



ENDOCYTE

The future of precision medicine

# Company Presentation

August 2018

Certain of the statements made in this presentation are forward looking, such as those, among others, relating to future spending, future cash balances, future use of capital, the timing of initiation and completion of clinical trials, the enrollment period for, and availability and reporting, of data from ongoing and future clinical trials, the successful completion of clinical trials, estimates of the potential market opportunity for the company's product candidates, and the company's future development plans including those relating to the completion of pre-clinical development in preparation for possible future clinical trials and those relating to future IND filings. Actual results or developments may differ materially from those projected or implied in these forward-looking statements. Factors that may cause such a difference include risks that the company or independent investigators may experience delays in the initiation and completion of clinical trials (whether caused by competition, adverse events, patient enrollment rates, shortage of clinical trial materials, regulatory issues or other factors); risks that data from prior clinical trials may not be indicative of subsequent clinical trial results; risks related to the safety and efficacy of the company's product candidates; risks that early stage pre-clinical data may not be indicative of subsequent data when expanded to additional pre-clinical models or to subsequent clinical data; risks that evolving competitive activity and intellectual property landscape may impair the company's ability to capture value for the technology; risks that expectations and estimates turn out to be incorrect, including estimates of the potential markets for the company's product candidates, estimates of the capacity of manufacturing and other facilities required to support its product candidates, projected cash needs, and expected future revenues, operations, expenditures and cash position. More information about the risks and uncertainties faced by Endocyte, Inc. is contained in the company's periodic reports filed with the Securities and Exchange Commission. Endocyte, Inc. disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

## Radio-ligand Therapies (RLT)



- $^{177}\text{Lu}$ -PSMA-617 is Ph 3 radiopharmaceutical with robust Ph 2 data for the treatment of mCRPC
- Differentiated MOA compared to current therapies for mCRPC
- Builds on expertise in PSMA-targeted conjugates and theranostics
- Portfolio of assets provides ability to pursue both  $\alpha$ - and  $\beta$ -emitting therapeutics to multiple indications




## Autologous Adaptor-Controlled CAR T Therapies



- Compelling pre-clinical data, entering Ph 1 Q4 2018
- Leverage expertise in CAR T Adaptor Molecule (CAM) technology to potentially address biggest challenges to current CAR T therapies
  - Novel control strategies for increased safety (e.g. control of cytokine release syndrome)
  - CAM control to avoid T-cell exhaustion
  - Multiple target recognition to address disease heterogeneity

Experienced leadership team building key capabilities to support execution

# Re-focused, innovative pipeline in proven therapeutic classes

PROGRAM	TRIAL DESIGN	INDICATION	PRECLINICAL	SAFETY / PROOF OF CONCEPT	PHASE 2/3	PARTNERS
<b>Radioligand Therapy (RLT)</b>						
<sup>177</sup> Lu-PSMA-617	<sup>177</sup> Lu-PSMA-617 + BSC/SC vs BSC/SC <sup>(1)</sup>	mCRPC			VISION Trial Currently Enrolling	
<sup>177</sup> Lu-PSMA-617	<sup>177</sup> Lu-PSMA-617 vs. Cabazitaxel	mCRPC			Phase 2 Currently Enrolling	
<sup>225</sup> Ac-PSMA-617	Single arm	mCRPC				
<b>CAR-T (Autologous Fluorescein CAR T-Cell, Adaptor Controlled)</b>						
FITC CAR-T + FITC-Folate CAM	Single arm	Osteosarcoma		4Q 2018		
FITC CAR-T + FITC-CAMs (various targets)		TBD				

<sup>1</sup>BSC (best supportive care) = palliative care; SC (standard of care) = potential use of a Novel Androgen Axis Drug (NAAD), such as abiraterone or enzalutamide, to be administered at physician's choice stratified for balance.

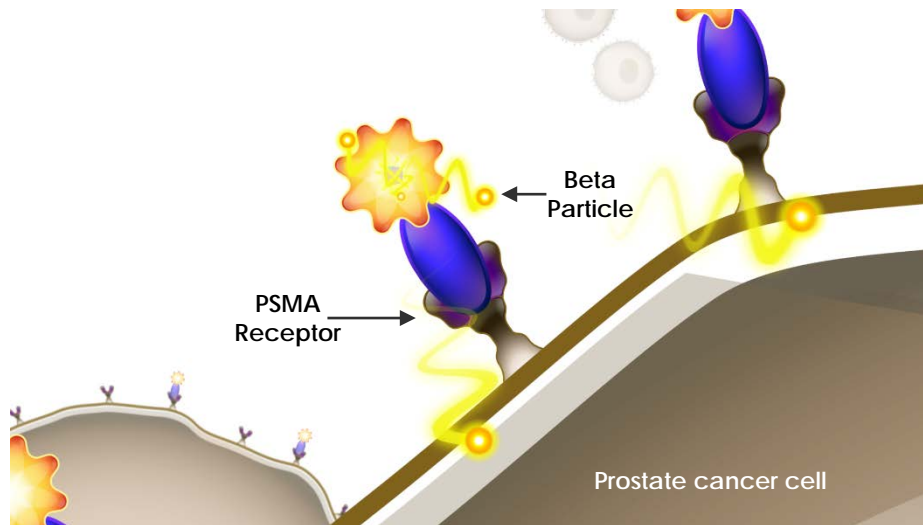
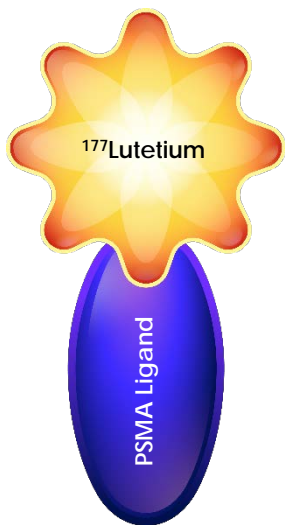


# $^{177}\text{Lu}$ -PSMA-617

Radioligand therapy (RLT) targeting a radioactive warhead,  $^{177}\text{Lu}$ Lutetium, to PSMA-expressing tumor cells in prostate cancer

# $^{177}\text{Lu}$ -PSMA-617 uses a small molecule ligand to target a radioactive atom to PSMA expressing cancer cells

$^{177}\text{Lu}$ -PSMA-617 pairs a PSMA targeting ligand (PSMA-617) to a radioactive atom ( $^{177}\text{Lu}$ ).



Drug conjugate binds to PSMA which is expressed in diseased cells at much higher levels than healthy tissue. Once bound, the  $^{177}\text{Lu}$  atom releases an energetic beta particle that results in lethal radiation killing the cancer cell.

