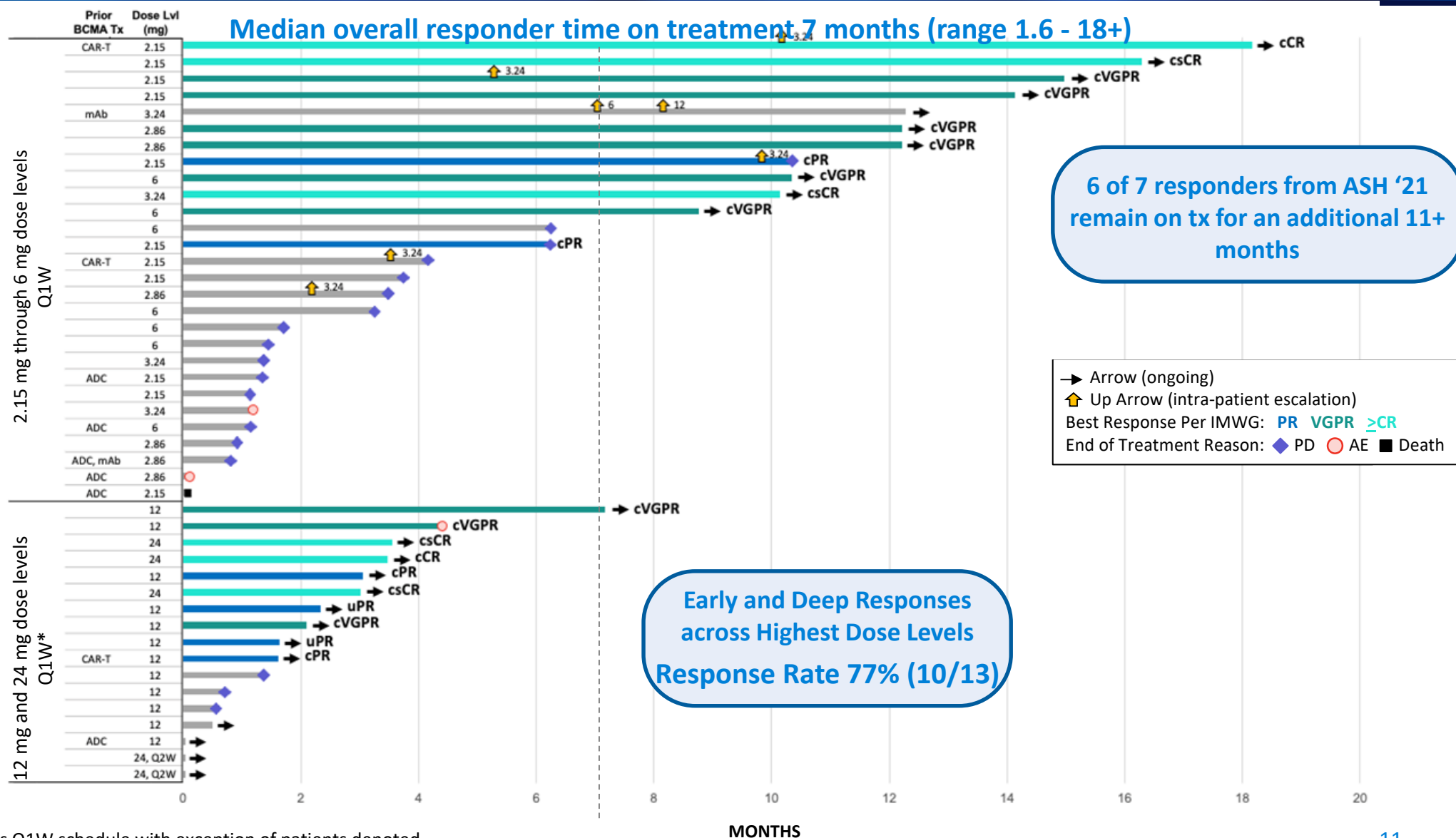
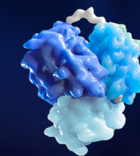
CRS

