



## Corporate Presentation

Nasdaq: PRTG  
January 2023

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**Immuno-Oncology Company with Four First/Best in Class Small Molecules in the Clinic**

**iNKT Agonist: Potential 1<sup>st</sup> Therapeutic to Increase PD-L1 Expression & PD-1 Effectiveness**

**Potential Best-In-Class Adenosine (A2A/A2B) Inhibitors, a Validated Mechanism of Action**

**Multiple Phase 1b/2 Data Catalysts in 2023 (Nine Next 18 Months in Multiple Tumor Types)**

**Experienced Team from Bristol Myers; 10 Oncology Approvals & Multiple Billion \$ Exits**

**Opportunities for Value-Creating Partnerships/License Agreements & Pipeline Expansion**

**Cost-Efficient Business Model: Potential Runway to Achieve Multiple Inflection Points**

# Proven Leadership with Oncology and Financing Expertise



**Ian Walters, MD**  
CEO, Chairman

 Bristol Myers Squibb™



THE ROCKEFELLER UNIVERSITY



**Rob Kramer, PhD**  
CSO

 Bristol Myers Squibb™

*Johnson & Johnson*



**Steve Innaimo**  
VP PM & Operations

 Bristol Myers Squibb™

**COVANCE**



**Justin Fairchild**  
VP Clin Dev

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FOR CANCER  
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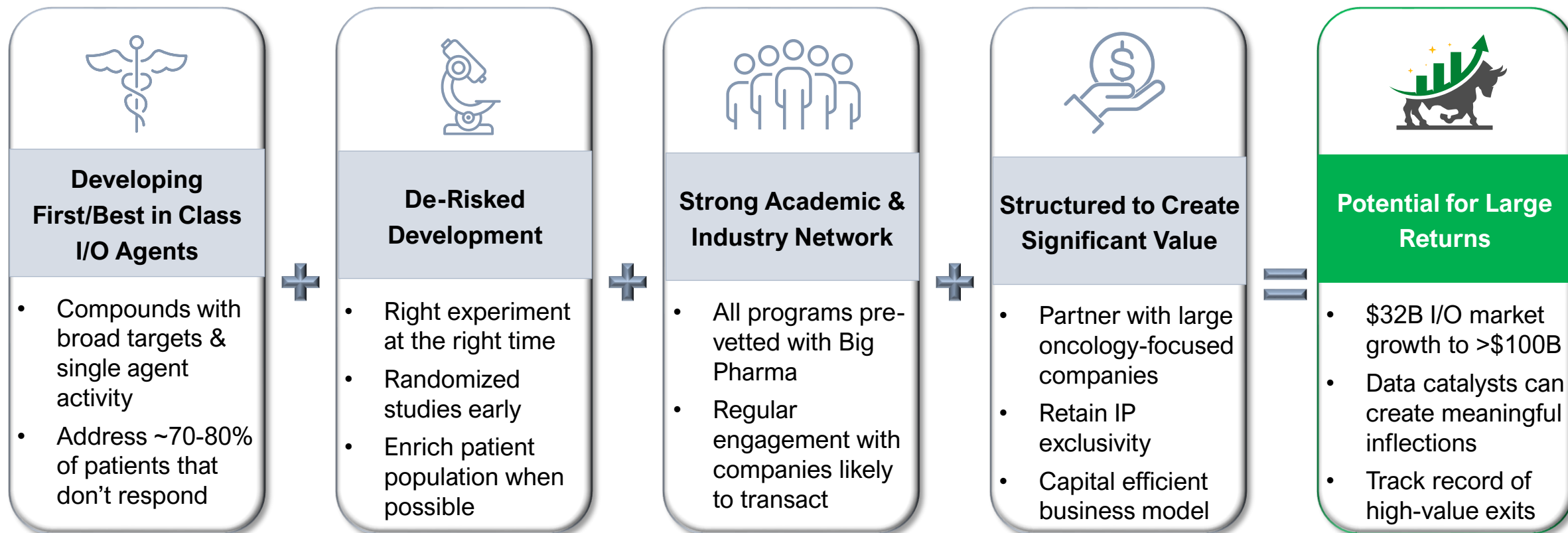
**Mark Simon**