## Benefits of Lutetium for Therapeutic Use

- 6.6 day half life
- <2 mm effective path length
- Commercially available supply



# $^{177}\text{Lu}$ -PSMA-617: Retrospective data analysis

German multi-center study in 145 mCRPC patients

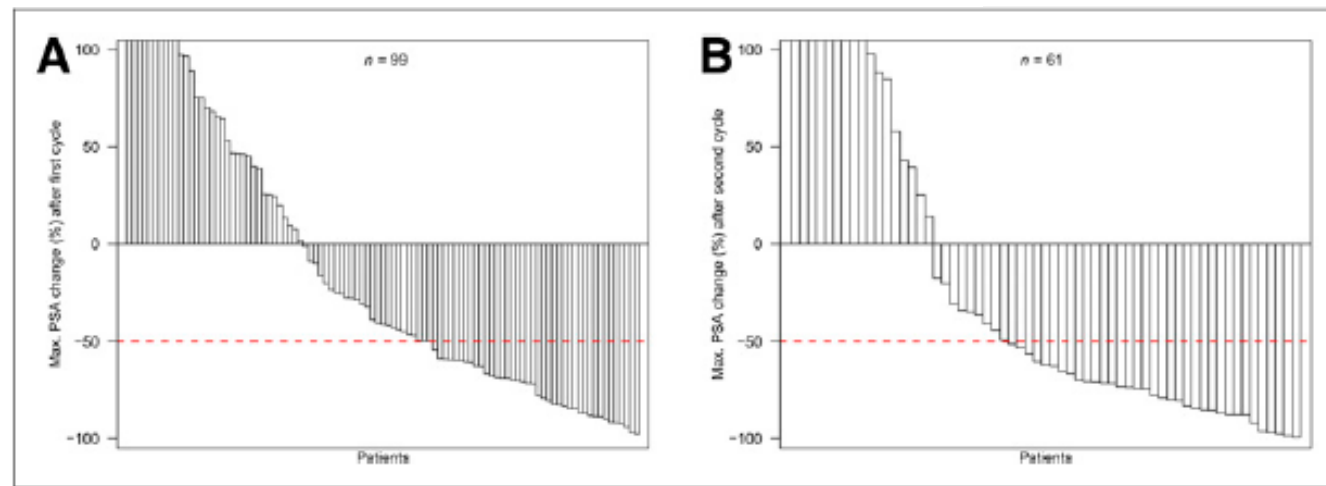
- Study included all patients with PSMA positive disease without regard to potential presence of PSMA negative disease
- Serial PSA levels for analyzing responses were available in 99 of 145 patients
- After the first therapy cycle, a PSA decline of  $\geq 50\%$  occurred in 40 of 99 patients (40%)
- After the second therapy cycle, a PSA decline of  $\geq 50\%$  occurred in 35 of 61 patients (57%)

## German Multicenter Study Investigating $^{177}\text{Lu}$ -PSMA-617 Radioligand Therapy in Advanced Prostate Cancer Patients

Kambiz Rahbar, Hojjat Ahmadzadehfar, Clemens Kratochwil, Uwe Haberkorn, Michael Schäfers, Markus Essler, Richard P. Baum, Harshad R. Kulkarni, Matthias Schmidt, Alexander Drzezga, Peter Bartenstein, Andreas Pfestroff, Markus Luster, Ulf Lützen, Marlies Marx, Vikas Prasad, Winfried Brenner, Alexander Heinzel, Felix M. Mottaghy, Juri Ruf, Philipp Tobias Meyer, Martin Heuschkel, Maria Eveslage, Martin Bögemann, Wolfgang Peter Fendler and Bernd Joachim Krause

*J Nucl Med.* 2017;58:85-90.  
Published online: October 20, 2016.  
Doi: 10.2967/jnumed.116.183194

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**FIGURE 3.** Waterfall plots of maximum PSA change (%) after first cycle (A) and after second cycle (B). PSA increase  $> 100\%$  was cropped due to simplification.

**TABLE 3**  
Adverse Events After <sup>177</sup>Lu-PSMA-617 as Determined by Blood Tests (*n* = 121) or Physician Reports (*n* = 145)

Organ system	Category	Evaluated for N	All grades	Grade 3–4
Blood and lymphatic disorders	Leukopenia	121	48 (40%)	4 (3%)
	Anemia	145	50 (34%)	15 (10%)
	Thrombocytopenia	121	38 (31%)	5 (4%)
Gastrointestinal disorders	AST elevation	121	27 (19%)	0 (0%)
	ALT elevation	121	11 (8%)	0 (0%)
	Xerostomia	145	11 (8%)	0 (0%)
	Nausea	145	9 (6%)	0 (0%)
	Dysgeusia	145	6 (4%)	0 (0%)
	Ascites	145	2 (1%)	0 (0%)
	Biliary obstruction	145	0 (0%)	1 (1%)
General disorders	Fatigue	145	19 (13%)	1 (1%)
	Pain	145	5 (3%)	0 (0%)
	Ileus	145	1 (1%)	0 (0%)
Urinary disorders	Renal failure	121	14 (12%)	0 (0%)
	Urinary tract infection	145	1 (1%)	0 (0%)
Cardiovascular disorders	Edema	145	2 (1%)	0 (0%)
	Lung embolism	145	0 (0%)	3 (2%)
Respiratory, thoracic, and mediastinal disorders	Pleural effusion	145	1 (1%)	0 (0%)
	Dyspnea	145	1 (1%)	0 (0%)
Neurologic disorders	Vertigo	145	1 (1%)	0 (0%)
	Stroke	145	0 (0%)	2 (1%)
Musculoskeletal disorders	Bone fracture	145	0 (0%)	3 (2%)

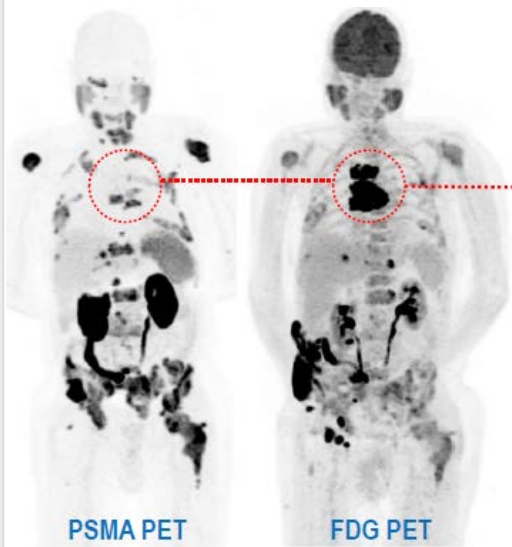
Rahbar, et al. J Nucl Med, 58, 1, 2017, 85-90.



