



# Spearheading Immunotherapies

**HARPOON**  
Therapeutics



**Investor Presentation**  
**August 2019**

# Forward-looking Statements

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This presentation contains forward-looking statements about Harpoon Therapeutics, Inc.. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including statements about our financial position, strategy, expectations regarding the timing and achievement of our product candidate development activities and ongoing and planned clinical trials, and plans and expectations for future operations. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to: our limited operating history; net losses; our expectation that we will incur net losses for the foreseeable future, and that we may never be profitable; our need for additional funding and related risks for our business, product development programs and future commercialization activities; the timing and success of preclinical and clinical trials we conduct; the ability to obtain and maintain regulatory approval of our product candidates; the ability to commercialize our product candidates; our ability to compete in the marketplace; risks regarding our license agreements; our ability to obtain and maintain intellectual property protection for our product candidates; and our ability to manage our growth. We operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. For a discussion of many of these and other risks and uncertainties, see our filings with the Securities and Exchange Commission, including the “Risk Factors” section in our Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q, which are available on the SEC’s website at [www.sec.gov](http://www.sec.gov). Except as required by law, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation to conform these statements to actual results or to changes in our expectations.

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# Harpoon Therapeutics – Investment Overview

<b>Therapeutic Focus</b>	Clinical-stage immunotherapy company
<b>Platform Technology</b>	Tri-specific T cell Activating Construct (TriTAC™) platform T cell engager technology, allows for “off-the-shelf” therapies
<b>Multiple Product Candidates</b>	HPN424 (PSMA TriTAC) Phase 1 in prostate cancer initiated August 2018 HPN536 (mesothelin TriTAC) Phase 1/2a in ovarian cancer and other solid tumors initiated April 2019 Two additional TriTACs expected to enter clinic in 2020
<b>Multiple Anticipated Clinical Catalysts in 2019/2020</b>	HPN424 – present of proof of concept data in H1 2020; expansion study initiation in 2020 HPN536 – present proof of concept data in 2020
<b>Strong Financial Position</b>	\$133.9 million in cash and investments at June 30, 2019 Successful IPO in February 2019 raised \$70.7 million net cash Current cash expected to fund operations into 2021



PSMA – prostate-specific membrane antigen

# Broad Pipeline of Wholly-Owned Immuno-Oncology Programs

*Four clinical stage TriTAC programs in 2020*

	Product Candidate	Target / Indication	Stage of Development				Anticipated Milestones
			Preclinical	Phase 1	Phase 2	Phase 3	
TriTAC	HPN424	PSMA / Prostate cancer	▶				H1 2020: POC dataset
	HPN536	MSLN / Ovarian, pancreatic and other solid tumors	▶				April 2019: Initiated Phase 1/2a clinical trial; 2020: POC data
	HPN217	BCMA / Multiple myeloma	▶				H2 2019: Submit IND Q1 2020: Initiate Phase 1
	HPN328	DLL3 / Small cell lung cancer	▶				2020: Submit IND and Initiate Phase 1