**ROBERTSON STEPHENS®**

**>10 Oncology Approvals, Several Billion \$ Exits**

# Our Formula for Success





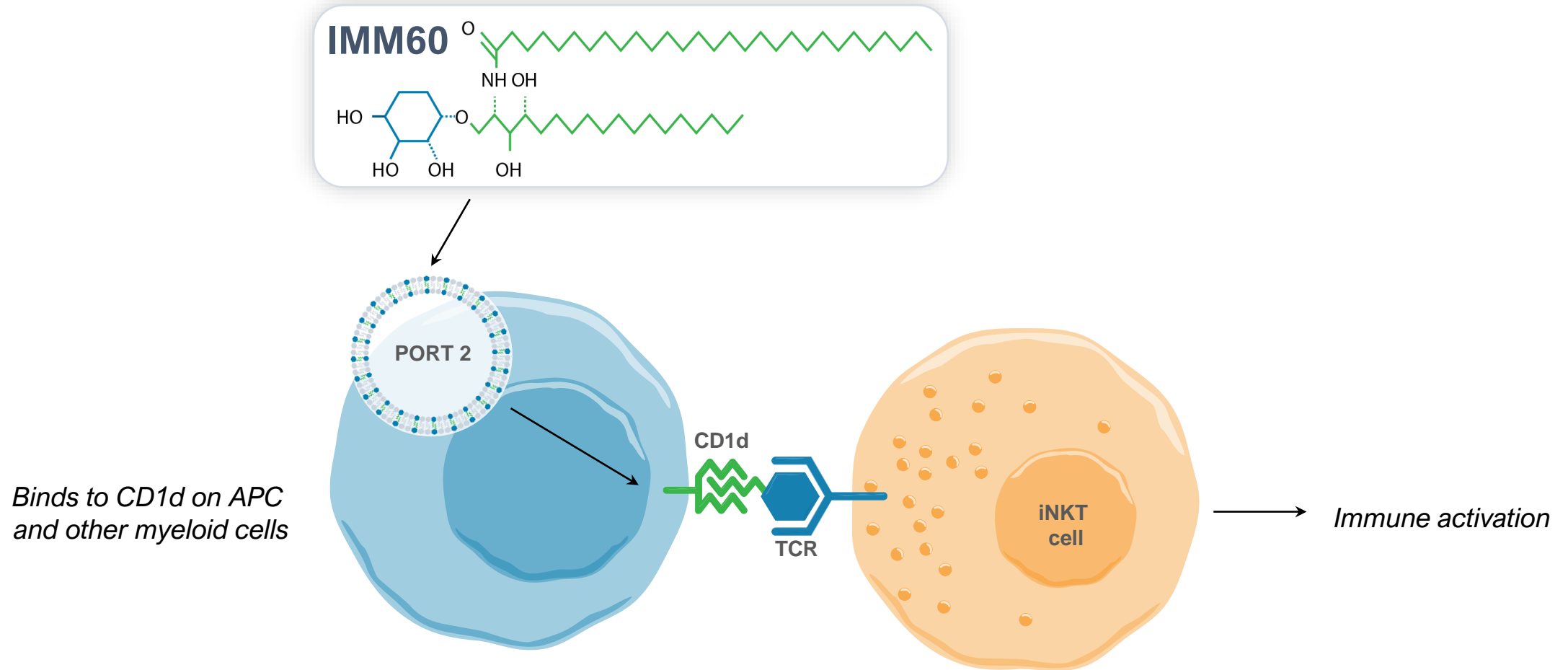
# iNKT agonists

*PORT-2, PORT-3*

Activating the innate,  
adaptive immune system  
and correcting the TME

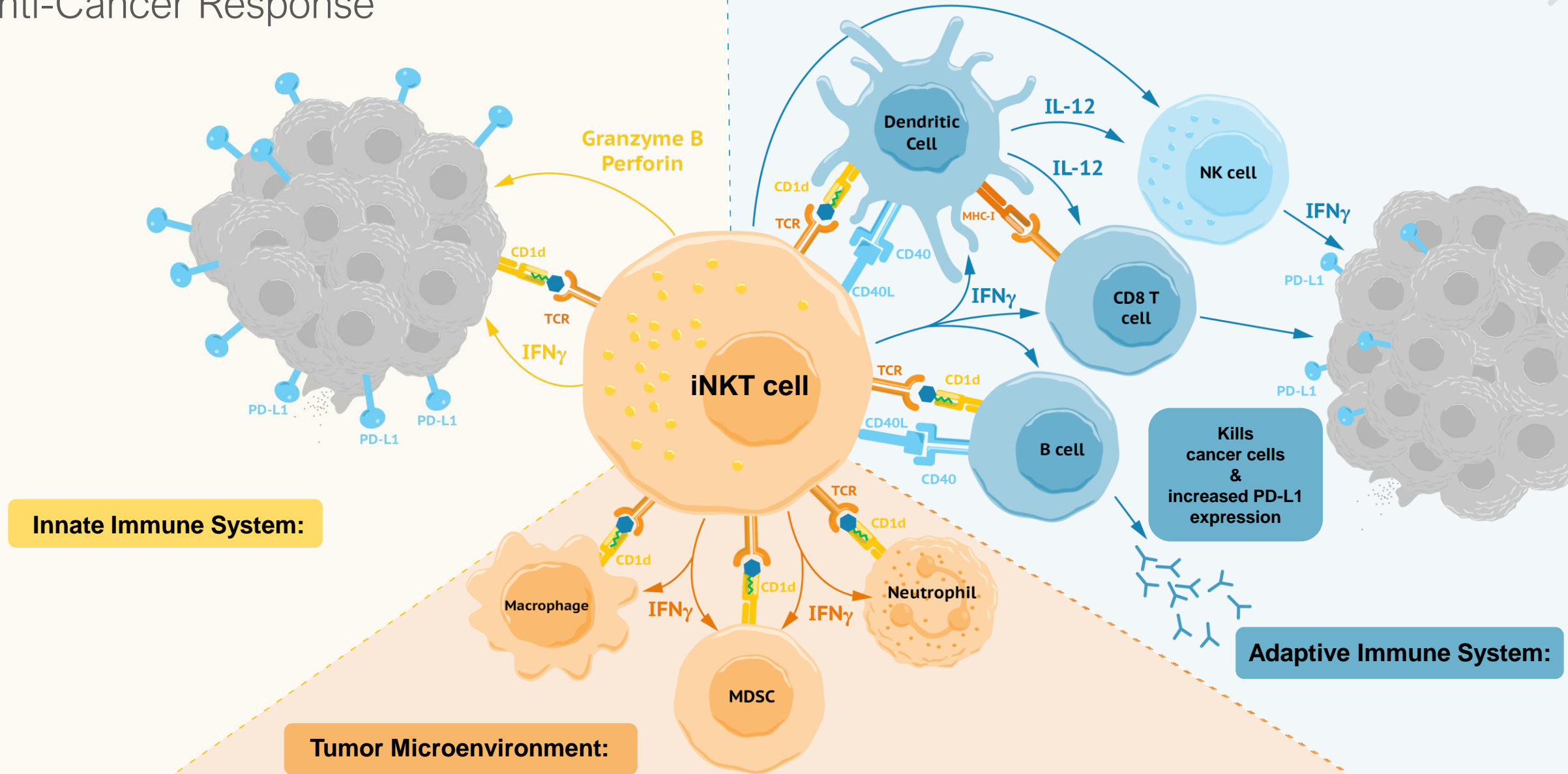
# Portage's iNKT Agonist (PORT-2): Rationally Designed Liposomal Formulation of IMM60

iNKT in charged liposome to protect lipid chain, aggregate in tumor, and promote Type 1 cytokine release




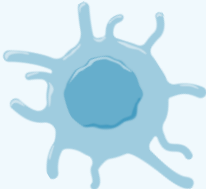
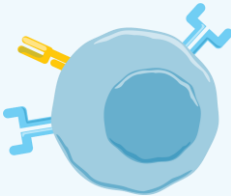
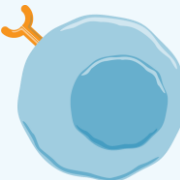
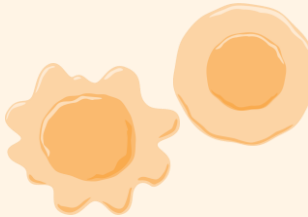