# $^{177}\text{Lu}$ -PSMA-617: Prospective clinical data

Results presented at 2017 ESMO garner significant investigator attention<sup>(1)</sup>

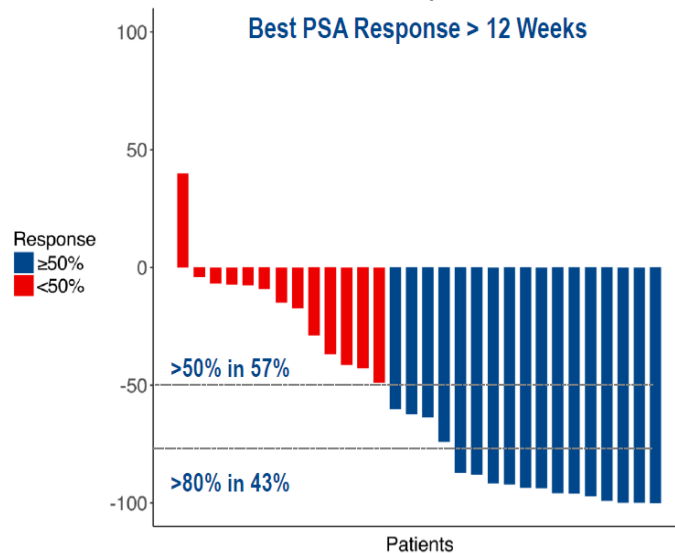
## Refined Patient Selection



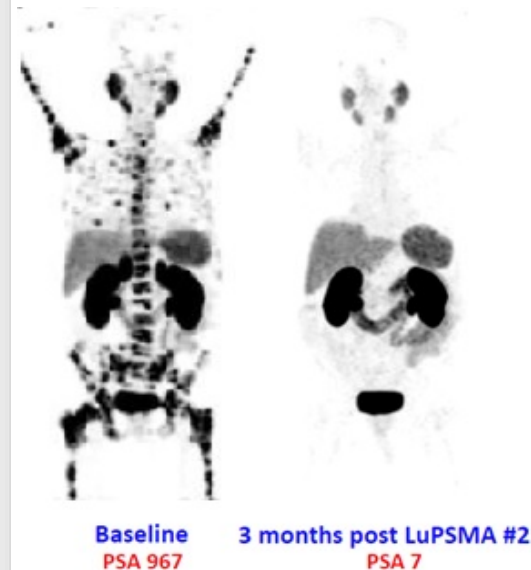
Patient excluded from trial.  
PSMA negative disease appears on FDG  
PET and not on PSMA PET.

## Driving Response

- 57% >50 PSA reduction
- 71% RECIST response



## Post Treatment Scan



PSMA positive disease not visibly  
detected from follow-up scan.

<sup>1</sup>Hofman, Michael (2017, Sept.). Lutetium-177 PSMA (LuPSMA) theranostics phase II trial. Presented at ESMO, Madrid, Spain.

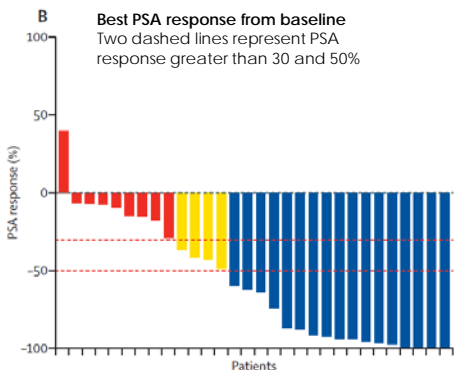
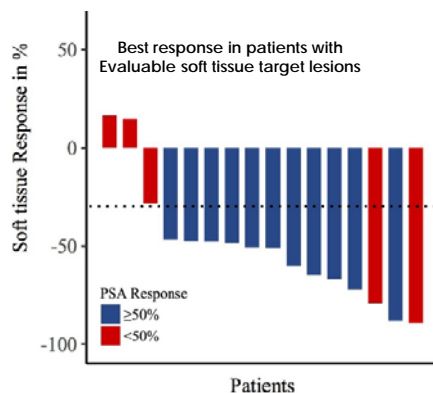
# Updated <sup>177</sup>Lu-PSMA-617 prospective data<sup>1</sup> confirm and improve on ESMO 2017 data

## THE LANCET Oncology

[<sup>177</sup>Lu]-PSMA-617 radionuclide treatment in patients with metastatic castration-resistant prostate cancer (LuPSMA trial): a single-centre, single-arm, phase 2 study

Michael S Hofman\*, John Violet\*, Rodney J Hicks, Justin Ferdinands, Sue Ping Thang, Tim Akhurst, Amir Iravani, Grace Kong, Anavind Ravi Kumar, Declan G Murphy, Peter Eu, Price Jackson, Mark Scalzo, Scott G Williams, Shahneen Sandhu

Efficacy Measure	Sept 2017 ESMO	May 2018 Lancet Oncology
Best PSA >50% Reduction	57%	57%
Best PSA >80%	43%	43%
PSA ≥ 96% Reduction	Not reported	20%
PSA Progression Free Survival	6.3 mo	7.6 mo
RECIST Response	71%	82%
Median Overall Survival	12.7 mo	13.5 mo



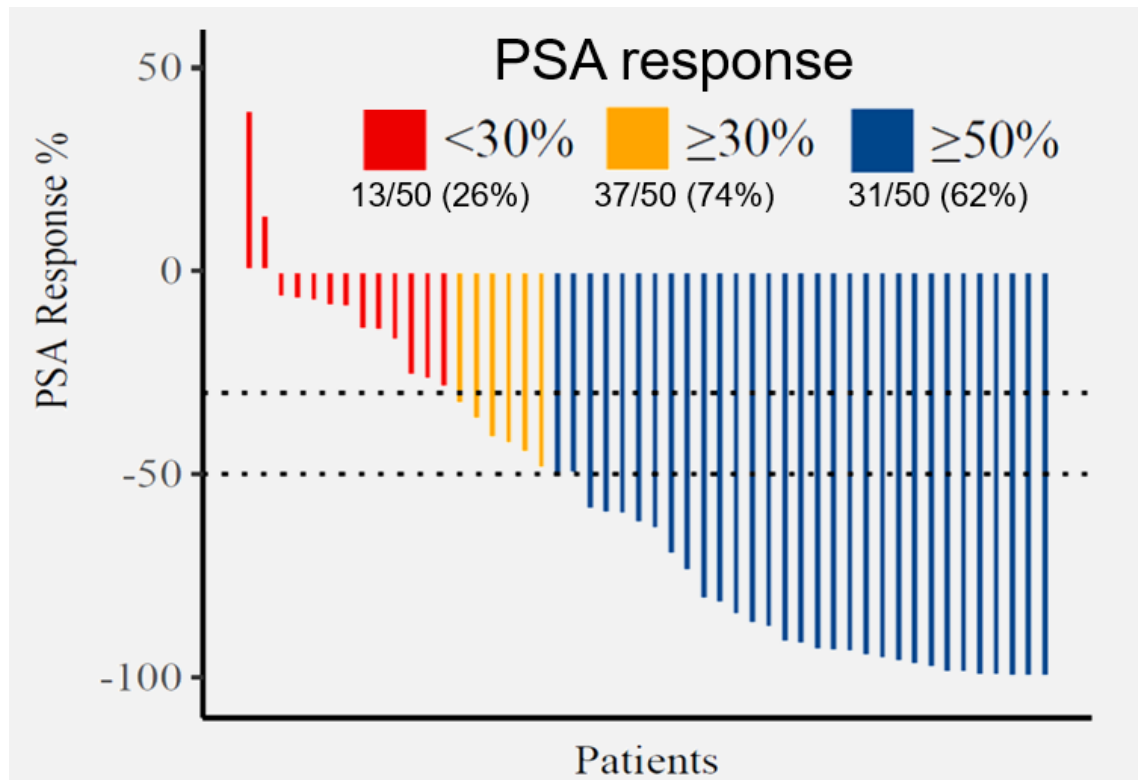
	Grade 1-2	Grade 3	Grade 4	Grade 1-2, attributed to LuPSMA*	Grade 3 attributed to LuPSMA*	Grade 4 attributed to LuPSMA*
Dry mouth	26 (87%)	0	0	26 (87%)	0	0
Lymphocytopenia	12 (40%)	13 (43%)	0	11 (37%)	11 (37%)	0
Thrombocytopenia	12 (40%)	5 (17%)	3 (10%)	8 (27%)	3 (10%)	1 (3%)
Fatigue	16 (53%)	1 (3%)	0	15 (50%)	0	0
Nausea	15 (50%)	0	0	15 (50%)	0	0
Anaemia	7 (23%)	7 (23%)	0	4 (13%)	4 (13%)	0
Neutropenia	12 (40%)	2 (7%)	0	8 (27%)	2 (7%)	0
Pain	8 (27%)	3 (10%)	0	5 (17%)	1 (3%)	0
Vomiting	10 (33%)	0	0	10 (33%)	0	0
Anorexia	8 (27%)	0	0	7 (23%)	0	0
Dry eyes	5 (17%)	0	0	5 (17%)	0	0
Weight loss	3 (10%)	0	0	3 (10%)	0	0
Disseminated intravascular coagulation	0	1 (3%)	0	0	0	0
Oculomotor nerve disorder	1 (3%)	0	0	1 (3%)	0	0
Spinal fracture	0	1 (3%)	0	0	0	0
Hip fracture	0	1 (3%)	0	0	0	0