MSLN – mesothelin, BCMA – B-cell maturation antigen, DLL3 – delta-like 3

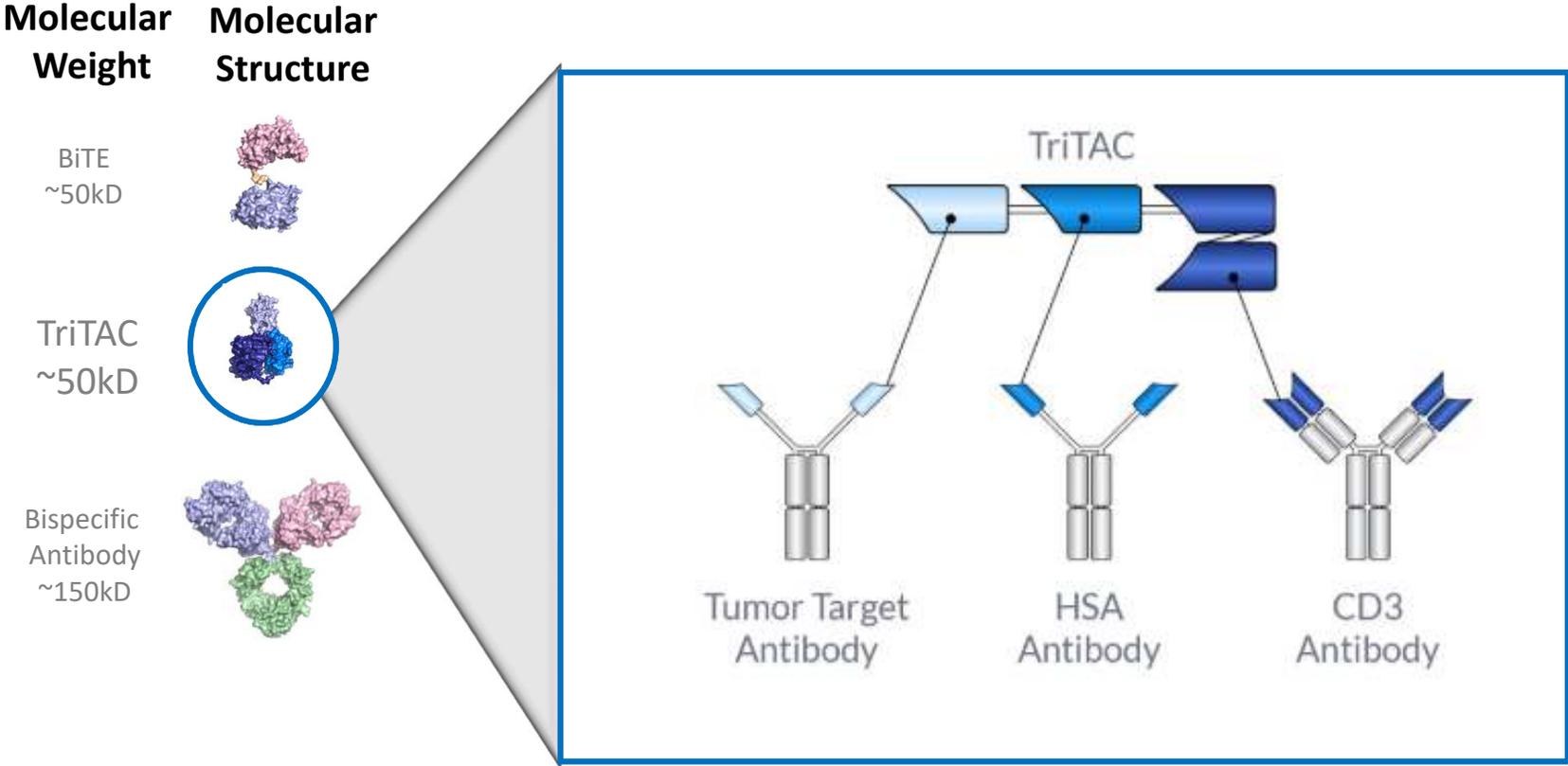
# TriTAC – Next Generation T Cell Engagers Address Limitations of Existing IO Therapies

	Checkpoint Inhibitors	CAR-T Cells	Bi-Specific T-Cell Engagers
COMPANY			
STRUCTURE		<p>CD28 or CD137 Domain</p>	
LIMITATIONS	<ul style="list-style-type: none"> <li>Requires tumor-specific T cells and MHC-I expression</li> <li>“Cold tumors” are unresponsive to checkpoint inhibitors</li> <li>Single-agent response rate limited compared to combination therapies</li> </ul>	<ul style="list-style-type: none"> <li>Limited activity or efficacy in solid tumors</li> <li>On-target toxicities (cytokine release syndrome, neurotox)</li> <li>Inability to dose-limit side effects</li> <li>Requires personalized manufacturing and treatment process</li> <li>Chemo pre-conditioning and hospitalization after infusion (often not reimbursed)</li> </ul>	<ul style="list-style-type: none"> <li>1<sup>st</sup> generation BiTEs require continuous IV administration</li> <li>Other T cell bispecifics use antibody (Fc) to extend half-life which may compromise tumor penetration and safety</li> </ul>
APPROVED IO DRUGS	<ul style="list-style-type: none"> <li>Yervoy (2011)</li> <li>Opdivo (2014)</li> <li>Keytruda (2014)</li> <li>Tecentriq (2016)</li> <li>Bavencio (2017)</li> <li>Imfinzi (2017)</li> </ul>	<ul style="list-style-type: none"> <li>Yescarta (2017)</li> <li>Kymriah (2018)</li> </ul>	<ul style="list-style-type: none"> <li>Blinicyto (2014)</li> </ul>



