

a genus

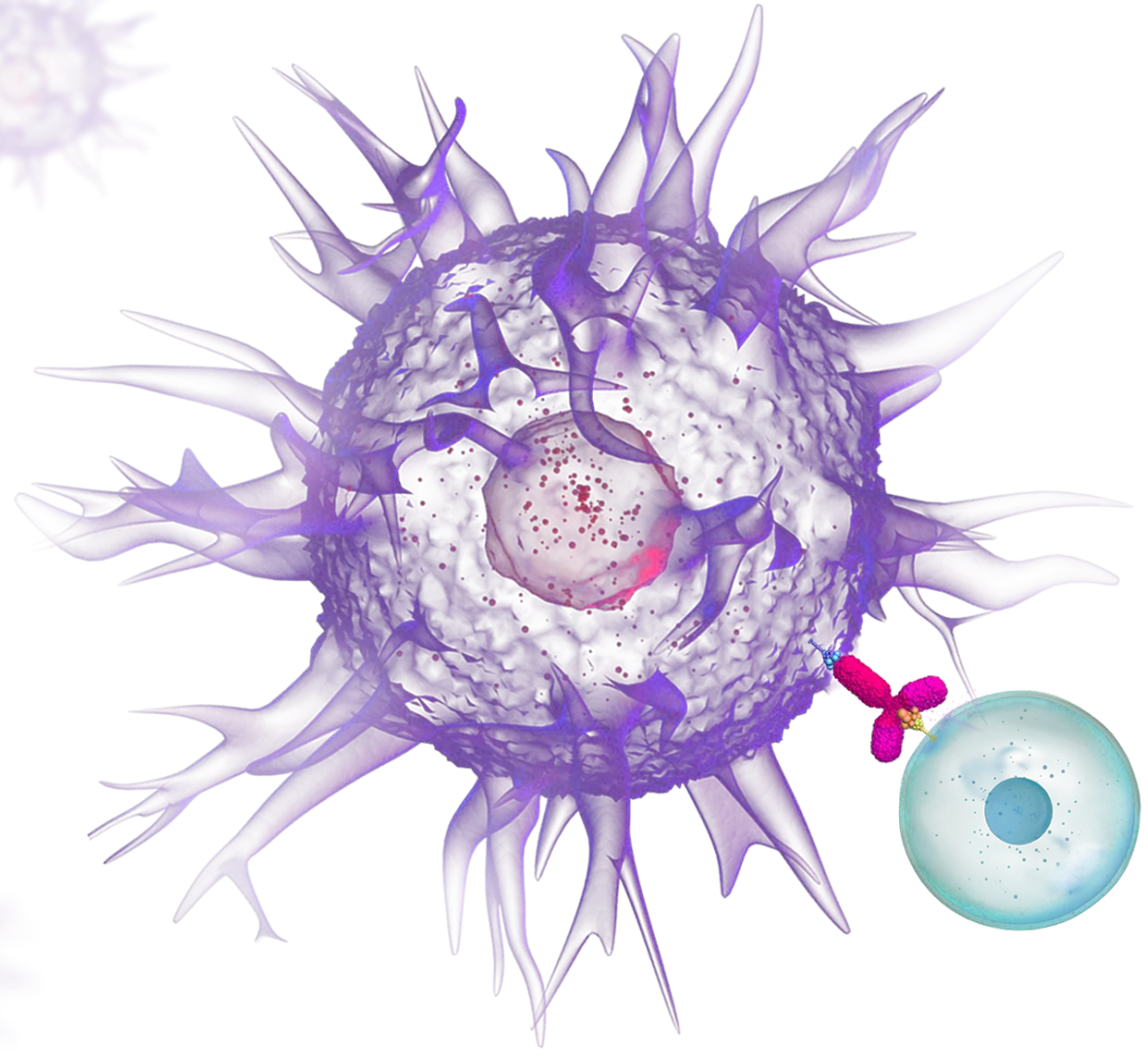
January 2024

# FORWARD-LOOKING STATEMENTS

*This presentation contains forward-looking statements that are made pursuant to the safe harbor provisions of the federal securities laws, including statements regarding Agenus', MiNK's, and SaponiQx's clinical development and regulatory plans (including the scope of any regulatory approval and the ability to obtain priority review) and timelines for product candidates including balstilimab, zalifrelimab, botensilimab, AGEN1327, AGEN1777, AGEN2373, AGEN1571, and AGENT-797; our commercialization plans and pipeline's potential to meet multiple blockbuster opportunities; anticipated safety, efficacy, potency, activity, superior responses, and durability; our goals, milestones and value drivers; anticipated commercial market opportunities (including partnering and licensing opportunities); our ability to collect milestone and royalty payments; our ability to continue to self-finance Agenus; our ability to develop first and best in class drug candidates, adjuvants, antigens and formulations; and our ability to meet manufacturing demands. Statements containing the words "may," "believes," "expects," "anticipates," "hopes," "intends," "plans," "will," "potential," or the negative of these terms and other similar words or expressions, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in any forward-looking statement. These risks and uncertainties include, among others, the factors described under the Risk Factors section of Annual Report on Form 10-K for the fiscal year ended December 31, 2022, and our subsequent Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission and made available on our website at [www.agenusbio.com](http://www.agenusbio.com). Agenus cautions investors not to place considerable reliance on the forward-looking statements contained in this presentation. Agenus makes no express or implied representation or warranty as to the completeness of forward-looking statements or, in the case of projections, as to their attainability or the accuracy and completeness of the assumptions from which they are derived. These statements speak only as of the date of this presentation, and Agenus undertakes no obligation to update or revise the statements, other than to the extent required by law. All forward-looking statements are expressly qualified in their entirety by this cautionary statement. Information that may be important to investors will be routinely posted on our website and social media channels.*