Data are n (%). Grade 1-2 adverse events occurring in >10% of the cohort and all grade 3 adverse events are presented. There were two grade 5 adverse events not attributed to LuPSMA: pneumonia (n=1), hepatic failure (n=1). LuPSMA-lutetium-177 prostate-specific membrane antigen-617. \*Possibly, probably, or definitely according to Common Terminology Criteria for Adverse Events.

Table 3: Treatment-emergent adverse events

<sup>1</sup>Hofman, Michael et al. The Lancet Oncology (2018, May)

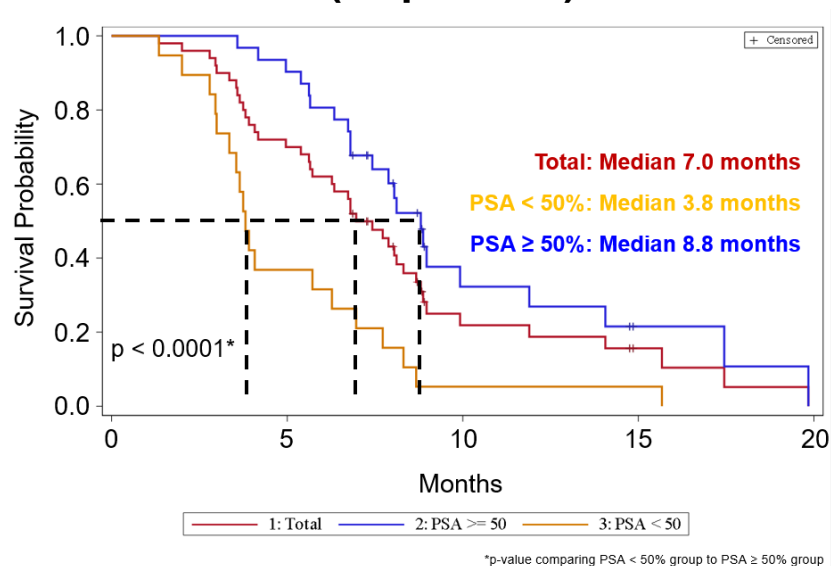
# Response rates sustained with trial expansion



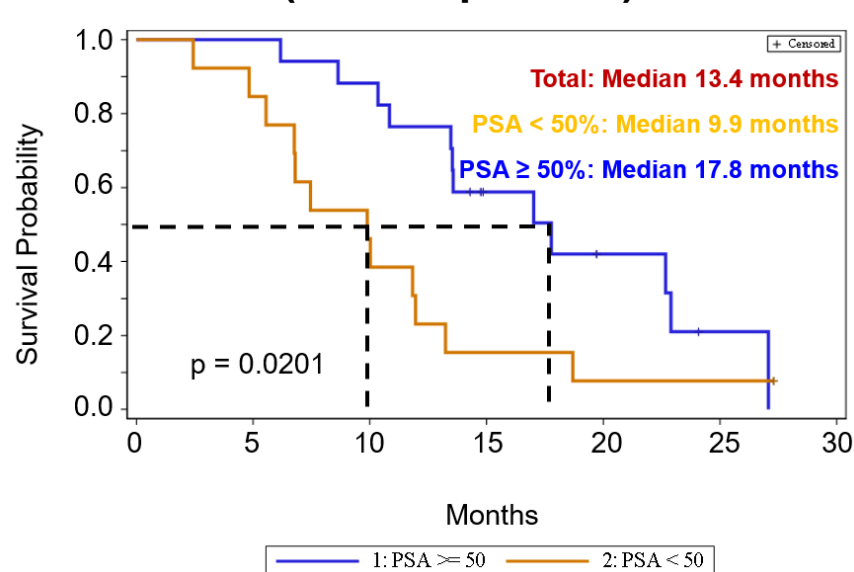
<sup>1</sup>Hofman, Michael (2018, June). Lutetium-177 PSMA617 theranostics in mCRPC: interim results of a phase 2 trial. ASCO 2018, Genitourinary cancer P5040.

# PSA PFS and overall survival correlate to PSA response & compare favorably to historical benchmarks

## PSA PFS (50 patients)



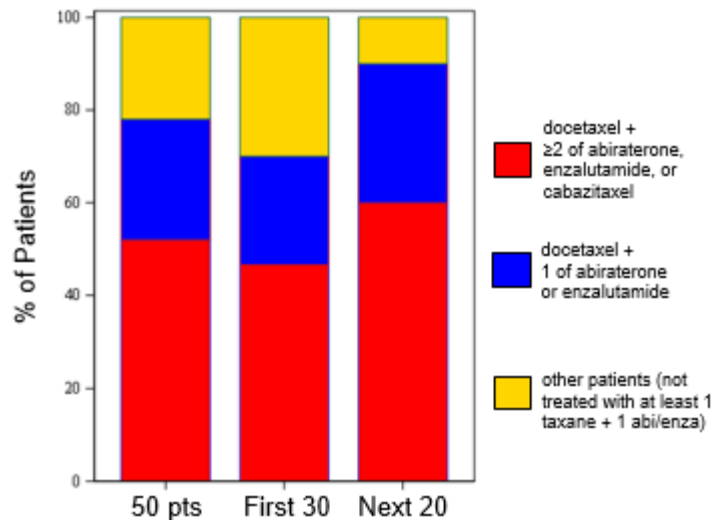
## Overall Survival (First 30 patients)



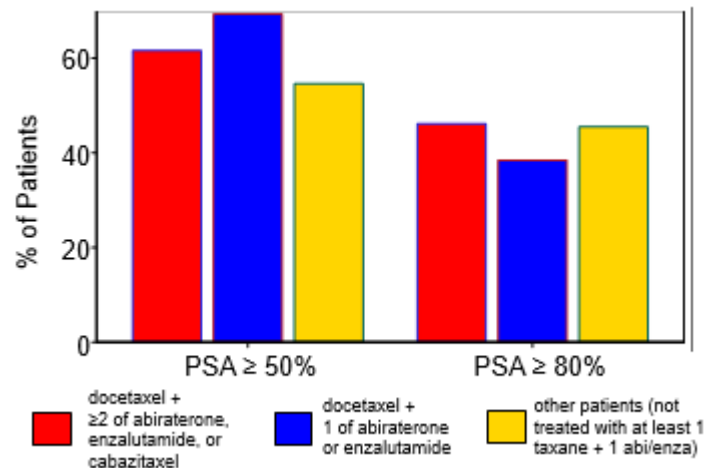
<sup>1</sup>Hofman, Michael (2018, June). Lutetium-177 PSMA617 theranostics in mCRPC: interim results of a phase 2 trial. ASCO 2018, Genitourinary cancer P5040.