MHC – major histocompatibility complex, CAR – chimeric antigen receptor

# TriTAC: Small Size and Flexibility, Albumin Domain Confers Extended Half Life

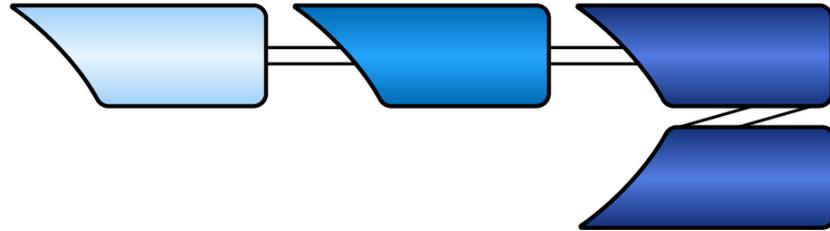


HSA – human serum albumin, BiTE – bispecific T cell engager

# Intellectual Property Strategy: Multiple Layers of Protection

## TriTAC

IP wholly owned by Harpoon



- **Issued patents** covering each binding domain



- **Issued platform patents** covering TriTAC domain orientation, with albumin binding in the middle of the construct



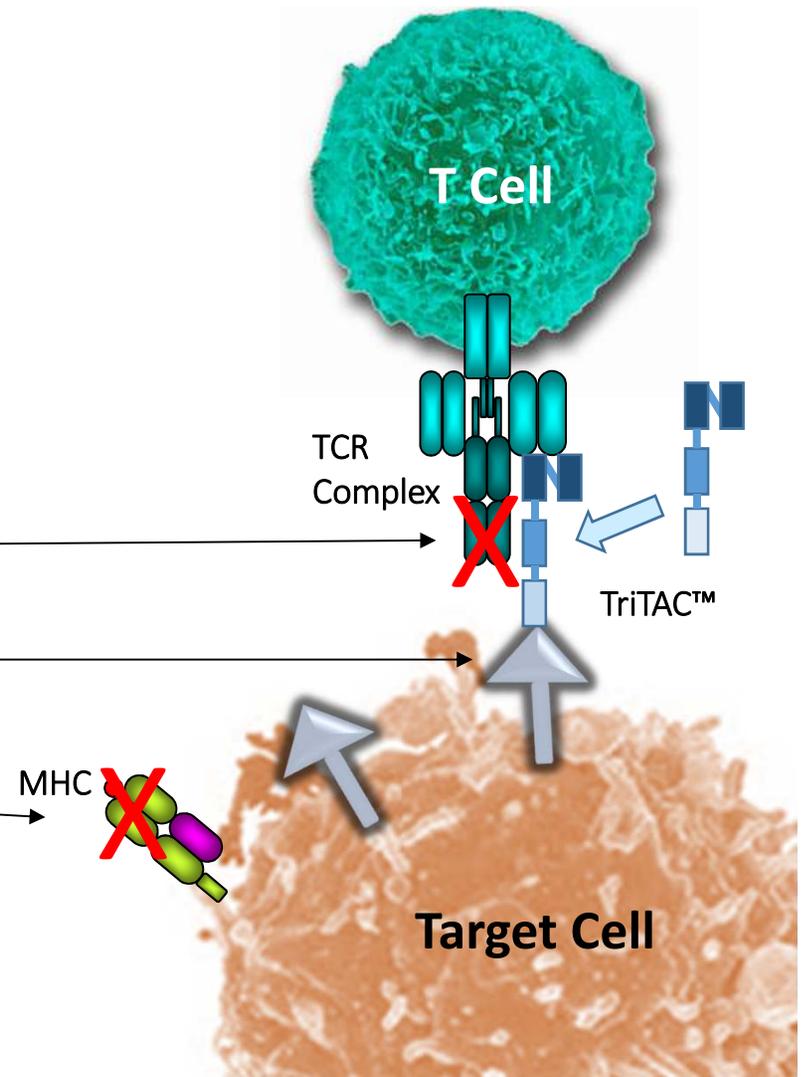
- **Pending patents** on each product sequence
  - HPN424, HPN536, HPN217, HPN328



# TriTACs Overcome Immune Escape Mechanisms and Induce Killing Independent of MHC Expression

MHC downregulation and mutations are a major tumor evasion mechanism

- Does not require a T cell clone with specific T cell receptor
- Any T cell can recognize a surface antigen
- Does not require MHC expression for recognition by T cell