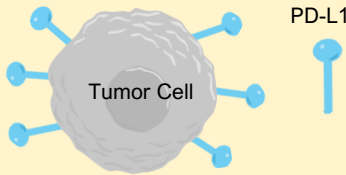






















# PORT-2 Stimulates Multiple Arms of the Immune System to Produce a Robust Anti-Cancer Response





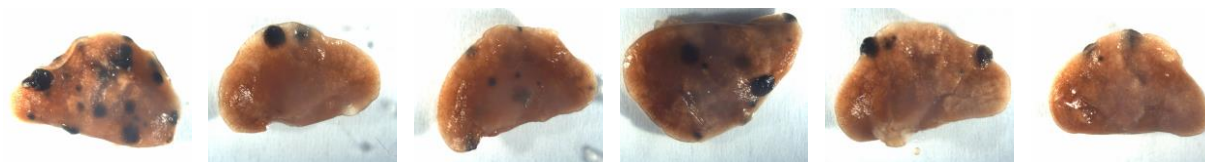
# Multiple Cell Types Involved with Anti-Cancer Response

	NK cell	Dendritic cell	B-cell	CD-8 T cell	MDSC & TAM	Antigen	PD-1
Target Cells							
Companies in the space	   	   	 	  	   	  	<ul style="list-style-type: none"> <li>• Upregulates PD-L1</li> <li>• Monotherapy activity in PD-1 resistant models</li> <li>• Combo restores sensitivity to PD-1 Ab</li> </ul> <p>+ <b>KEYTRUDA</b></p> <p>Enhanced activation</p>

- PORT-2 compound impacts all of these pathways, including changing the tumor directly
- Small molecule approach avoids the many challenges of large biologic compounds and cell therapies
- Focus on solid tumors, unlike many overvalued cell therapy companies

# PORT-2 Demonstrates Superior Response Versus PD-1 Antibody

## B16 melanoma lung metastases



IMM60 (0.5ng/mouse)

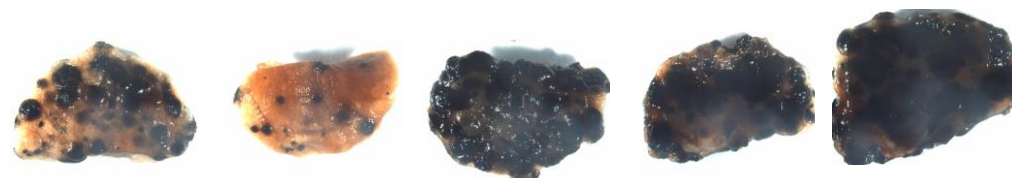
PORT-2



Vehicle + anti PD-1



Vehicle



Untreated

PORT-2 shows **better** response rates vs. anti-PD-1 in melanoma animals

# Interim Phase I Data Confirms PORT-2 Activity & Shows Good Safety (SITC 2022)

Tumor type	2 Melanoma 4 NSCLC
Age	64 (41,79)
Median prior therapies	5(3,7)
Prior PD-1	100%
Performance status	50% ECOG 0 50% ECOG 1

Figure 3

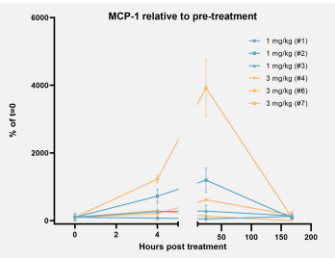


Figure 4

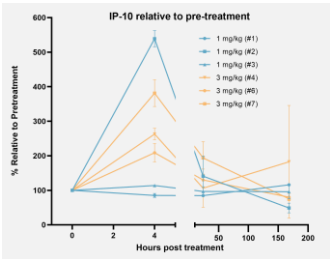


Figure 5

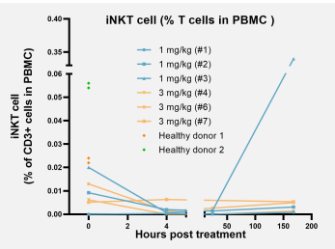
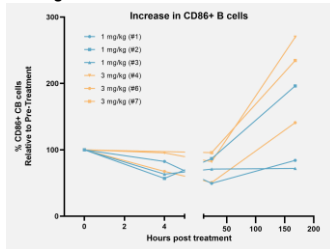


Figure 6



- MCP-1 (**Figure 3**) and IP-10 (**Figure 4**) showed increases in most subjects, no increases in IL-6, IL-4 and IL-10
- iNKTs downregulate their TCR when the agonist binds to the receptor, indicating activation of the iNKT (**Figure 5**)
- Increase in CD86+ B cells which is associated with tumor-specific antigen presentation and sensitivity to checkpoint inhibition<sup>a</sup> (**Figure 6**)

## Exposure/Safety:

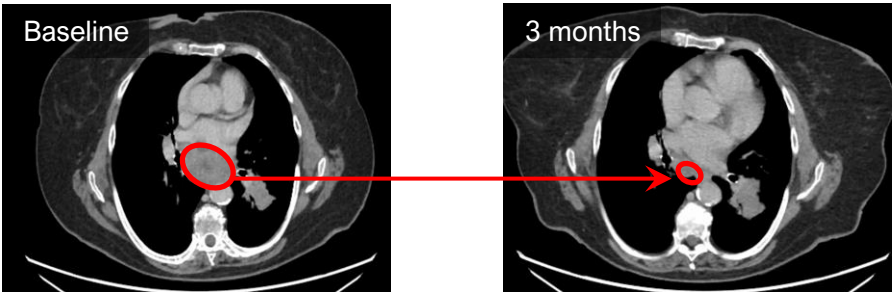
- 27 infusions administered to 6 patients [median 4 per patient]
- No SAEs, no DLTs were observed

Table 2: Adverse Events Related to IMM60 (n=6)

Adverse Event	Grade 1	Grade 2	Grade 3-5
Dizziness	1 (17%)	0	0
Fatigue	0	1 (17%)	0
Flu-like symptoms	1 (17%)	0	0
Hair Loss	1 (17%)	0	0
Headache	1 (17%)	0	0
Hypertension	0	1 (17%)	0
Vomiting	1 (17%)	0	0

Best response by RECIST was PD in all 3 patients at 1mg/m<sup>2</sup> dose. One of 3 patients treated at 3mg/m<sup>2</sup> had mixed response (melanoma patient previously failed anti-PD-1 and targeted therapy), see images below.