# Differentiated mechanism of action yields consistent response independent of prior therapy

## Most patients received 3 or more prior therapies in metastatic setting



## Response rates similar for less pre-treated compared to most pre-treated patients



<sup>1</sup>Hofman, Michael (2018, June). Lutetium-177 PSMA617 theranostics in mCRPC: interim results of a phase 2 trial. ASCO 2018, Genitourinary cancer P5040.

# PSA-response predictive of clinical & regulatory success in mCRPC

Only COMET-1 trial evaluated patient population similar to the Australian <sup>177</sup>Lu-PSMA-617 trial

	Study (Phase - Completion Yr.)	Prior Chemo?	Prior ADT?	OS (HR)	PSA Response (≥50% reduction)	Time to PSA Progression	ORR <sup>3</sup> (RECIST)	Approved in mCRPC?	Comparator
 PSMA-617	Australian LuPSMA <sup>1</sup> (Ph2 in expansion)	Yes	Yes		62%	7.0 mo.	82%		
	TROPIC (Ph3 – 2009)	Yes	No	0.70	39%	6.4 mo.	14%	2010	mitoxantrone
	COU-AA-301 (Ph3 – 2010)	Yes	No	0.65	29%	10.2 mo.	14%	2011	placebo
	AFFIRM (Ph3 – 2011)	Yes	No	0.63	54%	8.3 mo.	29%	2012	placebo
	ALSYMPCA (Ph3 – 2011)	Yes	No	0.70	6%	3.6 mo.	NR	2013	placebo
	COMET-1 (Ph3 – 2014)	Yes	Yes	0.90	6%	4.2 mo.	5% <sup>2</sup>	No	prednisone
	SUN 1120 (Ph3 – 2011)	Yes	No	0.91	6% <sup>2</sup>	NR	6%	No	placebo
	CA184-043 (Ph3 – 2012)	Yes	No	0.85	13%	NR	NR	No	placebo

<sup>1</sup>Hofman, Michael et al. The Lancet Oncology (2018, May); <sup>2</sup>Data from Phase 2 studies (Phase 3 data not reported); <sup>3</sup>In soft tissue lesions; NR=Not Reported

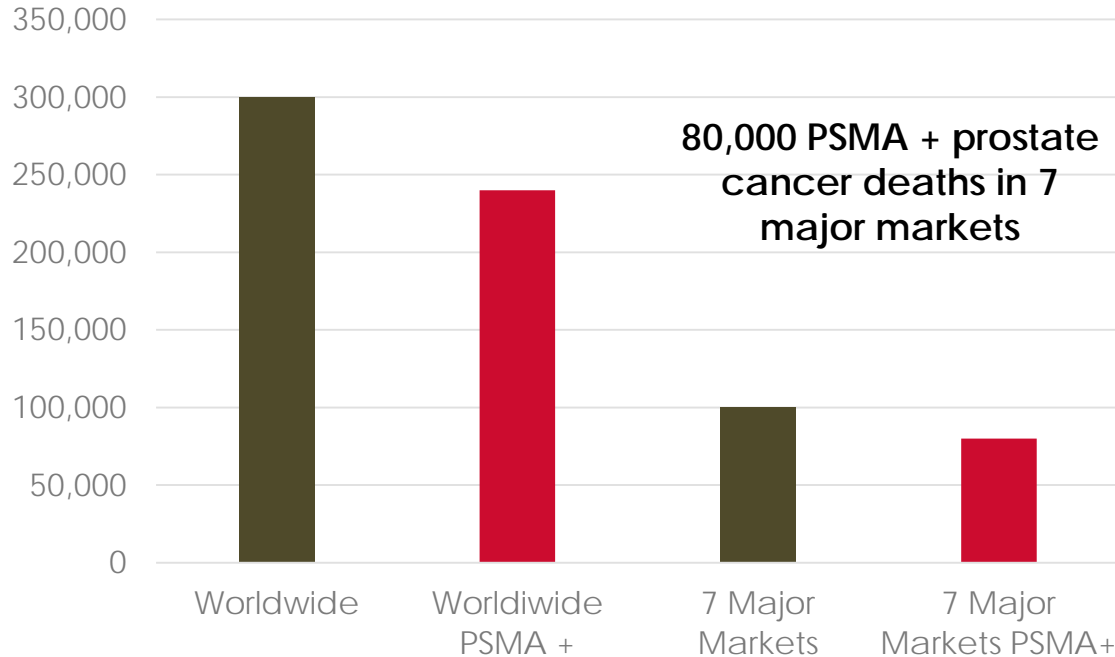
P≤0.001

P>0.001 to 0.05

P>0.05

# Large opportunity even in late-stage, metastatic setting

## Annual Prostate Cancer Patients Deaths<sup>1</sup>



<sup>1</sup>2016 Facts and Figures, American Cancer Society, and International Agency for Research on Cancer, World Health Organization