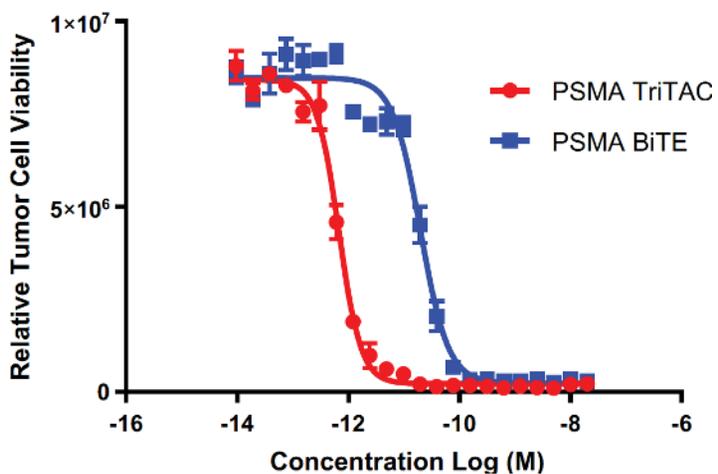


# Preclinical Validation of TriTAC Platform

Data Supports Once Weekly Treatment in Humans

## TriTAC Potency

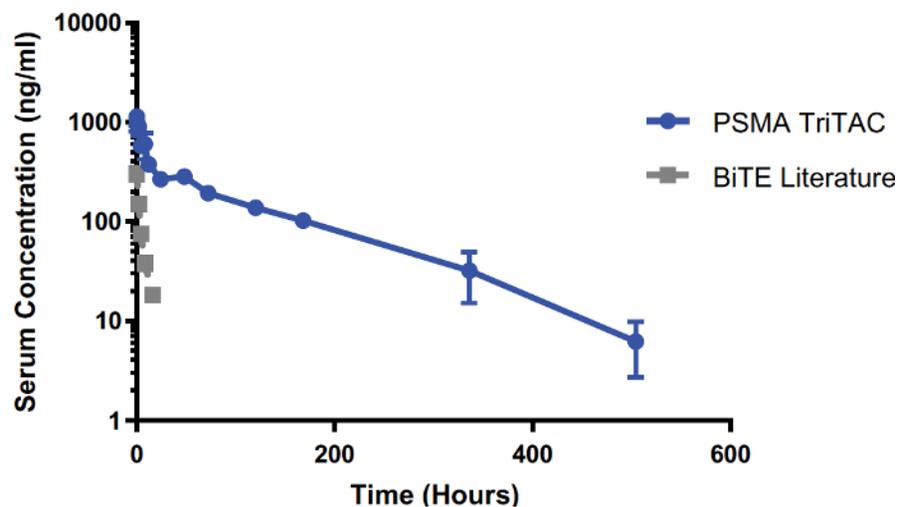
Comparison of TriTAC and BiTE Mediated Cell Killing



- TriTACs observed to be more potent than the comparative BiTE molecule, and can induce T cells to kill tumor cells in both cell-based and animal models

## Extended Half Life

Serum Levels of PSMA TriTAC



- TriTACs observed to have a terminal half-life of 80+ hours vs < 2 hours reported in Blincyto literature

# Benefits of TriTACs - the Next Generation of T Cell Engagers

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## Extended Half-Life and Stability

- Stable in bloodstream and long-serum half-life allow for treatment without continuous IV administration
- Once-weekly dosing

## Active at Low Antigen Level

- Active at low levels of antigen expression where other treatment modalities lose efficacy
- Does not require high levels of target antigen expression to engage T cells to kill disease cells (based on preclinical studies)

## MHC Independence

- Direct T cells to kill target cells independent of MHC expression
- Expected to be able to generate greater and more durable therapeutic responses than MHC dependent approaches

## Small Size and Tissue Penetration

- Small size expected to allow for faster diffusion into human tumor tissue
- Designed for greater potential in solid tumors

## Modularity

- Structure is modular and antigen binding domain designed to be easily switched out
- Allows for potential rapid discovery and development of new product candidates

## Safety Design Elements

- No potential for Fc receptor binding
- Single-armed CD3 binding reduces likelihood of non-specific T cell activation

## Conventional Manufacturing

- Less complex manufacturing than personalized or cell-based therapies
- Off-the-shelf therapies

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## HPN424 TriTAC (PSMA)