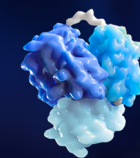


Grading per ASTCT 2019 Criteria
All patients shown who received ≥1 dose HPN217

HPN217: Time on Treatment at Target Doses ≥ 2.15 mg

Deep Early Responses Observed at Highest Exposures





Profile Emerging with Opportunity to be Best-in-Class T Cell Engager Targeting BCMA

Active Agent¹

- **77% (10/13) ORR** observed across highest step-dose levels (12 and 24 mg)
- **Responses occurred early and were durable**; for patients with at least 9 months follow up, the median responder time on treatment is 12 months
- 18 of 21 responders remain on study treatment with sustained response, **with many responses deepening over time**

Well Tolerated Safety Profile Emerging

- Transient CRS in 29% of patients across highest step-dose levels (12 and 24mg)
- Post ASH 2022, 1 patient experienced Gr3 CRS and Gr1 ICANS at 24 mg target dose followed by post-traumatic Grade 5 subdural hematoma
- **Overall, low incidence of CRS across the patient population studied to date**

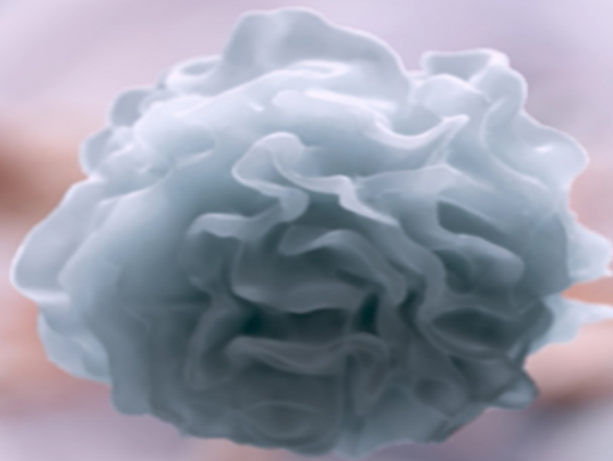
Anticipated Near-Term Milestones

- **Dose expansion and backfill cohorts continue to enroll at target dose of 12mg and 24mg**
- **Phase 1 study enrollment anticipated to complete** in 1H 2023, with up to potentially 94 patients, based on data from dose escalation cohorts
- Anticipate identification of a recommended Phase 2 dose(s) by YE 2023
- **Data update** anticipated in 2H 2023

¹ Relative to other BCMA-targeted TCEs in heavily pretreated patients across the highest step-dose cohorts

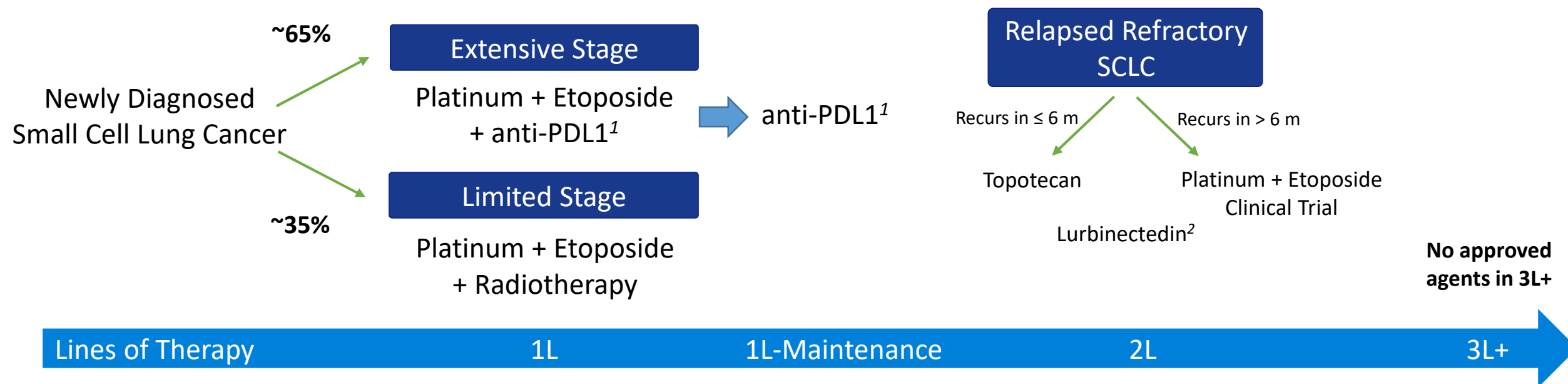
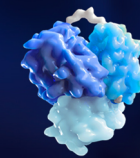
² ICANS means Immune effector cell-associated neurotoxicity syndrome