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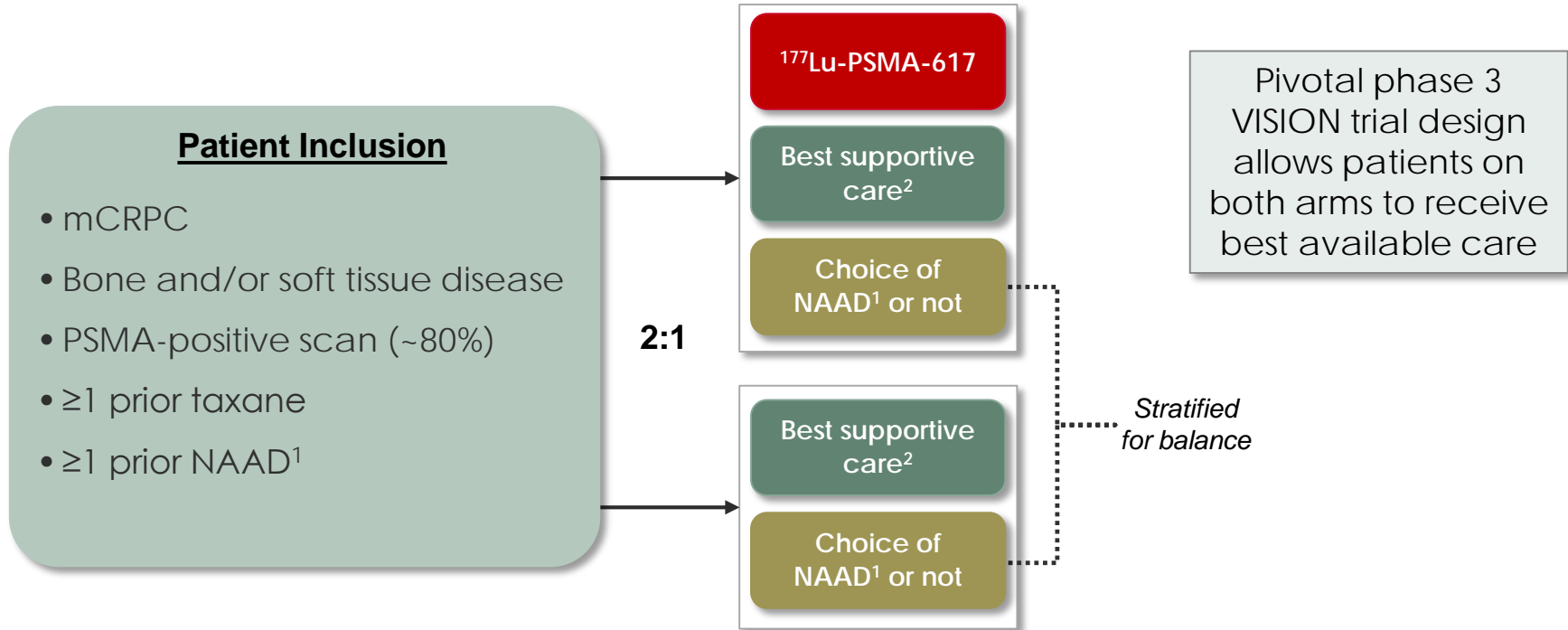
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# $^{177}\text{Lu}$ -PSMA-617 Phase 3 VISION Trial Design



# Pivotal phase 3 VISION trial design

An international, prospective, open-label, multi-center, randomized Phase 3 Study of  $^{177}\text{Lu}$ -PSMA-617 in treatment of patients with progressive PSMA-positive metastatic castration resistant prostate cancer



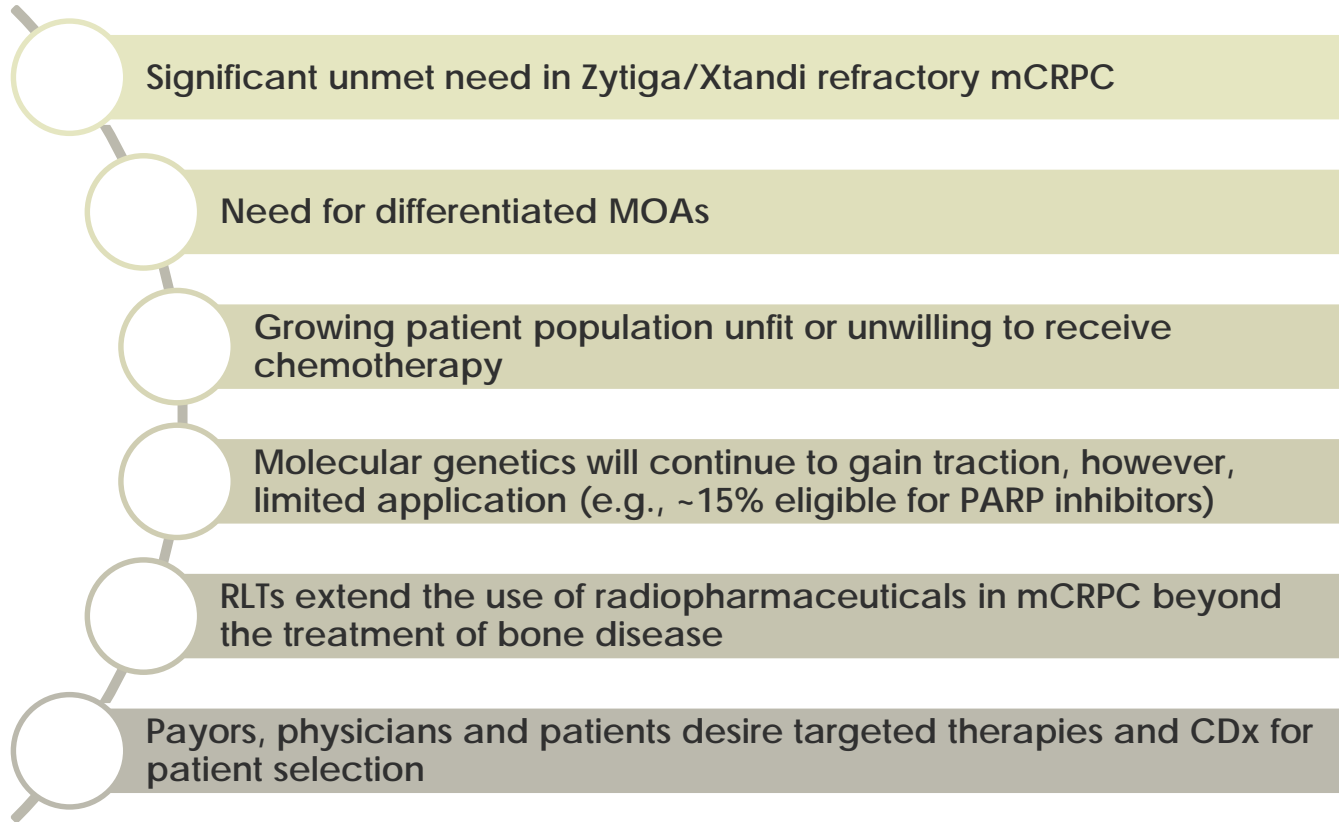
<sup>1</sup>NAAD = novel androgen axis drug = abiraterone or enzalutamide; <sup>2</sup>Best supportive care = palliative.


- Enrollment
  - Up to 750 patients for ~490 overall survival (OS) events
  - Early efficacy stops at 50% and 70% of events
- Statistics
  - 90% overall power, Type I error rate of 0.025 (1-sided)
  - Observed HR's to meet p-value at each assessment: 0.669, 0.754 and 0.825
  - Vs. assumed 10 month OS control, corresponds to 4.9, 3.3, and 2.1 month improvement
- Endpoints
  - Primary – Overall Survival
  - Secondary
    - Radiographic progression-free survival (rPFS)
    - Overall response rate (RECIST)
    - Time to symptomatic skeletal events
- Stratification
  - Choice of NAAD (yes or no)
  - ECOG score (0-1 vs 2)
  - LDH (high vs low)
  - Liver metastasis (yes or no)
- Planned FDA discussion
  - Shift to rPFS endpoint at interim analyses for accelerated approval

- Clear unmet need in patient population
- Rapid timelines to endpoints
- Add-on therapy improves likelihood of success (vs. head-to-head)
- Evidence of NAADs enhancing PSMA expression<sup>1</sup>
- Best supportive & standard care provided for both arms
- Sets the stage for potential earlier line use of <sup>177</sup>Lu-PSMA-617
- Powered well with opportunity for early stops

<sup>1</sup>Evans, et. al., Proc Natl Acad Sci U S A. 2011 Jun 7;108(23):9578-82. doi: 10.1073/pnas.1106383108. Epub 2011 May 23.