Our Mission

**To End the Suffering  
of Cancer Patients**



# AGENUS BY THE NUMBERS

**29+ years**

Pioneering immuno-oncology (I-O) since 1994

**9 clinical assets**

>20 industry-sponsored clinical studies ongoing for owned and partnered I-O compounds

**\$825 Million**

Upfront cash and achieved milestone payments from strategic partners

**275 employees**

Experienced leadership team in developing and commercializing novel oncology therapeutics

**83,000 sq ft.**

Current good manufacturing practice (cGMP) biologics production facility underway: clinical and commercial-grade drug substance and drug product

**BOTENSILIMAB**

**~750 patients**

Dosed with botensilimab (BOT) or botensilimab/balstilimab (BOT+BAL) combo in ongoing Phase 1 & 2 studies in advanced, refractory solid tumors

**Responses in 9 tumor types**

Clinical responses noted in 9 advanced, refractory solid tumors treated with BOT or BOT+BAL

**FDA Fast Track in CRC\***

Granted in April 2023 for BOT+BAL combo in heavily pretreated metastatic microsatellite stable (MSS) colorectal cancer (CRC) without active liver mets; BLA filing planned for mid 2024

4 \*Fast Track designation is for patients who are heavily pretreated and resistant or intolerant to a fluoropyrimidine, oxaliplatin, and irinotecan, and who have also received a VEGF inhibitor, and EGFR inhibitor and/or a BRAF inhibitor, if indicated

# BOT+BAL: REMARKABLE RESPONSES IN RESISTANT PATIENTS

- 1 Planned BLA Filing Mid 2024 for BOT+BAL in 2/3L+ Metastatic MSS Colorectal Cancer (CRC)
- 2 Opportunity to Significantly Improve Patient Benefit in Stage 3 Neoadjuvant CRC
- 3 Potential for Multiple Supplemental BLA Filings: *Pancreatic (2025), Melanoma (2025), Lung (NSCLC)*
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# COLORECTAL CANCER: GROWING PREVALENCE WITH LARGE UNMET NEED

CRC is the 3<sup>rd</sup> most common cause of cancer mortality globally<sup>1</sup>

Despite advances in treatment of CRC, long term survival remains low<sup>2,3</sup>

- **3-year relative OS for patients with metastatic CRC is ~30-35%**
- **5-year relative OS for patients with metastatic CRC is ~15%**

~1.9M

People diagnosed annually with CRC worldwide<sup>1</sup>

~380K

~20% of patients diagnosed have metastatic disease<sup>2</sup>

~360K

95%<sup>4</sup> of metastatic CRC patients have MSS CRC<sup>3</sup>



# GOAL: DELIVER FIRST BLA FOR BOT+BAL IN MID 2024

Target Indication: Metastatic 2/3L+ MSS CRC in patients with no active liver mets (NLM)

## High Unmet Need

- CRC is the 2<sup>nd</sup> most common cause of cancer mortality in the US<sup>1</sup> and in Europe<sup>2</sup>
- 20% patients have metastases<sup>3</sup>
- MSS CRC represents 95% of metastatic CRC patients<sup>4</sup>
- CRC diagnosis rapidly shifting to a younger age; 43% of diagnosis will be in 45–49-year-olds<sup>5</sup>

## Robust Clinical Responses

- 2/3L+ Metastatic MSS CRC with NLM:
- Overall Response Rate (ORR): 24%<sup>6</sup>
  - 12-Month Overall Survival (OS): 74%
  - Disease Control Rate (DCR): 80%
  - Median OS not reached after 12 months of follow-up (vs. 12.9 months with standard of care [SOC])
  - Manageable safety profile
- n=70 efficacy evaluable, median 4 prior lines of therapy; 25% failed prior I-O therapy*

## Accelerated Approval Path

- FDA Fast Track designation in Metastatic MSS CRC with NLM\*
- Phase 2 enrollment complete (n=230); Study objective: dose optimization and contribution of components
- Includes SOC arm (lonsurf or regorafenib)
- Phase 3 planned in 1L for 2024 (subject to further regulatory interactions)
- BLA planned mid 2024