TriTAC®
HPN328
Targeting DLL3



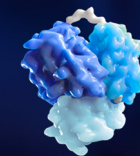
Small Cell Lung Cancer Standard of Care

Limited effective options available in the relapsed/refractory setting



HPN328: Trial Design and Demographics

A Phase 1/2 Open-Label, Multi-Center, Dose Escalation / Expansion, Safety & PK Study



- **Target population**

- SCLC relapsed after platinum chemotherapy
- Other high-grade neuroendocrine cancers R/R to standard of care (SOC) or no SOC available

- **Trial objectives**

- Assess safety and tolerability at increasing dose levels
- Characterize PK and PD
- Evaluate preliminary anti-tumor activity

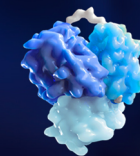
- **Dosing and administration**

- Weekly IV infusion

- **Status**

- 29 patients enrolled at the end of 2022
- Currently enrolling backfill patients in 1mg – 6mg cohort; enrollment continuing in dose escalation 1mg – 12 mg cohort

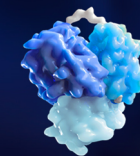
Baseline Characteristics	Total N = 22
Age (yr), Median (range)	61 (43 – 73)
ECOG performance status 0-1, n (%)	22 (100)
Brain / Liver metastases, n (%)	8 (36) / 11 (50)
Disease	n (%)
Small Cell Lung Cancer	15 (68)
Neuroendocrine Prostate Cancer	2 (9)
Other Neuroendocrine Neoplasm	5 (23)
Prior Lines of Therapy	n (%)
1	5 (23)
2	5 (23)
≥3	12 (54)
Median (range)	3 (1-6)
Prior immune checkpoint inhibitor (αPD-1/αCTLA4, αPD-L1)	18 (82)



- Recent priming dose DLTs inform optimization of priming dose to support further escalation of target dose¹
- TriTAC platform designed to minimize CRS risk and allow for greater escalation of target dose, and re-escalation of target dose is underway
- **No** DLTs at target dose
- Target dose MTD **not yet reached**

HPN328: Clinical Summary

Anti-tumor Activity Seen in Small Cell Lung Cancer at Higher Doses

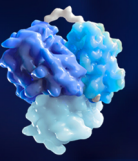


- HPN328 was observed to be active ¹
 - 71% (5/7) of SCLC patients at doses $\geq 1.215\text{mg}$ had target lesion shrinkage
 - 25% (3/12) of SCLC patients across all doses with $>30\%$ Target Lesion Shrinkage
 - 1 Confirmed Partial Response, durable beyond 6 months
- Treatment duration ≥ 5 months was observed in 7 of 20 (35%) patients
- Median half-life of 71 hours, with linear pharmacokinetics
- **Update as of February 2023:** 1 additional Confirmed Partial Response was observed in a SCLC patient in the 2-12mg QW cohort who remains on treatment