# Metastatic Prostate Cancer: >\$5B Global Market Opportunity\*

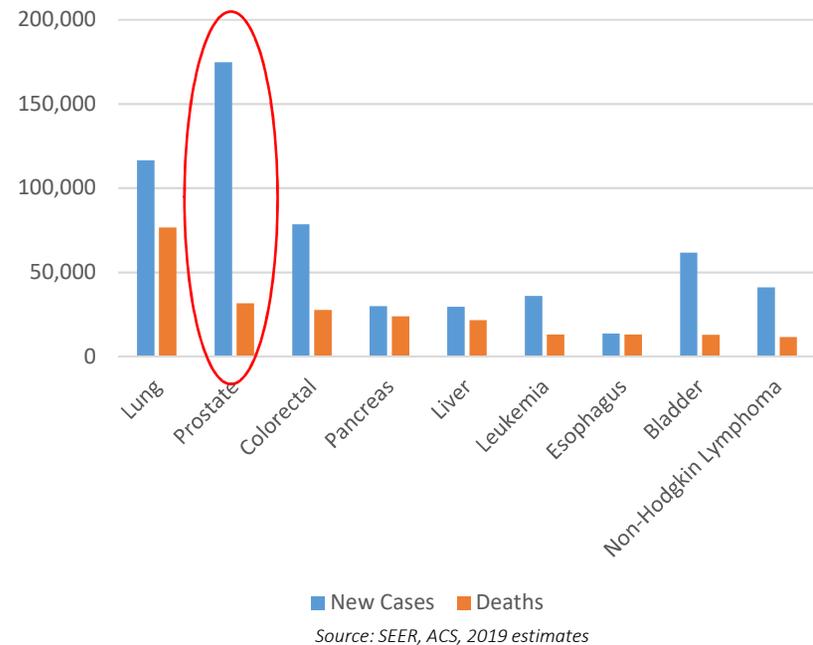
## ~ 174K new cases of prostate cancer annually in the U.S.

- >31K U.S. deaths per year (2<sup>nd</sup> leading cause of cancer death in men)
- Mean survival time for mCRPC = 13 months
- 5-year survival rate is ~30% in more aggressive forms
- ~ 23% initially diagnosed with advanced disease

## Significant unmet need for patients with incurable mCRPC

- Continued high mortality rates of advanced disease
- Potential “fast to market” strategy for high-risk patient subgroups

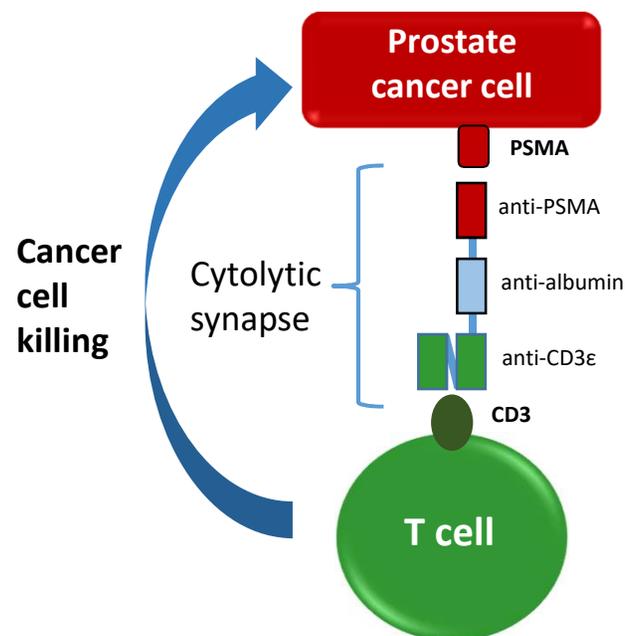
## U.S. Incidence and Mortality of Cancer in Men



\* Based on combined sales in 2017 of later-generation anti-androgen drugs such as Zytiga and Xtandi.

# HPN424 Targets PSMA - A Highly Expressed and Validated Target for Prostate Cancer

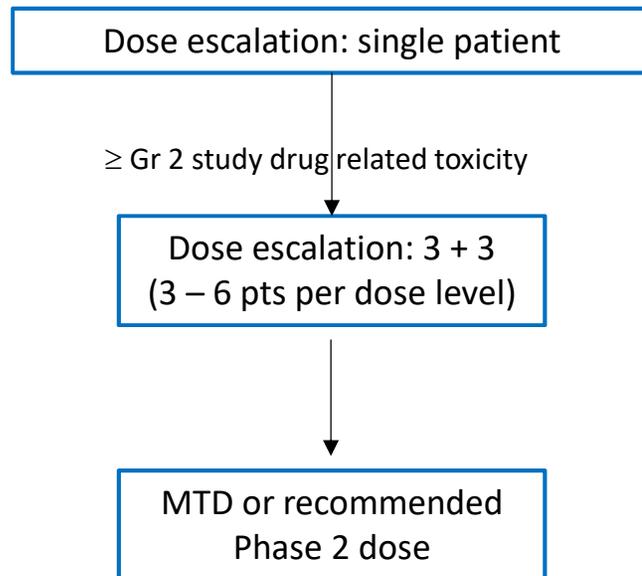
- Designed to bind to human PSMA, CD3, and albumin
- Redirects T cells to kill PSMA-expressing target cells
- Target overexpressed in malignant cells, with limited expression in normal tissue
- Clinically validated by encouraging response data from Amgen's BiTE targeting PSMA in mCRPC patients
- Phase 1 trial initiated in patients with mCRPC cancer in August 2018