# Strong rationale for development of RLT in mCRPC





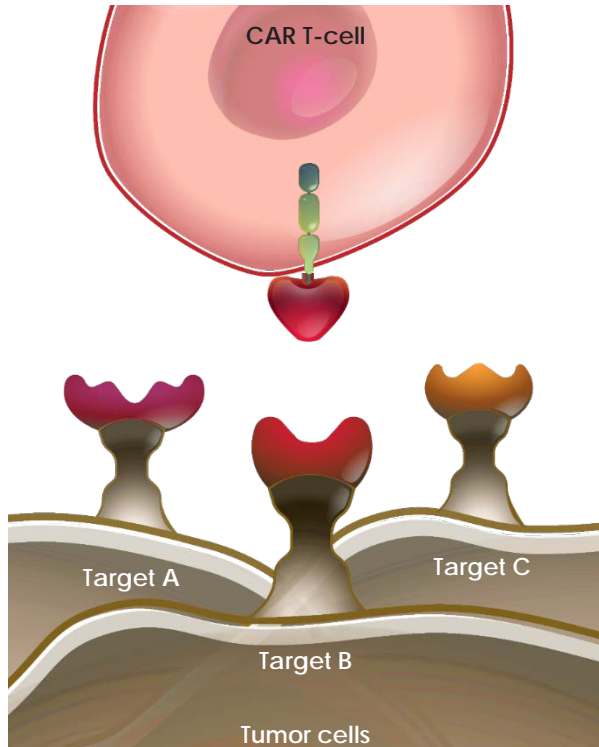
# Adaptor controlled CAR T-cell program

Universal<sup>1</sup>, autologous CAR T-cells targeting  
FITC paired with various small molecule, FITC  
CAR T adaptor molecules (CAMs) to target  
multiple tumor antigens

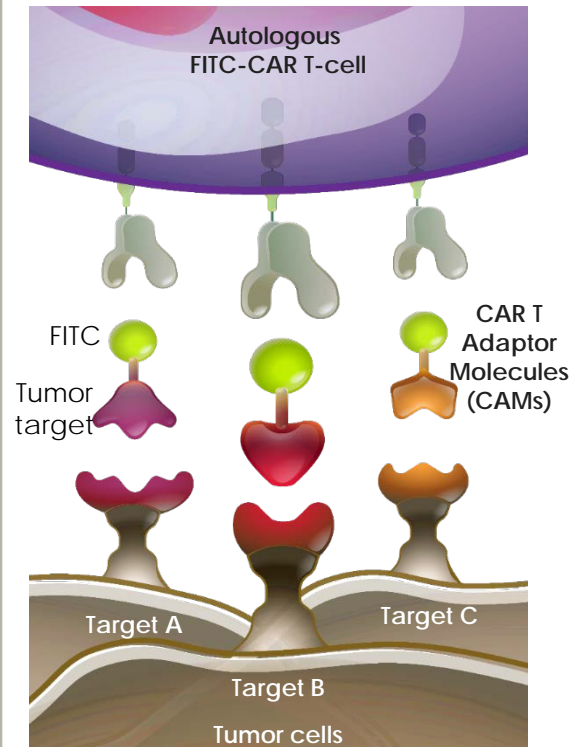
<sup>1</sup>Universality refers to the ability to use the same CAR construct to treat any number of indications through the use of CAMs

# Novel CAR T approach provides potential for greater control over immune response

## Traditional Approach



## Endocyte Approach



## Novel Approach

- Universal, autologous CAR T binds to FITC
- CAM provides bridge from CAR T to tumor
- CAM dosing enables antigen control

## Potential benefits

- Manage or avoid cytokine release syndrome (CRS)
- Manage T-cell exhaustion
- Address tumor heterogeneity

## Business strategy

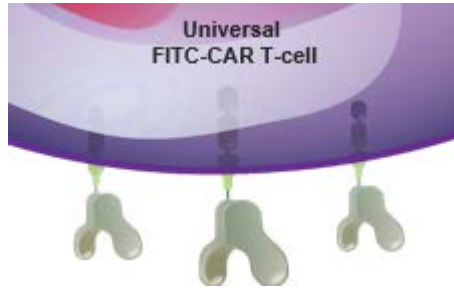
- POC with single CAM in osteosarcoma
- Development of multiple CAMs for variety of tumor targets
- Seek partnership(s) following POC

<sup>1</sup>Folate receptor (FR) is the initial target for PoC, but the concept applies to any cell surface antigen with an associated small molecule ligand (e.g. cholecystokinin-2 receptor (CCK2R), neurokinin-1 receptor (NK1R))

# Endocyte's CAR T: Potentially for controlled, personalized immune response

1

Autologous FITC CAR T-Cell Administration



CAR T-cell distributes throughout the body (inactive)

2

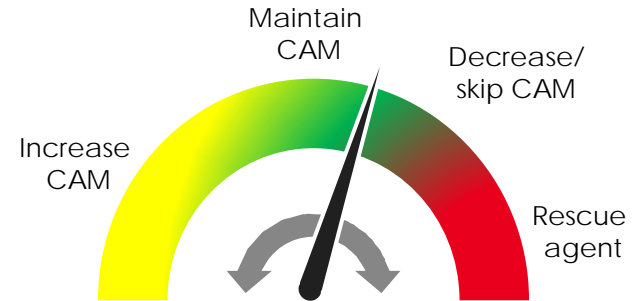
Initial CAM Dose



CAM is the antigen to "bridge" T-cell to targeted disease

3

Subsequent CAM Doses Tailored to Patient Immune Response



CAM's properties yielded control of immune response in preclinical models

# Collaboration with SCRI enhances speed to clinic and likelihood of success

 ENDOCYTE  
Endocyte and Seattle Children's Research Institute to Collaborate on Endocyte's Small Molecule Drug Conjugate Bi-Specific Adaptor Molecules for CAR T-cell Therapies  
*Collaboration pairs leading SMDC technology with recognized CAR T-cell research expert*  
*Plans to develop next generation CAR T-cell therapeutic platform with potential for improved safety and efficacy in solid tumor indications*

**Dr. Michael Jensen**

Scientific Co-founder of Juno Therapeutics  
Founding Director of Ben Towne Center for  
Childhood Cancer Research at SCRI



## SCRI-Endocyte-Purdue Collaboration

- Preclinical work with EC17 CAM
  - CAR T-specific work by Dr. Jensen
  - CAM-specific work by Endocyte/Purdue<sup>1</sup>
- Optimization & GMP-grade manufacturing of CAR vector Q4 2017
- Imaging study to assess FR-positivity in osteosarcoma patients (2018)
- Pediatric osteosarcoma IND filed (Q4 2018)