HPN328 Patient Case 1: Relapsed ES-SCLC

53% Reduction in Sum of Target Lesion Diameters at Week 10: Confirmed PR

Data as of October 10, 2022

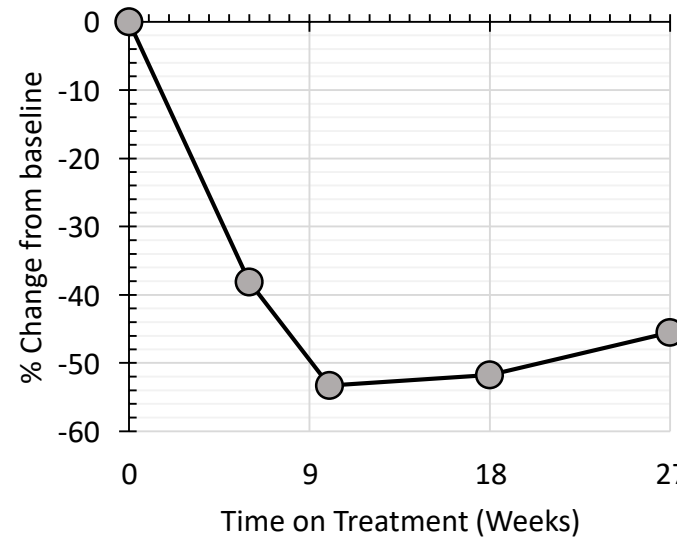


Patient History

- 61-year-old female
- Diagnosed Jan 2021 with extensive-stage SCLC
- Location of metastases:
 - TLs: lung, liver x2, lymph nodes x2
 - Non-TLs: lung x2, liver
- Prior systemic treatment:
 - carboplatin + etoposide + atezolizumab
- Time on most recent prior systemic treatment: 20.1 weeks
- Upon study entry, **stable disease as best response** to most recent prior systemic treatment

Results

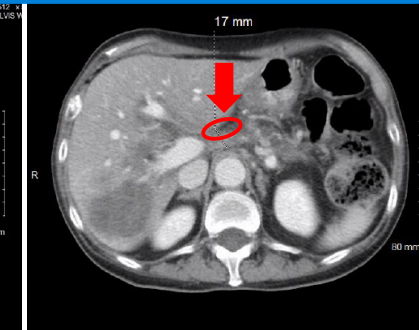
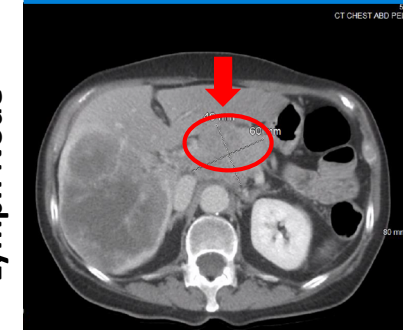
- Initiated HPN328 at 1.215mg/week, later dose escalated
- **Confirmed PR at week 10**
- Continued treatment with HPN328 for 33 weeks



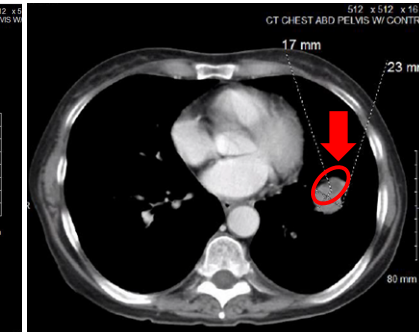
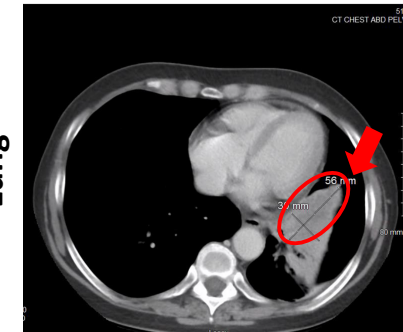
Pre-Treatment

Week 10 On Treatment

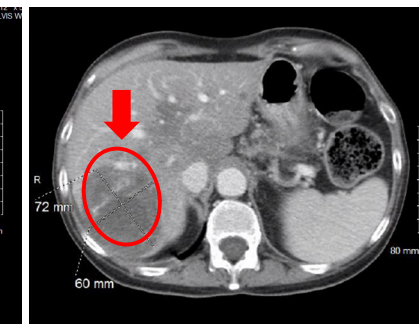
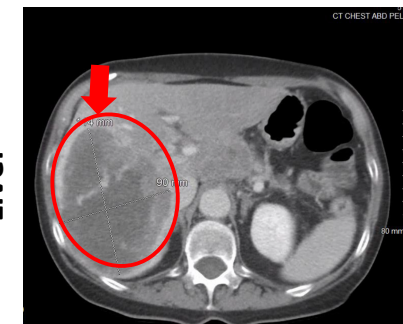
Lymph Node