*HPN424 is a tri-specific single chain molecule of ~50 kDa*

# HPN424 – Design of Open-label Ongoing Phase 1 Trial

## Part 1 – Dose escalation



## Part 2 – Expansion

~20 pts treated at recommended  
Phase 2 dose determined in Part 1

- Target population
  - Patients with mCRPC
  - Disease progression on the prior systemic regimen
  - At least two prior systemic therapies approved for mCRPC
- Trial objectives
  - Assess safety and tolerability at increasing dose levels
    - AEs
    - Time on trial
  - Pharmacokinetic and pharmacodynamic data
    - Single-dose and multi-dose pK
    - T-cell activation: cytokines and chemokines
    - Circulating tumor cells (CTC)
  - Evaluate preliminary anti-tumor activity
    - PSA levels
    - CT and bone scans
- Dosing & administration
  - Weekly IV infusion of HPN424

# HPN424 - Phase 1 Trial Update & Next Steps

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- Trial initiated August 2018 – Update as of July 31, 2019
  - Dose escalation through multiple cohorts ongoing – seventh cohort underway
  - Weekly infusions well tolerated for multiple cycles
  - Increase in cytokines indicates T cell activation
  - Cytokine-mediated adverse events are transient, manageable
    - No discontinuations due to AEs
    - No dose limiting toxicities
    - Addition of weekly premedication with dexamethasone tapered over several weeks has successfully limited cytokine-related adverse events
    - Several patients have completed the dex taper and have successfully received HPN424 without dex
  - Evidence of half-life extension supports once-weekly schedule
- Initiation of expansion cohort expected in 2020
  - Increase enrollment and continue dose escalation
  - Identify recommended Phase 2 dose
  - Planning for medical conference presentation of POC data H1 2020

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## HPN536 TriTAC (MSLN)

# MSLN - Associated with Tumors with High Unmet Need and Low Survival Rates

**Ovarian Cancer**

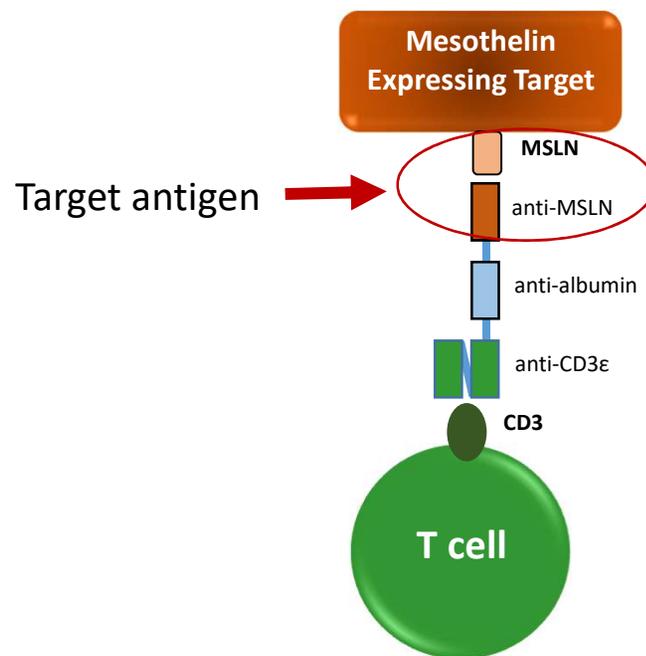
- 5<sup>th</sup> most common cause of cancer death among women in the U.S.
  - ~22,000 new cases per year
  - More than 70% diagnosed with advanced disease
- 5-year survival rate is 47%; ~14,000 die annually
- Current treatment is rarely curative but provides moderate symptom relief and limited increase in survival

Cancer Type	New Patients Diagnosed in the U.S.	MSLN Expression Level (%)
Non-Small Cell Lung Cancer	199,000	60-65*
Ovarian Carcinoma	22,000	60-65
Pancreatic Carcinoma	55,000	80-85
Mesothelioma	2,600	85-90
Triple-Negative Breast Cancer	40,000**	34-42