## Evidence of monotherapy activity



Mediastinal Lesion

Decreased. **4cm** to **1.9cm**

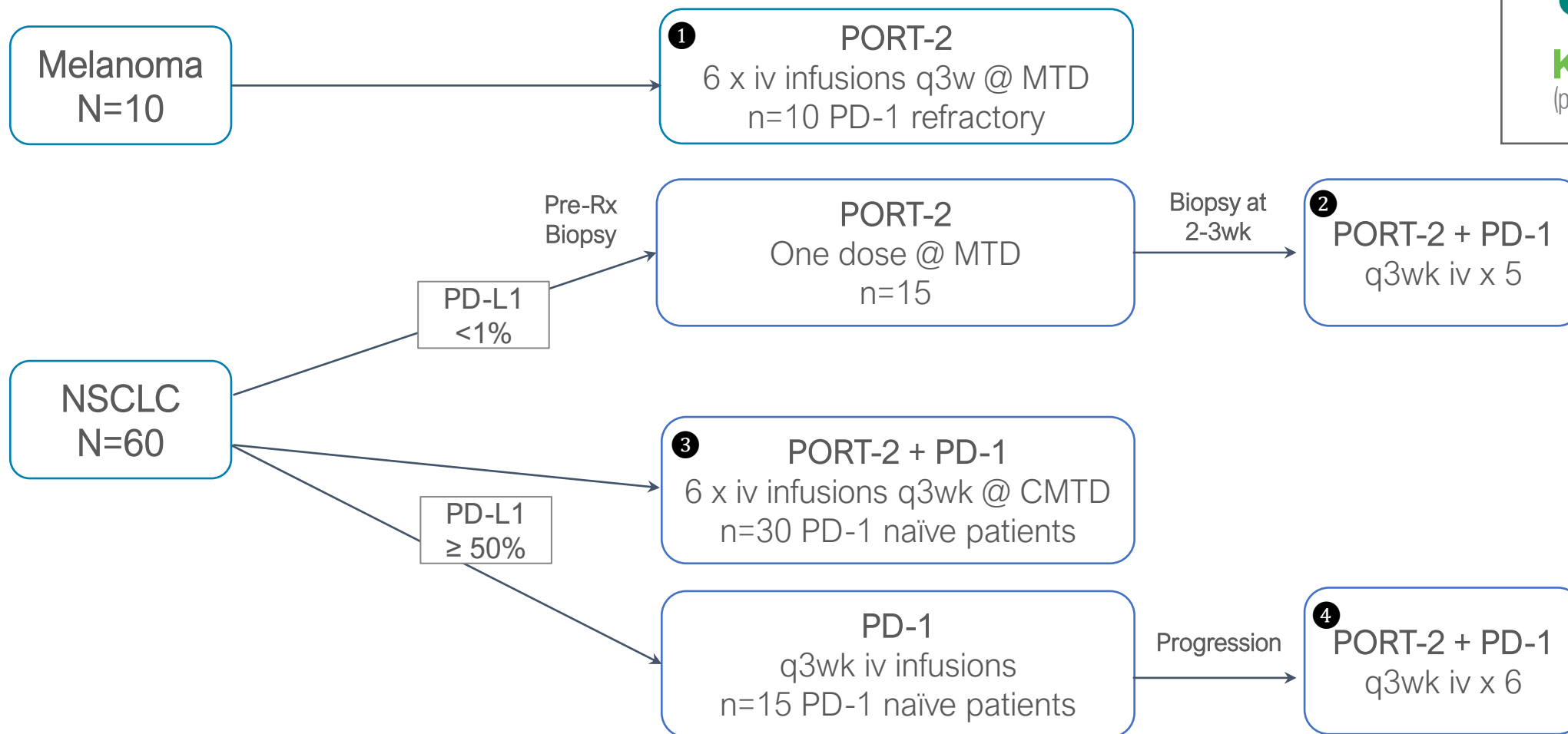
## Additional data in 2023:

High dose cohort of patients receiving PORT-2 monotherapy (total patients to receive monotherapy n=18)