Lung



Liver



53% reduction at wk 10

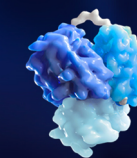
Unaudited patient data based on entries provided in open clinical database as of 10/10/2022 (subject to change)

HPN328 Patient Case 2: Relapsed ES-SCLC

72% Reduction in Sum of Target Lesion Diameters

Deepening of response over time continuing beyond ASCO 2022 data

Data as of October 10, 2022

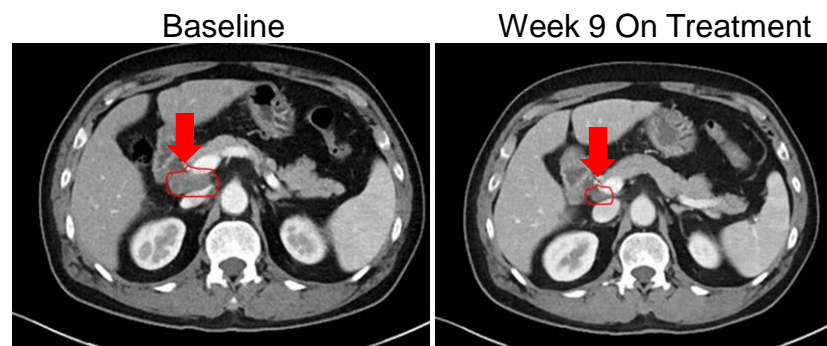


Patient History

- 67-year-old male
- Diagnosed in April 2020 with extensive-stage SCLC
- Location of metastases
 - TLs: liver x2, lymph nodes x2
 - Non-TLs: liver, lymph nodes x2, spleen, bone, brain
- Prior systemic treatment
 - Carboplatin + Etoposide + Toripalimab
 - Cisplatin + Etoposide
 - Lurbinectedin
- Time on most recent prior systemic treatment
 - 10.9 weeks
- Upon study entry, partial response as best response to most recent prior systemic treatment but unable to tolerate further treatment

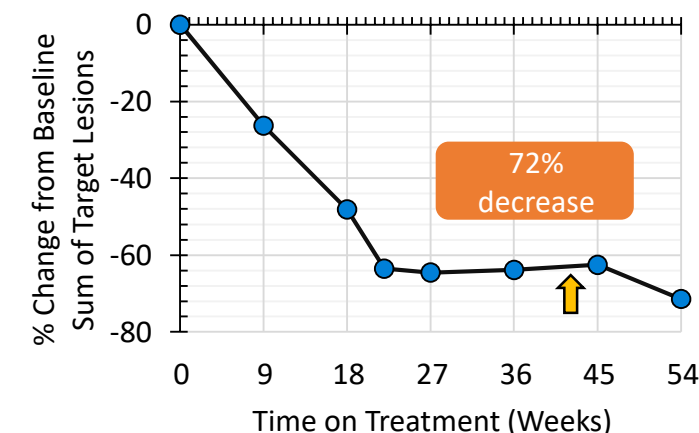
Results

- **HPN328 3.6 → 7.2 mg/week (increased to 12 mg/week)**
 - Well tolerated
- **72% reduction in sum of target lesion diameters**
 - Asymptomatic brain metastasis identified at week 2
 - Systemic disease responding to HPN328
 - RECIST v1.1: Target Lesions: PR; Overall: PD
 - 60% cells positive for DLL3
- **Deepening of radiographic target lesion response over time**
- **Remains on HPN328 treatment beyond 54 weeks**
 - At ASCO 2022 (April 21, 2022 data) was at 27 weeks
 - Current data: **ongoing clinical benefit observed beyond 1 year**