\* Represents MSLN expression levels across all lung cancer types.  
 \*\* Calculated as 15% of SEER-estimated breast cancer incidence

# HPN536 – Targets MSLN for the Treatment of Ovarian Cancer and Other MSLN-Expressing Tumors

- Designed to bind to human mesothelin, CD3, and albumin
- Redirects T cells to kill MSLN-expressing target cells
- Target overexpressed in malignant cells, with limited expression in normal tissue
- Clinically validated and is overexpressed on a wide array of cancer types: ovarian, pancreatic, mesothelioma, NSCLC, TNBC
- Phase 1/2a trial initiated in patients with ovarian cancer in April 2019

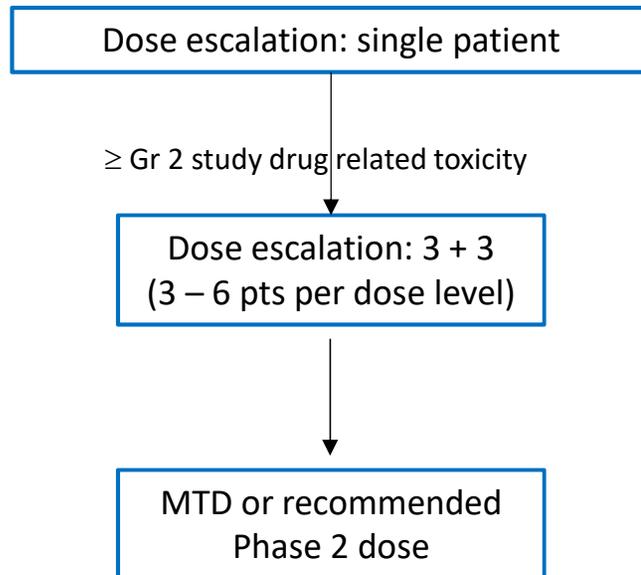


*HPN536 is a tri-specific single chain molecule of ~50 kDa*

# HPN536 – Design of Open-label Ongoing Phase 1/2a Trial

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## Part 1 – Dose Escalation



## Part 2 – Expansion

3 parallel cohorts, ~20 patients each:  
Ovarian, Pancreatic and  
Mesothelioma cancers  
Treated at recommended Phase 2  
dose determined in Part 1

- Target population
  - Patients with advanced cancers associated with mesothelin expression who have failed standard available therapy
  - Initial focus on ovarian cancer, expansion planned to pancreatic and mesothelioma cancers
- Trial objectives
  - Assess safety and tolerability at increasing dose levels
  - Pharmacokinetic and pharmacodynamic data
  - Evaluate preliminary anti-tumor activity
- Dosing & administration
  - Weekly IV infusion of HPN536
  - Successfully dosed through two cohorts (*as of July 2019*)
  - Expect POC data in 2020

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## HPN217 TriTAC (BCMA)

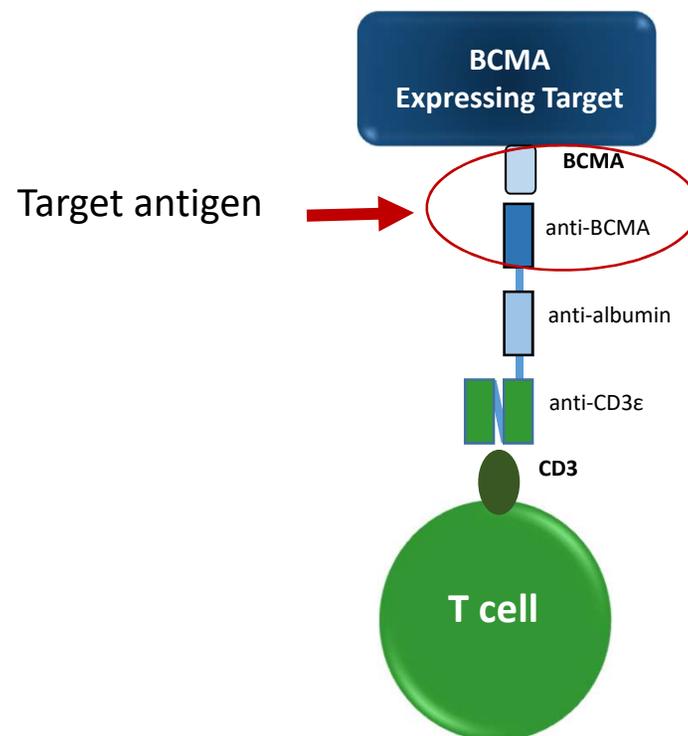
# BCMA - Validated Target for Multiple Myeloma