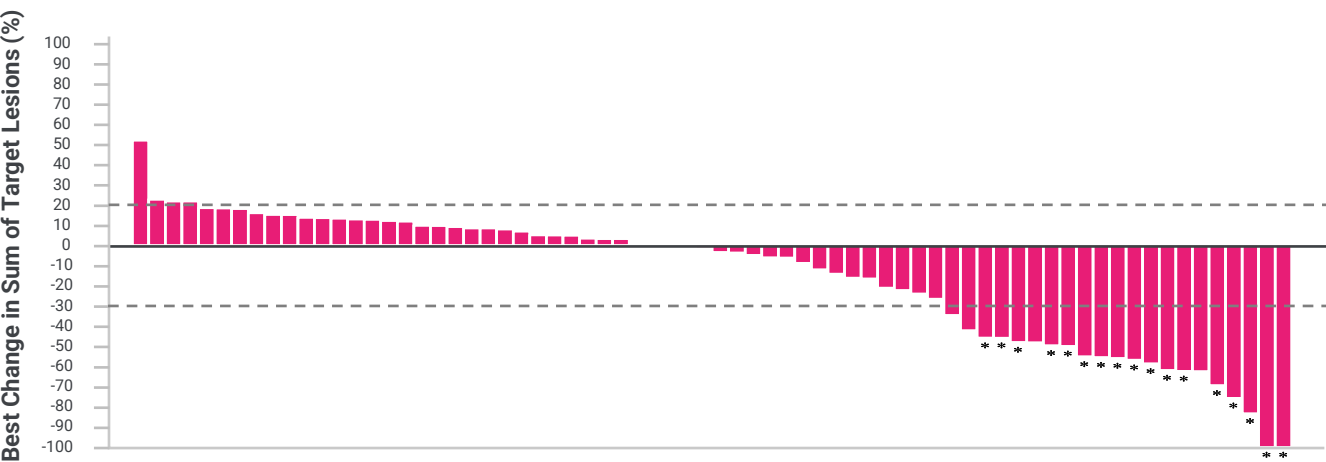
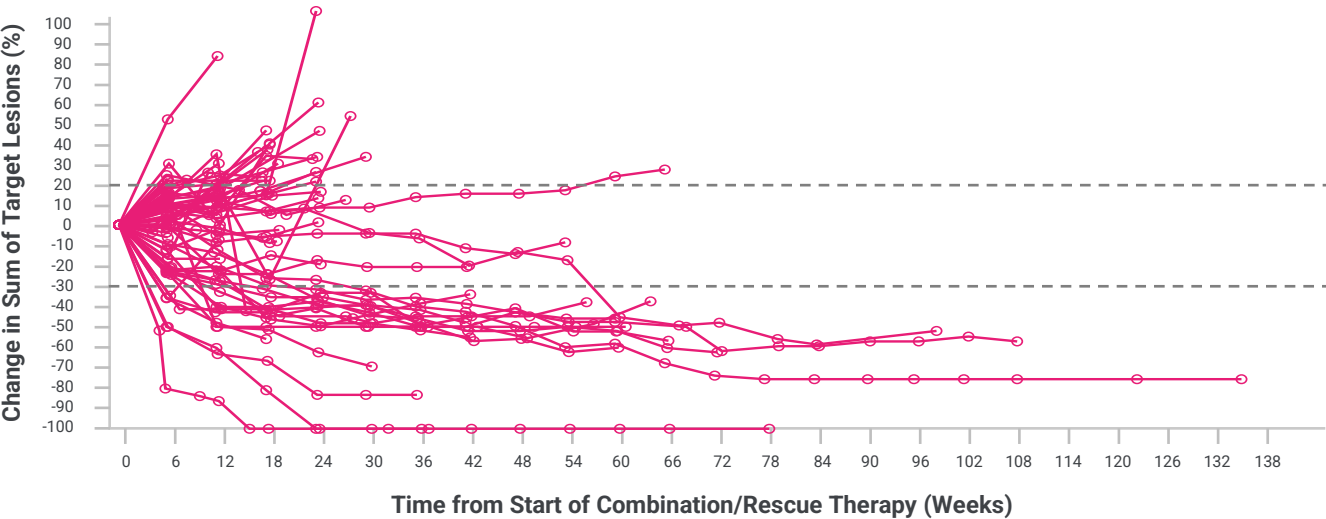
8 \*Fast Track designation is for patients who are heavily pretreated and resistant or intolerant to a fluoropyrimidine, oxaliplatin, and irinotecan, and who have also received a VEGF inhibitor, and EGFR inhibitor and/or a BRAF inhibitor, if indicated

Source: 1. Siegel et. al. CA Cancer J Clin, 2023. 2. Dyba, et al. NIH 2021. 3. Ciardiello F et al. CA Cancer J Clin. 2022. 4. CancerMPact® Treatment Architecture U.S., CRC 2021. 5. Colorectal Cancer Statistics, ACS 2023 6. Agenus Corporate Event, ESMO 2023



# ROBUST RESPONSES IN METASTATIC 2/3L+ MSS CRC NLM

8x improvement in ORR to reported standard of care in patients with NLM disease



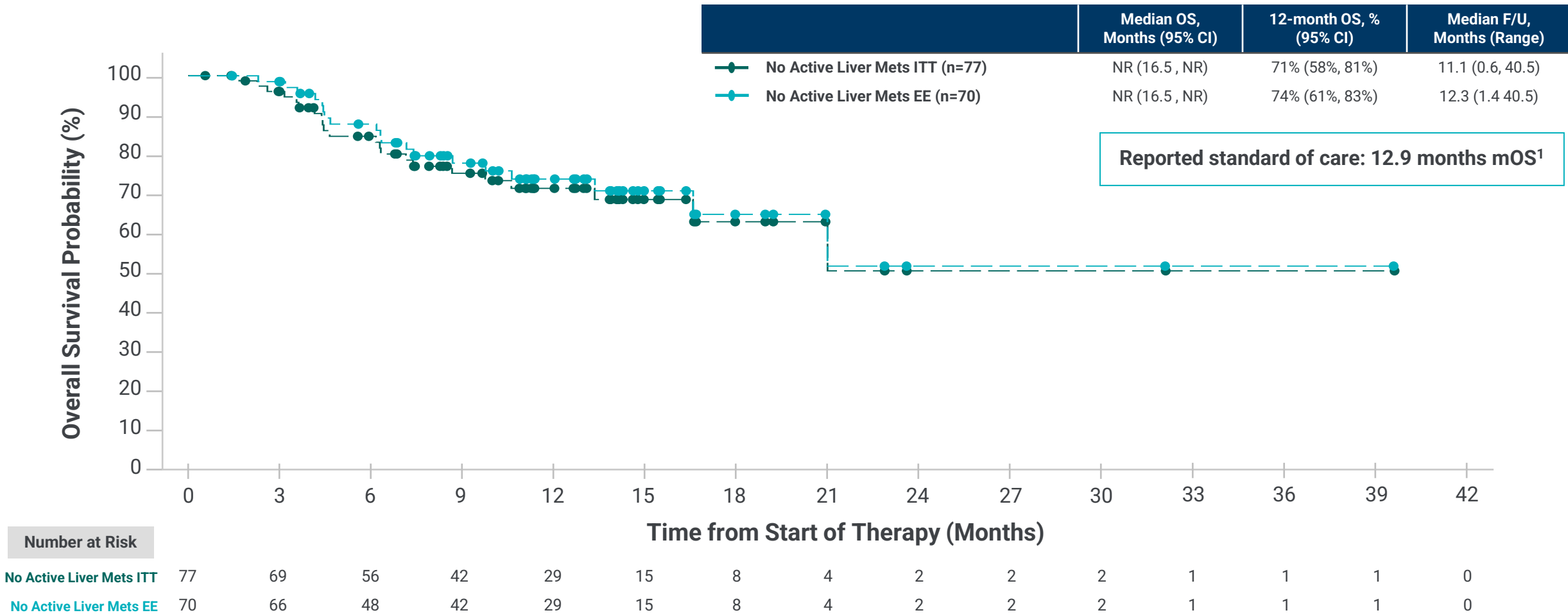
2/3L+ metastatic MSS CRC with No Active Liver Mets Efficacy Evaluable Population (n=70)	
Confirmed ORR, % (95% CI)	24% (15%, 36%)
BOR, n (%)	
CR	1 (1%)
PR	16 (23%)
SD	39 (56%)
PD	14 (20%)
DCR (CR + PR + SD), % (95% CI)	80% (69%, 89%)
Responses ongoing	10 (59%)
Median follow-up, months (range)	12.3 (1.4 – 40.5)