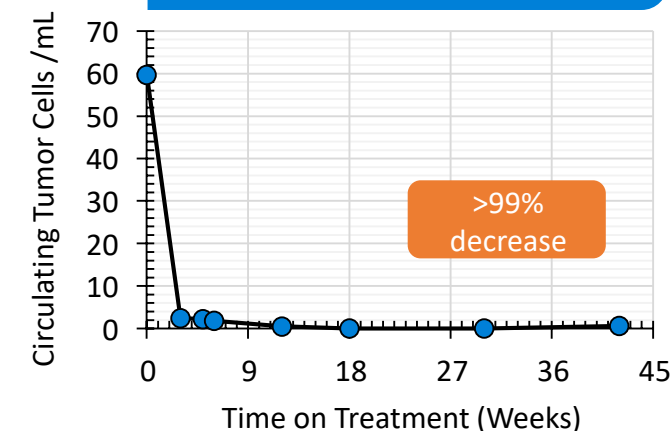


Response in peri-portal lymph node

Deep, durable target lesion shrinkage

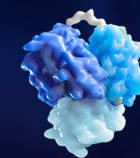


Durable >99% decrease in CTCs



↑ = Dose Increase

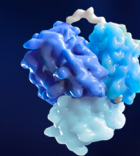
HPN328: Anticipated Next Steps



- Continue Phase 1 enrollment in the dose exploration study
 - Monotherapy cohorts:
 - 1 mg – 6 mg step dose cohort enrolled and cleared for escalation
 - 1mg – 12mg step dose cohort enrolled and cleared for escalation
 - 29 patients were enrolled at year end 2022
 - Enrollment started in Q2W dosing cohorts for HPN328 monotherapy planned
 - Combination cohorts:
 - Begin enrollment in 2H2023 of additional cohorts in the Phase 1 dose escalation part of the study to evaluate HPN328 in combination with atezolizumab in SCLC
- Anticipate Phase 1 interim data in 2H 2023 for the highest target doses studied
 - Plan enrollment up to potentially 70 patients with ≥ 1 on-treatment scan by end of Q2 '23*
- Plan for enrollment of up to 100 patients in monotherapy (including backfill) by mid-2023*
- Phase 1 dose exploration expected to complete in 2H-2023, including the identifying of a recommended Phase 2 dose(s) in the monotherapy setting by YE 2023

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 timeline to enable a Phase 1 dose exploration study dependent on availability of resources

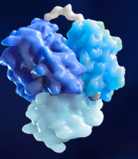
Tumor	EpCAM Expression ¹ (% mod./high expression by IHC)	HPN601 Population ^{2,3} (est. annual incidence in USA)
Prostate	89	171,000
NSCLC	74	147,000
Breast	46	128,000
Colon	94	99,000
Endometrial	88	58,000
Thyroid	87	46,000
SCLC	75	22,000
Gastric	74	21,000
Ovarian	73	16,000
Esophageal	65	12,000
Neuroendocrine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

¹Based on Spizzo et al., J Clin Pathol, 2011. ²Estimated 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 proteintlas.org.

T Cell Engager	Route of Admin.	Clinical Results
Solitumab / 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.

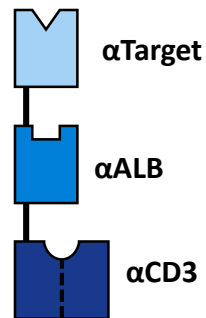
Harpoon's T Cell Engager Platforms Designed to Address Broad Number of Targets and Tumor Types