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- BCMA is a TNFR super family member expressed in nearly all multiple myeloma samples
- Several modalities in development
  - CAR-Ts (bluebird)
  - Antibody drug conjugates (GSK)
- Early data from CAR-T and ADC have clinically validated the target
- Clinical data from bispecific T cell engager AMG 420 (continuous IV administration BiTE)
  - Data presented at ASCO 2019 Annual Meeting demonstrated encouraging clinical responses in patients with relapsed / refractory multiple myeloma in a FIH dose escalation study
    - There were 13/42 responders (9 patients with complete response, 2 very good partial responses, 2 partial responses)
    - At MTD of 400ug/d, there was a 70% ORR (7/10 patients)
      - ◆ 5 of 7 patients achieved minimal residual disease - negative complete response or stringent complete response
      - ◆ All 7 responses at this dose started in the first cycle (overall median time to response was 1.4 months)
      - ◆ Median duration of response at 400ug/d was 9 months (range: 5.8-13.6 months) with two patients ongoing on treatment

# HPN217 - Targets BCMA for the Treatment of Multiple Myeloma and Other BCMA-Expressing Tumors

- Designed to bind to human BCMA, CD3, and albumin
- Redirects T cells to kill BCMA-expressing target cells
- Validated target: Amgen presented promising clinical responses on continuous IV BiTE candidate (AMG420)
- IND-enabling activities underway, expect to file IND in second half of 2019 and initiate Phase 1 in Q1 2020



*HPN217 is a tri-specific single chain molecule of ~50 kDa*

# AbbVie Discovery Collaboration Signed in October 2017

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## TERMS OF AGREEMENT

- Discovery collaboration to create TCR-TriTACs: up to 2 soluble TCRs (provided by AbbVie)
  - Does not compete with Harpoon targets
  - AbbVie gets target-specific product IP (no reach-through)
- Harpoon and AbbVie responsible for research and discovery activities
- AbbVie responsible for all preclinical / clinical development and commercialization

## ECONOMICS

- \$17M upfront payment
- Up to \$600M in aggregate development, regulatory, and commercial sales milestones
- Tiered royalties at percentages in mid-single digits

# Seasoned Management Team with Deep Expertise in Oncology

STRONG HISTORY OF R&D INNOVATION, IMPACT ON PATIENTS AND VALUE TO STOCKHOLDERS



**Jerry McMahon, Ph.D.**  
President and CEO



**Georgia Erbez**  
Chief Financial Officer



**Natalie Sacks, M.D.**  
Chief Medical Officer



**Holger Wesche, Ph.D.**  
Chief Scientific Officer



**Che Law, Ph.D.**  
VP, Translational  
Medicine



**Susan Dana Jones**  
SVP, Product  
Development



**Rachael Lester**  
VP, Corporate  
Development



**Christopher Whitmore,**  
**CPA**  
VP, Finance

CONTRIBUTED TO MANY DRUG APPROVALS AND COMMERCIALIZATION AT OTHER COMPANIES INCLUDING



# Financial Snapshot – Strong Cash Position

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		Notes
Cash	\$133.9M	<ul style="list-style-type: none"> <li>As of June 30, 2019</li> <li>Includes net proceeds from IPO</li> <li>Cash expected to fund operations into 2021</li> <li>No debt</li> </ul>
Shares Outstanding	24.6M	<ul style="list-style-type: none"> <li>As of August 1, 2019</li> </ul>
Market Capitalization	\$358M	<ul style="list-style-type: none"> <li>As of August 1, 2019</li> </ul>
Non-affiliated Institutional Ownership	50.0%	<ul style="list-style-type: none"> <li>As of May 15, 2019</li> </ul>

## Potential Clinical Milestones

Milestone	Timing
<b>HPN424:</b> Preliminary Phase 1 data	January 2019 ✓
<b>HPN536:</b> Initiate Phase 1/2a clinical trial	April 2019 ✓
<b>HPN217:</b> Submit IND	H2 2019
<b>HPN217:</b> Initiate Phase 1 clinical trial	Q1 2020
<b>HPN424:</b> Presentation of interim Phase 1 data at medical conference	H1 2020
<b>HPN536:</b> Proof of Concept	2020
<b>HPN424:</b> Initiate expansion cohort	2020
<b>HPN328:</b> Submit IND and initiate Phase 1 clinical trial	2020

Anticipate four TriTAC product candidates in the clinic in 2020

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PSMA – prostate-specific membrane antigen