Data from cohort of patients receiving PORT-2 in combination with Keytruda

# IMPORT-201: Phase 2 Evaluates Front Line NSCLC and Refractory Melanoma

In collaboration with



**Multi-arm study with four Phase 2 readouts in 2023/2024**

# Adenosine Portfolio

Unique position to modulate adenosine in 4 different ways

**PORT-6** A2AR Inhibitor

**PORT-7** A2BR Inhibitor

**PORT-8** A2AR/A2BR Dual Inhibitor

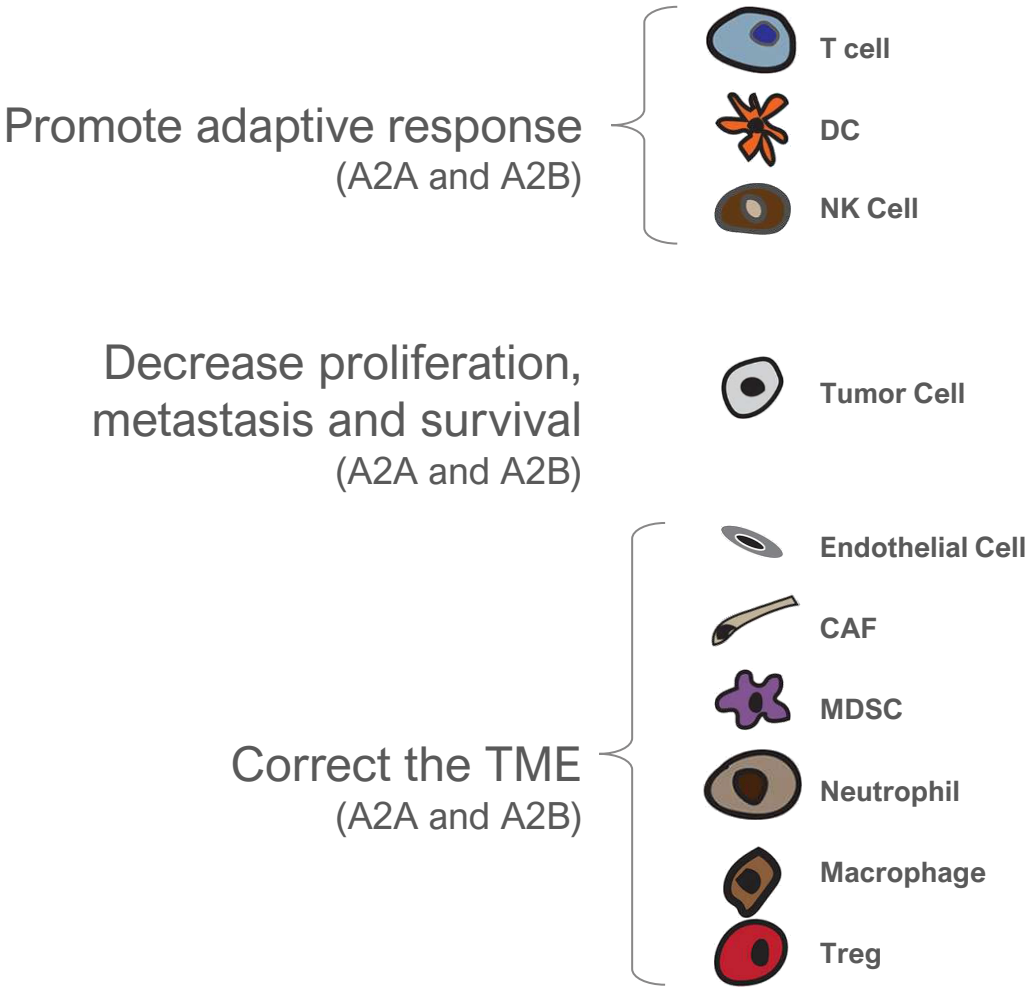
**PORT-9** Gut-Restricted A2BR Inhibitor

Adenosine agents in development by many Pharma & Biotech

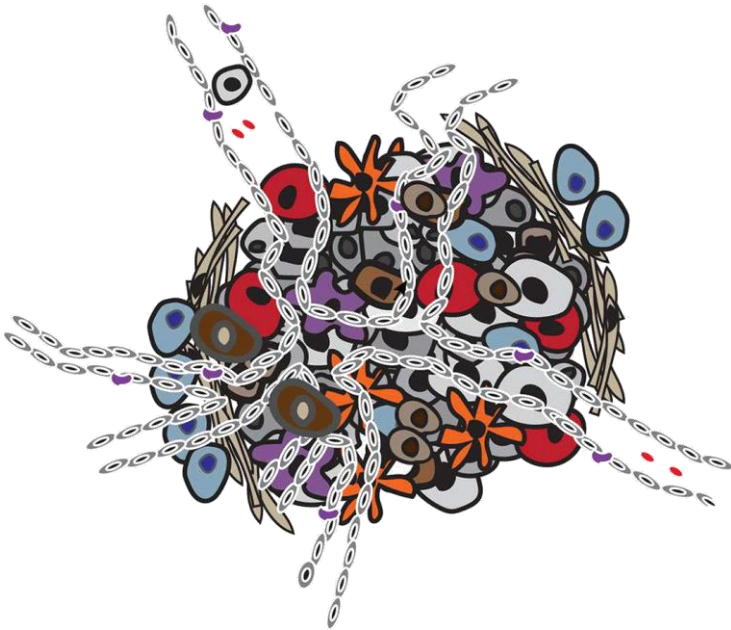
- Validated mechanism impacting multiple immune cells
- Portage acquired adenosine platform for \$18M in stock + \$3M cash
- Gilead paid Arcus \$450M for 2 adenosine compounds