In the intent to treat (ITT) population with no active liver metastases (n=77), ORR was 22% and DCR was 73%

Reported standard of care: 2.8% ORR<sup>1</sup>

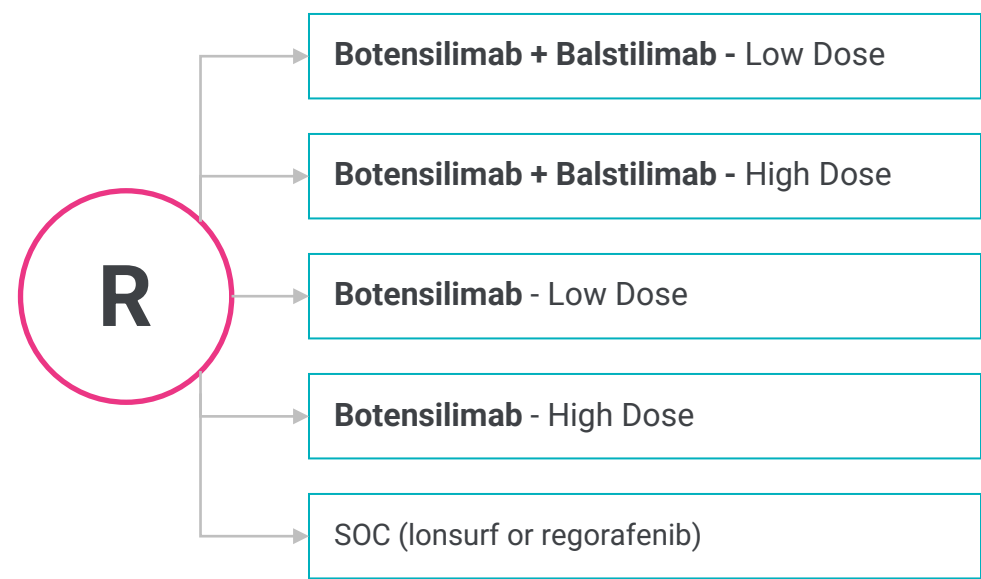
# ENHANCED OVERALL SURVIVAL IN 2/3L+ METASTATIC MSS CRC NLM

Median follow up 12.3 months; median overall survival (mOS) not yet reached



# PHASE 2 STUDY IN REFRACTORY 2/3L+ METASTATIC MSS CRC NLM

Ongoing global, randomized phase 2 study, enrollment completed October 2023



## Objective

- Dose optimization
- Contribution of components

## Patient Population

- 2/3L+ MSS colorectal adenocarcinoma that is refractory to chemotherapy
- No active liver mets (NLM)

## Target Endpoints

- Primary: ORR
- Secondary: DOR, Progression Free Survival (PFS), OS, Safety, Pharmacokinetics (PK)/Immunogenicity

# GO-TO-MARKET STRATEGY

Experienced leadership team in place to deliver successful launch of BOT upon approval

## Clinical Team with I/O Pioneers

- ✓ **KOL relationships across 40+ countries** facilitating scientific exchange
- ✓ **25+ podium & clinical presentations** at major medical conferences
- ✓ **PIs from the top cancer centers** (Dana Farber, City of Hope, Weill Cornell etc.)