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

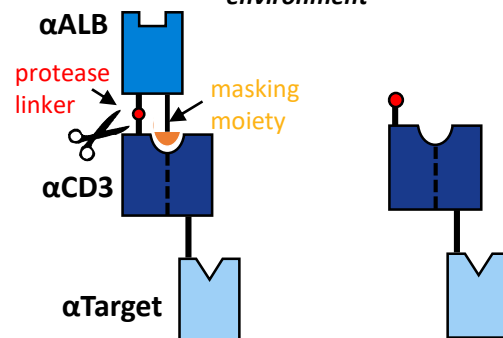
Prodrug

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

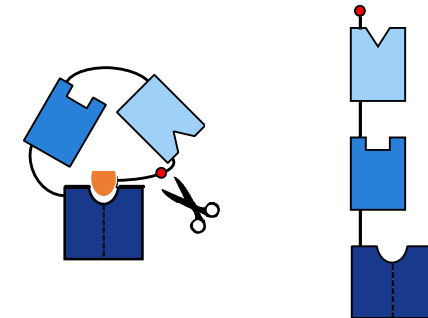
TriTAC-XR™

Prodrug activation in systemic circulation

Prodrug

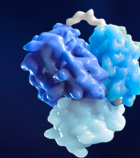
Slow activation in circulation

Active

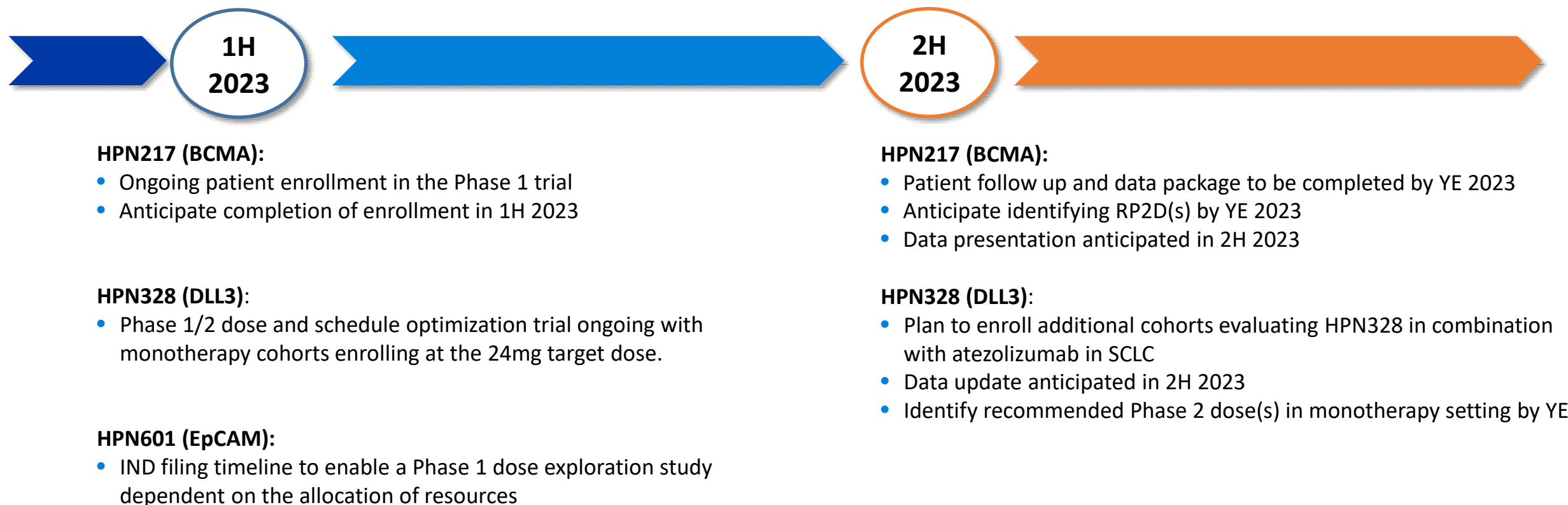


- Designed to maximize systemic exposure while minimizing CRS
- Heme malignancies and solid tumors with potential expansion to non-oncology
- Finalizing platform validation

Summary and Anticipated Milestones



- Advancing pipeline of next-generation T cell engagers address broad patient populations with high unmet needs
- Strategic prioritization to focus resources on ongoing clinical programs in or nearing the clinic
- Clinically meaningful activity in hematology and solid tumor Phase 1 studies
- Current cash and equivalents of \$61.4 million* including \$25M preferred equity financing in March 2023 is expected to fund operations into the second half of 2024



HARPOON
Therapeutics

Nasdaq: HARP