# Leveraging A2A and A2B Alone or in Combo Allows for Customization of Treatment



Tumor is complex system governed by numerous immune cells

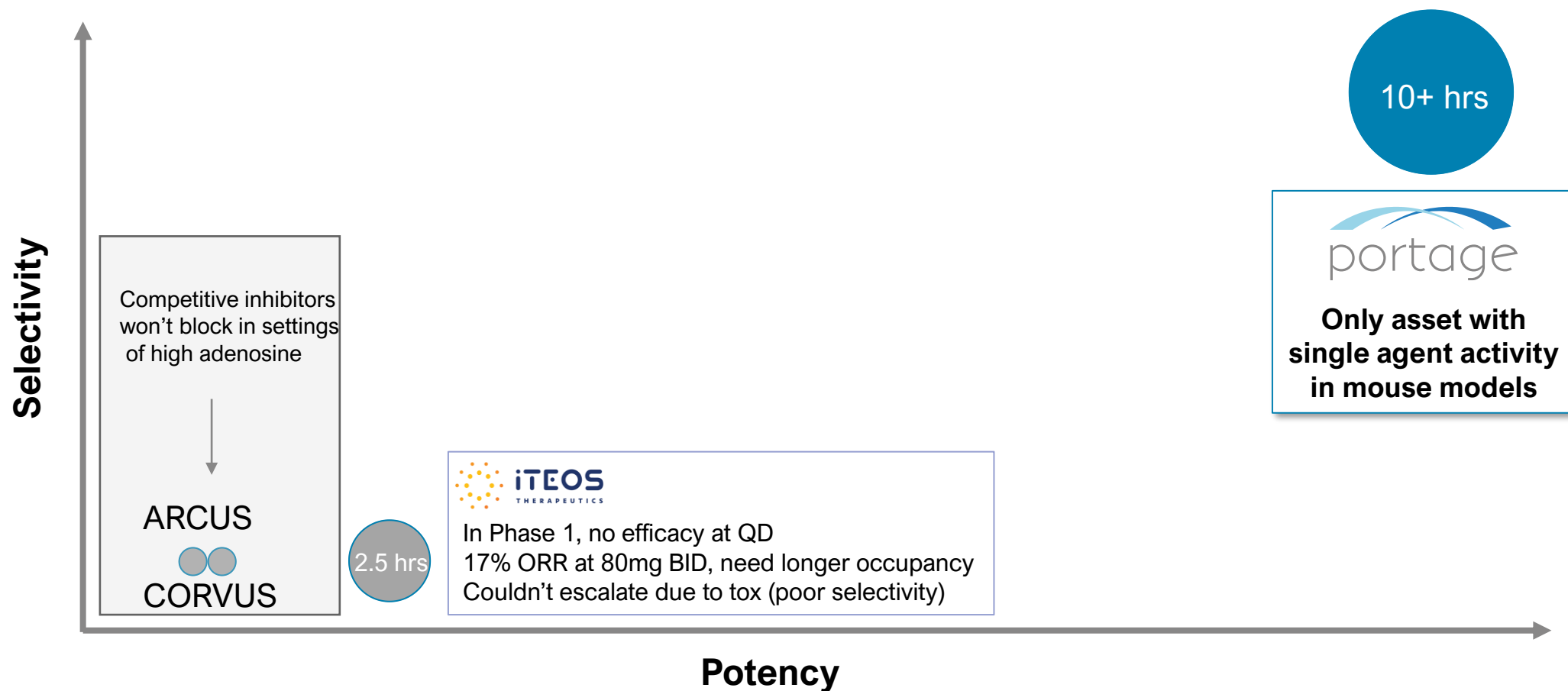


# Difference in A2A Small Molecules

Portage's PORT-6 is best in class for potency, selectivity and durability

Relative profiles of A2A antagonists based on public profiles

Bubble size illustrates how long receptors are occupied





# Fast Follower with Superior Profile Offers Major Competitive Advantages

Use biomarker and clinical data to enrich patient population



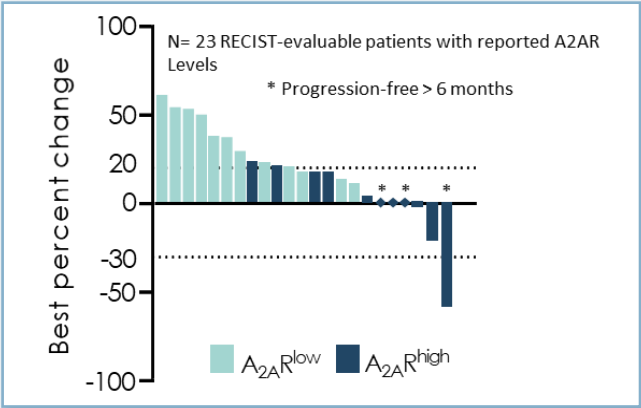
Tumors with High Adenosine

Tumor type	% A2A high*
RCC	50
BC	38
NSCLC	34
Gastric	32
Prostate	26

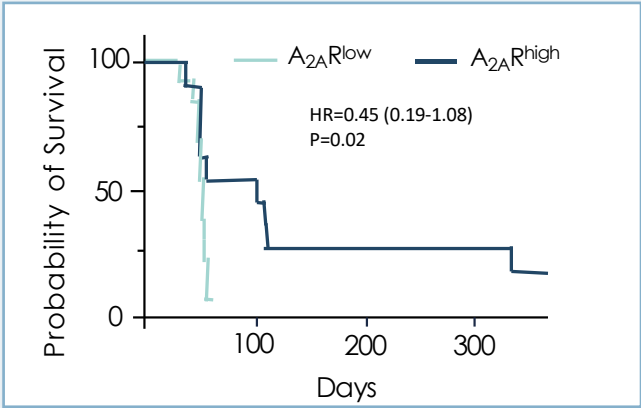
## Positive effect of adenosine antagonist in patients with high adenosine expression demonstrated

iTEOS independent monotherapy activity in biomarker defined population (data from retrospective analysis ASCO 2021)

Best % Change in Tumor Lesion by High/Low A<sub>2</sub>A<sub>R</sub> levels



Survival curve by High/Low A<sub>2</sub>A<sub>R</sub> levels



# PORT-7: Highly Selective and Potent A2B Adenosine Receptor Antagonist

## Functional Receptor Antagonism

Receptor	Ki (nm)	Selectivity
A2B	9	1
A1	>30,000	>3000x
A2A	>10,000	>1000x
A3	>30,000	>3000x

## Binding Affinity

Receptor	Ki (nm)	Selectivity
A2B	13	1
A1	300	23x
A2A	1,800	138x
A3	60,000	>4,000x

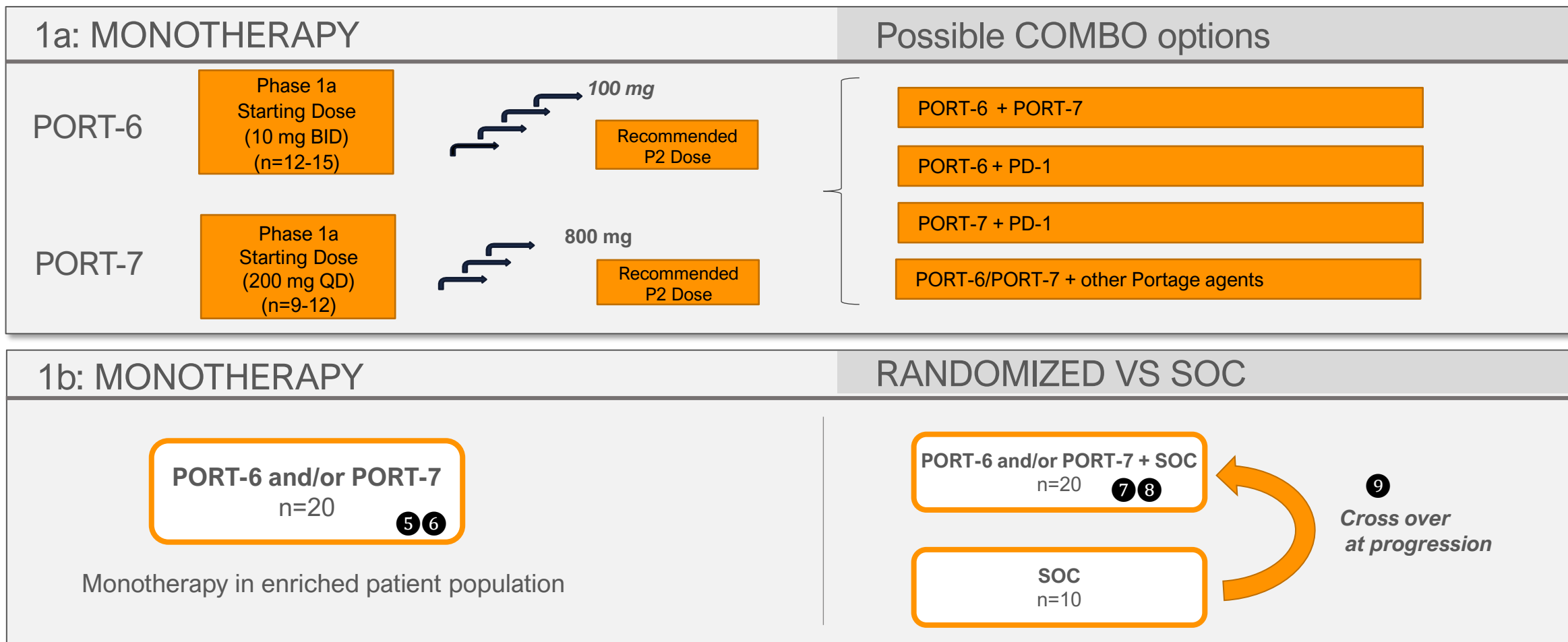
High potency and selectivity may provide important safety and efficacy advantages