### Chief Medical Officer

Steven O'Day



### VP, Clinical Development

Joseph Grossman



## Extensive Medical Affairs Engagement

- ✓ **25+ FTEs with big pharma and biotech experience** (BMS, Amgen, BeiGene, Turning Point, Agios etc.)
- ✓ **Multiple KOL meetings at ASCO 2023 and ESMO 2023** with major tertiary care research centers in US, EU, Japan and CIS
- ✓ **Extensive engagement** with globally-renowned GI & CRC oncologists as investigators on Phase 1 & 2 studies



### Chief Medical Affairs Officer

Nils Eckardt



### Chief Strategic Advisor

Todd Yancey



## Commercial Preparedness

- ✓ **Robust planning for commercial launch**
- ✓ **Fully integrated cGMP manufacturing capabilities underway**



### Chief Commercial Officer

Robin Taylor



### Chief Manufacturing Officer

Al Dadson



# FULLY INTEGRATED COMMERCIAL cGMP MANUFACTURING FACILITY

## 📍 Agenesis West (Emeryville, CA)

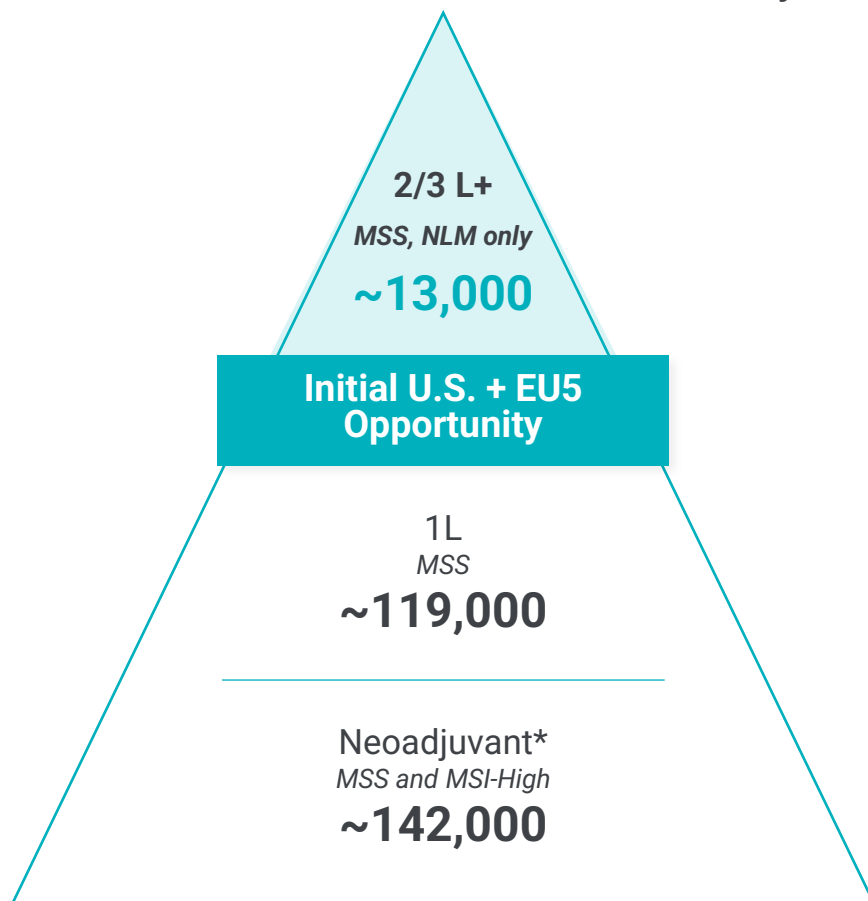
- ~83,000 sq foot commercial cGMP facility
- Enhances operational flexibility and efficiency through end-to-end clinical and commercial production:
  - Drug substance manufacturing
  - Drug product fill/finish
  - Visual Inspection
  - Packaging & labeling
  - Distribution
  - Warehousing



# BOT+BAL HAS THE POTENTIAL TO BECOME A BACKBONE CRC THERAPY

Initial opportunity in NLM subpopulation in late-line setting with clinical data being generated in earlier treatment settings

## U.S./EU5 CRC Patients Treated Annually



### 2/3L+ MSS CRC

- >300 patients treated with BOT/BAL
  - ORR: 24% ; 74% 12-month OS ; mOS: not reached (n=70)
- Fast Track designation granted by FDA
- BLA filing planned mid 2024

### 1L MSS

- Planned Phase 3 confirmatory study (pending regulatory alignment)
- BOT/BAL + Bevacizumab + FOLFOX vs. Bevacizumab + FOLFOX
- Investigator Sponsored Trial (IST) ongoing @ City of Hope (NCT05627635) designed to evaluate tolerability with chemo

### Neoadjuvant MSS and MSI-H

- Treatment with BOT/BAL pre-surgery
- IST ongoing @ Weill-Cornell in MSS & MSI-H CRC (NCT05571293)
- IST expanding; initial data at ESMO 2023 event; data readout expected in 2Q 2024

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## PATIENT CHALLENGES IN METASTATIC, LATE-LINE SETTINGS

Colon cancer spreads most often to the liver, sometimes the lungs and less often to the abdomen and other areas. Treatment options vary by patient but can be invasive and taxing, potentially including:

- Colectomy to remove the colon tumor
- Colostomy with colostomy bag to remove waste
- Surgery and ablation for liver and lung tumors
- Nerve damage from chemotherapy
- Radiation-induced menopause
- Radiation-induced bone loss







“

***"Individuals with stage IV cancer face the worst kind of deadline: The deadline that their advanced disease is going to someday take their life if we don't make greater advances."***

*- Dr. Rich Goldberg, GI Oncologist, West Virginia University Cancer Institute, Advisor to Fight CRC's Path to a Cure Research Report*