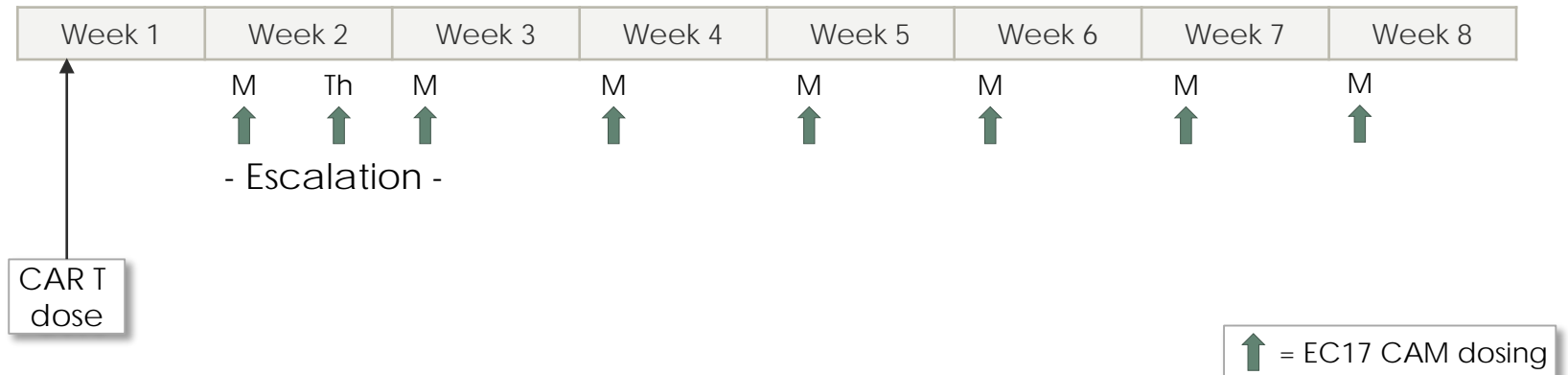
<sup>1</sup>Development of additional CAMs directed to distinct tumor targets via Endocyte's research collaboration with Purdue University



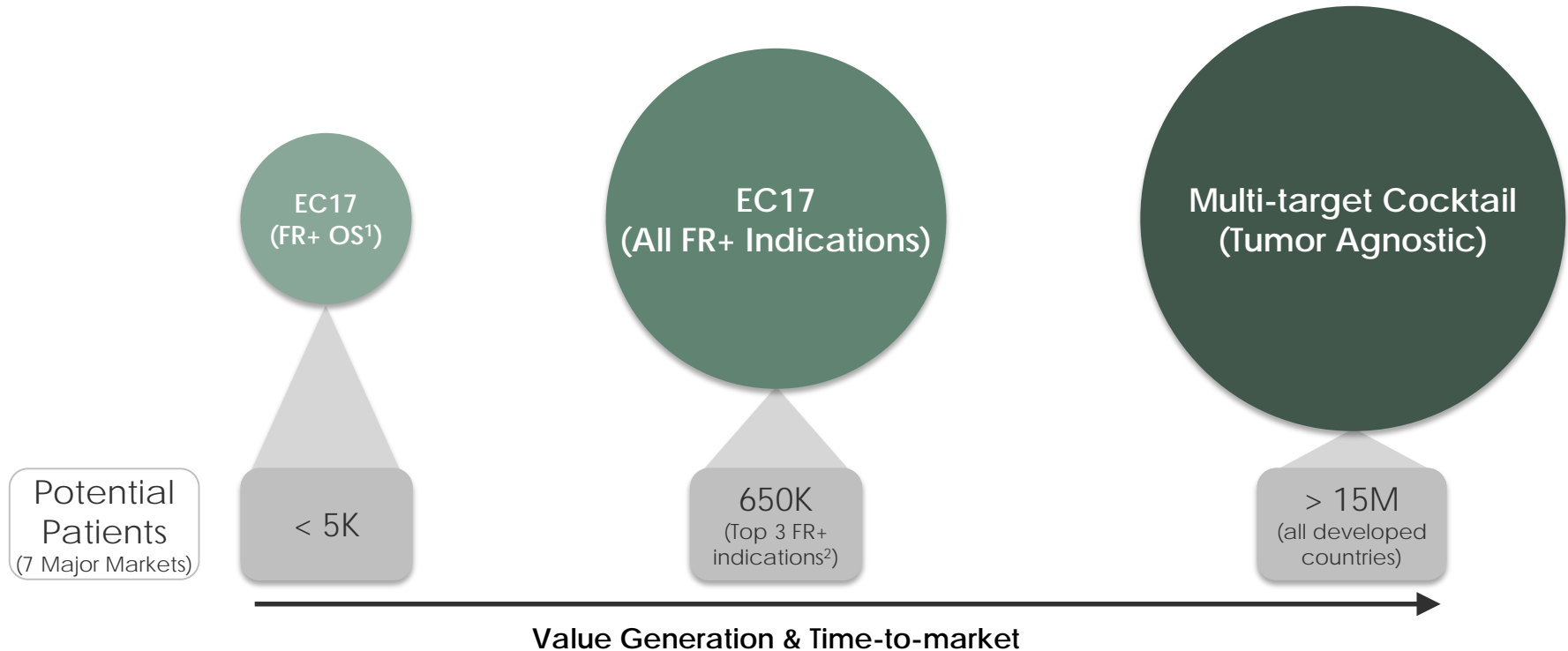
# CAR T phase 1 trial design in osteosarcoma

CAR T trial design employs intra-patient dose escalation of CAM

- Pre-clinical evidence of CAM dose escalation prevents cytokine release syndrome and T-cell exhaustion
- Immune response assessed following each CAM dose allowing immediate feedback on activity



# Collaboration provides fast-to-market strategy with blockbuster market potential in next indications



<sup>1</sup>Pediatric osteosarcoma; <sup>2</sup>Non-small cell lung cancer, Ovarian cancer, Triple negative breast cancer

# Recent and upcoming milestones

✓	Oct '17	In-license of $^{177}\text{Lu}$ -PSMA-617
✓	Nov '17	Acquired active IND for $^{177}\text{Lu}$ -PSMA-617
✓	Feb '18	Successful end of Phase 2 meeting with the FDA
✓	Feb '18	1 <sup>st</sup> patient enrolled in TheraP Phase 2 trial
✓	Feb '18	Lutetium clinical supply agreement
✓	May '18	Patrick Machado and Dawn Svoronos elected to Board
✓	June '18	First enrollment in phase 3 registration trial of $^{177}\text{Lu}$ -PSMA-617
✓	June '18	50-patient data readout of investigator initiated Phase 2 trial of $^{177}\text{Lu}$ -PSMA-617 in mCRPC at Peter MacCallum Cancer Centre
•	2018	Publications on other ongoing investigator initiated clinical trials of $^{177}\text{Lu}$ -PSMA-617 in prostate cancer patients (2018)
•	Q4 '18	CART IND

# Financial summary

Dollars (millions)	Full Year 2017	Jun YTD 2018
R&D	25.9	12.9
G&A	13.8	8.4
Acquired in-process R&D	16.5	-
Total Operating Expenses	56.2	21.3
Net Income (loss)	(55.1)	(20.2)
Ending Cash Balance	97.5	166.8
Shares Outstanding (millions)	48.3	70.0

- Follow-on financing closed 3/2/18, net proceeds to Endocyte of ~\$81M, ~20.5 million new common shares issued
- Company expects cash, cash equivalents and investments balance at the end of 2018 to exceed \$130 million.
- No additional <sup>177</sup>Lu-PSMA-617 license-related payments until NDA filing