- Activity in 4T1, CT26, and other disease models (asthma, fibrosis, sickle cell)
- IND approved for pro-drug

# ADPORT-601: Adaptive Phase 1a/1b Study

A2AR (PORT-6) indications: Prostate Cancer, Non-small Cell Lung Cancer, Head & Neck Cancer, Renal Cell Cancer with high A2A expression

A2BR (PORT-7) indications: Colorectal Cancer, Non-small Cell Lung Cancer, Endometrial Cancer, Ovarian Cancer with high A2B expression



# Strong U.S. and Global IP Positions on Platforms and Products

## Broad and deep intellectual property covering:

### iNKT Agonists

- Composition, formulations with antigens, other I/O agents
- Liposomes/particles

### Adenosine Inhibitors

- Composition of matter patents
- Use patents filed

### Nanolipogel & DNA Aptamers

- Optimized co-delivery platforms
- New IP for aptamers
- Composition patents for products

### VLP Delivery Platform

- First-in-class systemic STING agonist

Many Applications  
Pending Worldwide

**>60**  
Issued Patents

**2031-2036**  
Patent Exclusivity

# Nine Phase 1b/2 Data Catalysts Anticipated to Drive Value

iNKT Platform

	PLATFORM	TECHNOLOGY	ASSET	INDICATION	STAGE	# of PTS	DATA MILESTONES
1	PORT-2	iNKT Agonists Liposomal Formulations	IMM60	Melanoma + NSCLC	Phase 1	18	ASCO 23
	PORT-2	iNKT Agonists Liposomal Formulations	IMM60	Refractory Melanoma	Phase 2	10	ASCO 23/24 SITC 23/24
	PORT-2	iNKT Agonists Liposomal Formulations	IMM60 + Keytruda®	Front line PD-L1 + NSCLC	Phase 2	30	ASCO 23/24 SITC 23/24
	PORT-2	iNKT Agonists Liposomal Formulations	IMM60 + Keytruda®	PD-L1 – NSCLC 2 <sup>nd</sup> /3 <sup>rd</sup> line	Phase 2	10	ASCO 23/24 SITC 23/24
4	PORT-2	iNKT Agonists Liposomal Formulations	IMM60 + Keytruda®	PD-L1 + NSCLC 2 <sup>nd</sup> line	Phase 2	15	ASCO 23/24 SITC 23/24

Adenosine Platform

	PLATFORM	TECHNOLOGY	ASSET	INDICATION	STAGE	# of PTS	DATA MILESTONES
5	PORT-6 PORT-7	A2AR Inhibitor A2BR Inhibitor	TT-10 TT-4	A2A and A2B exp Solid Tumors	Phase 1a	21-27	SITC 23/24 ASCO 24
	PORT-7	A2BR Inhibitor	TT-4	A2B exp Solid Tumors	Phase 1b	20	SITC 24
	PORT-6	A2AR Inhibitor	TT-10	A2A exp Solid Tumors	Phase 1b	20	ASCO 24 SITC 24
	PORT-6 combo	A2AR Inhibitor	TT-10 + CPI	A2A exp Solid Tumors	Phase 1b	20	SITC 24
	PORT-7 combo	A2BR Inhibitor	TT-4 + CPI	A2B exp Solid Tumors	Phase 1b	20	SITC 24
9	PORT 6/7 combo	A2AR Inhibitor A2BR Inhibitor	TT-10 + TT-4 + CPI	BM enriched	Phase 1b	20	SITC 24

# Summary Financial Data

Cash Balance (9/30/22)	~\$15.0 million
Committed Purchase Lincoln Park Capital^	\$30 million
Debt	\$-
Shares Outstanding (11/29/22)	17,061,744
Insider Ownership	51%
Public Float*	49%
Options & RSUs Outstanding (9/30/22)	1,596,040
Warrants Outstanding (9/30/22), expired unexercised October 2022	33,888
Net Cash Used in Operating Activities (Quarter Ended 9/30/22)	\$(2.5 million)
Expected Quarterly Burn in 2023	~\$5 million

^Portage has the right (sole discretion/no obligation), to sell up to \$30 million shares over agreement's 36-month term based on prevailing market prices at the time of each sale, subject to certain conditions

\*Includes ~3.5M Shares subject to lock-up agreements (6-12 mo) in recent 2 stock transactions

# Accelerating I/O Development in Untapped Growth Areas



## Novel, Clinical Stage I/O Portfolio with Small Molecule Focus

- Manufacturing simplicity, low capital investment
- Nine phase 1b/2 clinical data reads over next 2 years



## Engine for Efficient Drug Development & Commercialization

- Expert scientific oversight
- Lean structure with financial flexibility/good cash runway