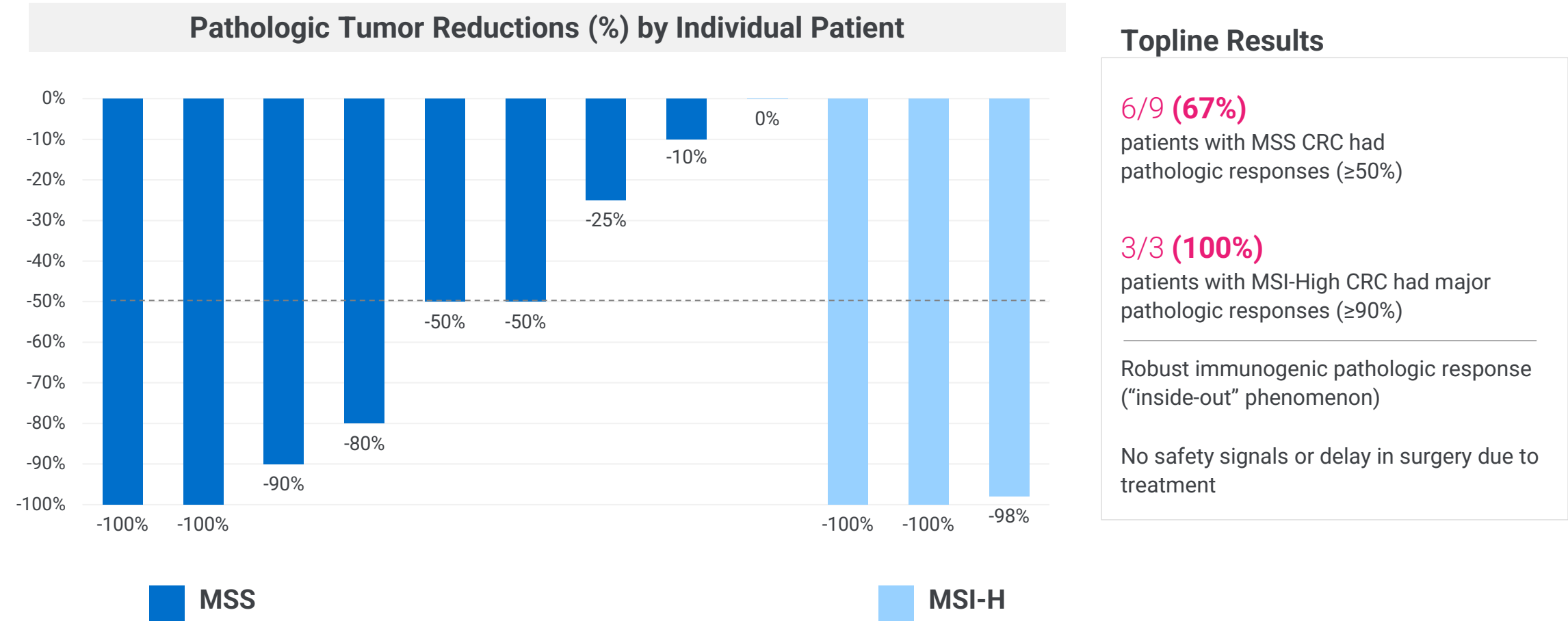
# EXPANSION INTO EARLIER TREATMENT LINES IN MSS CRC

Investigator sponsored studies support ongoing development and registrational strategy

Institution	IST / Disease Setting	Anticipated Data Readout
  <b>Marwan Fakih, MD</b>	<b>1L MSS CRC</b> BOT/BAL + Bev + FOLFOX vs. Bev + FOLFOX	<ul style="list-style-type: none"><li>• 1H 2024</li></ul>
  <b>Pashtoon Kasi, MD</b>	<b>Neoadjuvant MSS &amp; MSI-H CRC</b> BOT/BAL pre-surgery	<ul style="list-style-type: none"><li>• 4Q 2023 Pilot study (n=12)</li><li>• Pilot study submitted to 2024 medical meeting</li><li>• Updated data in 2Q 2024</li></ul>

# “WINDOW OF OPPORTUNITY” NEOADJUVANT CRC: PROMISING RESULTS

Treatment with one dose of BOT and two doses of BAL led to significant tumor reduction within approximately four weeks; well tolerated





## BOT: POTENTIAL PARADIGM SHIFT IN THE PATIENT EXPERIENCE AT EARLIER STAGES OF DISEASE

- BOT as potential backbone therapy in combination with other immunotherapies
- Biological basis: stronger immune system should respond more favorably
- Potentially avoid invasive surgeries and chemo toxicities
- Data from ISTs in CRC to inform sponsored study path forward in neoadjuvant and/or 1L setting

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*“With confirmation in a larger cohort and/or a randomized clinical trial, these patients potentially could be spared the toxicity of adjuvant chemotherapy.”*

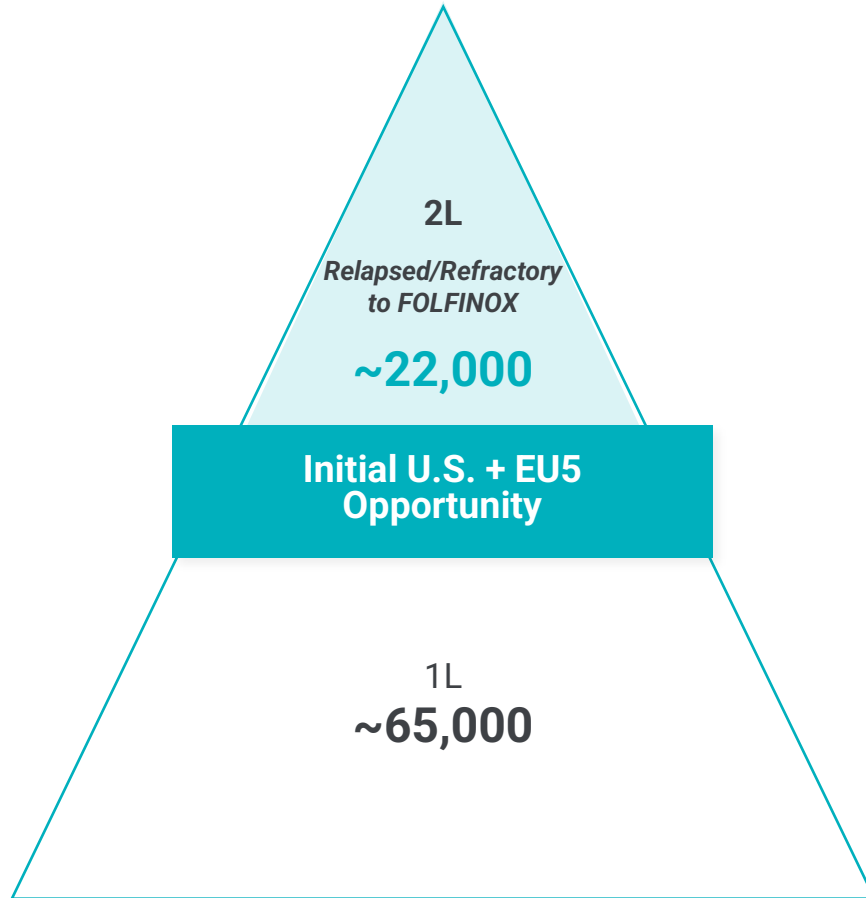
*- Kasi et al. Oncogene 2023*

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# BOT + CHEMO AS POTENTIAL BACKBONE 2L PANCREATIC THERAPY

U.S./EU5 PDAC Patients Treated Annually



## 2L Pancreatic Cancer

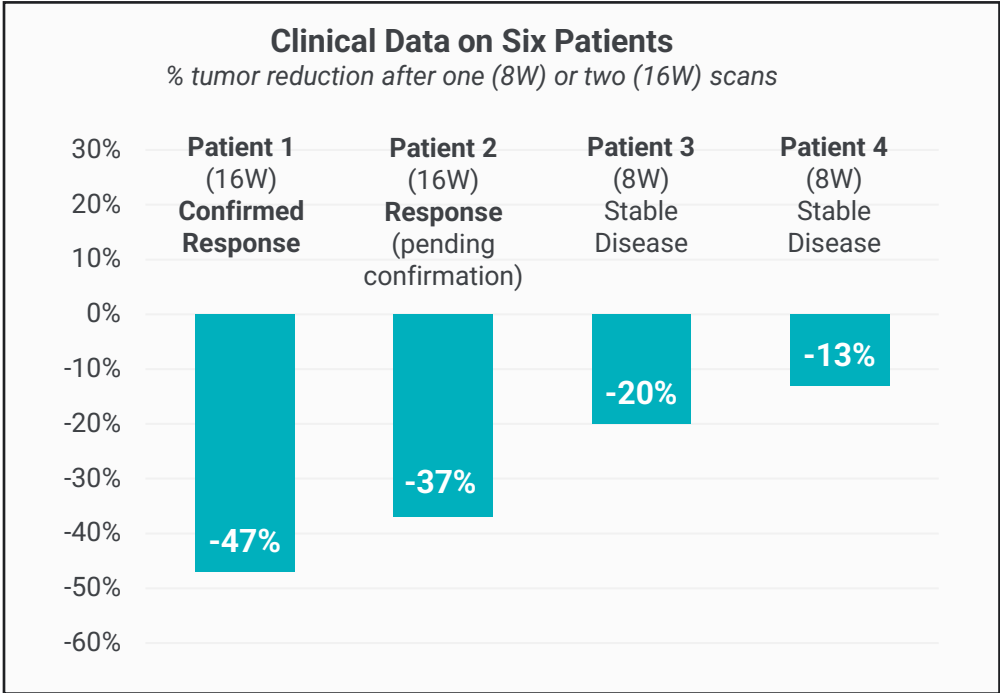
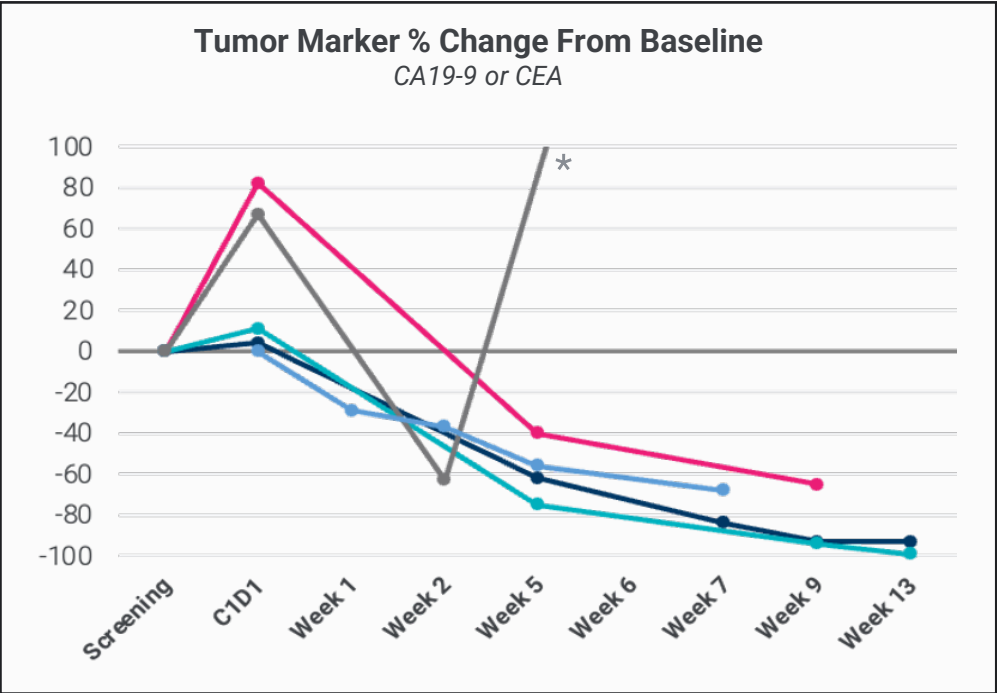
- Phase 2 with BOT + gem/Abraxane (n=60)
- High unmet need: SOC has <15% ORR, 7-8 month median overall survival
- Potential sBLA filing 2025