## Preferred Partner for Pharma in I/O

- Deep industry network facilitates engagement with big pharma and biotech
- Packaged for commercialization/acquisition



## Expert Leadership with Track Record of Success

- Proven success, more than 10 oncology approvals
- Formation of Biohaven Pharmaceuticals, sale to Pfizer





# Appendix

# IMPORT-201: Dose Escalation with Best-in-Class Design for NSCLC and Melanoma

## Phase 1/2 Trial

### Primary investigator

Mark Middleton, Churchill Hospital,  
Oxford: 3 additional sites

### Primary endpoint

Safety

### Secondary endpoints

Response, PFS at 6 months,  
frequency of iNKT cells, frequency  
of Ag specific T cells, frequency  
MDSCs & other immune related  
parameters

### Dose escalation (monotherapy)

3+3 design  
6 x iv infusions  
q3w @ 1/3/9 mg/m<sup>2</sup>  
Max. n=18

↓  
MTD

PORT-2

### Dose escalation (combination therapy)

3+3 design  
6 x iv infusions  
q3w @ MTD-1 Max. n=12

↓  
Combination MTD ('CMTD')

PORT-2 + PD-1

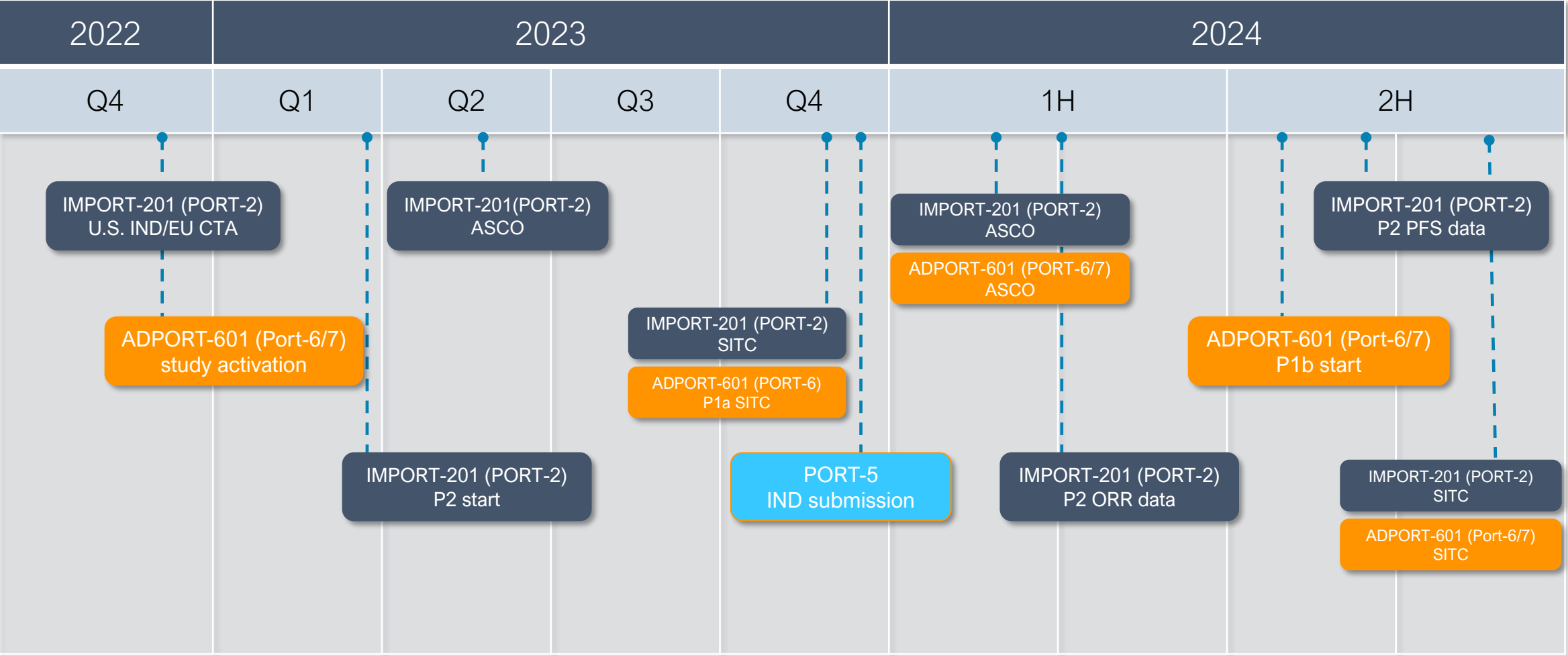
**Phase 1 in refractory melanoma and NSCLC**

# PORT-6: Potential Best-in-Class A2A - Better Selectivity, Potency, Durability

Key Parameters		PORT-6 Portage <sup>1</sup>	EOS-850 iTeos <sup>2</sup>	CPI-444 Corvus <sup>3</sup>	AB928 Arcus <sup>4</sup>	Significance
Potency (cAMP functional inhibition of A2AR)	IC50	<b>0.40 nM</b>	2.24 nM	17.03 nM	--	PORT-6 is >5x more potent than next best IC50
	Ki	<b>0.065 nM</b>	--	--	1.4 nM	Port-6 22x more potent than Arcus on Ki measure
Selectivity against A1 Receptor (Safety)		<b>&gt;150,000x</b>	270x	54x	43x	A1R associated with CNS and CV toxicity
Receptor Occupancy		<b>10+ hours</b>	2.5 hours	0.3 hours	--	Prolonged PD effect: Key attribute given high concentrations of adenosine in TME
Tumor Concentration		<b>10x vs plasma</b>	--	--	1.6x vs plasma	High concentration in tumor tissue required for effective antagonism of tumor expressed receptors
Single Agent Efficacy (% Tumor Reduction)		<b>54% (p&lt;0.05)</b> CT26 Colon Cancer	<10% (p=ns) CT26 Colon Cancer	<10% (p=ns) CT26 Colon Cancer	~20% B16f10 Melanoma	Competing compounds only show effect in combination with other agents

1 Data on File  
 2 AACR 2019  
 3 Cancer Immunology Research 2018  
 4 ASCO GU 2020, SITC 2018

# Key Upcoming Clinical Development Milestones\*



\*At conferences we will present multiple arms & tumor types