## 1L Pancreatic Cancer

- Potential registrational study: BOT + SOC (FOLFIRINOX) vs. FOLFIRINOX

# CLINICAL DATA IN 2L PANCREATIC CANCER

Patients (n=6) dosed with 150mg BOT + gem/abraxane after FOLFIRINOX failure for metastatic disease; all patients had liver metastases



\*5<sup>th</sup> patient had clinical progression and is now off study  
6<sup>th</sup> patient is awaiting their first scan



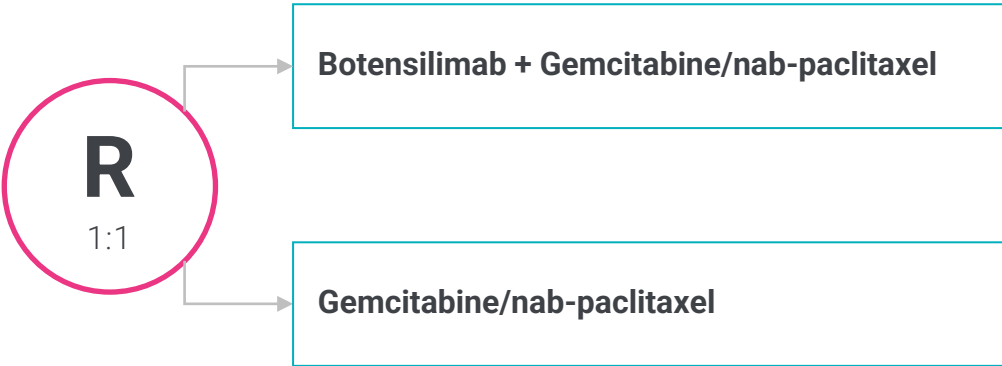
# PHASE 2 ONGOING IN 2L PANCREATIC CANCER

Designed to address key regulatory requirements

## Part A (Safety Lead-In)

- DLT evaluable patients get high dose or low dose depending on DLTs observed
- Determine Part B dose

## Part B (Randomization)



## Objective

- Dose optimization
- Contribution of components

## Patient Population

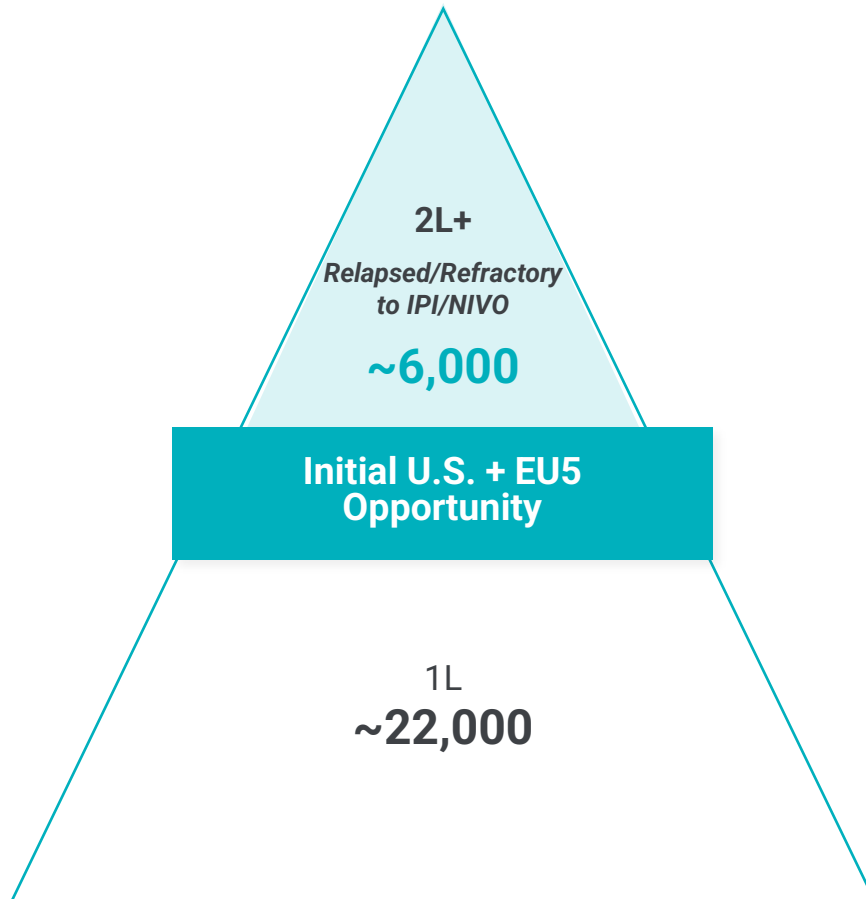
- 2L metastatic Pancreatic Ductal Adenocarcinoma (mPDAC) post FOLFIRINOX

## Target Endpoints

- Primary: PFS
- Secondary: DOR, PFS, ORR, Safety, PK/Immunogenicity

# BOT+BAL AS BACKBONE MELANOMA THERAPY

## U.S./EU5 Melanoma Patients Treated Annually



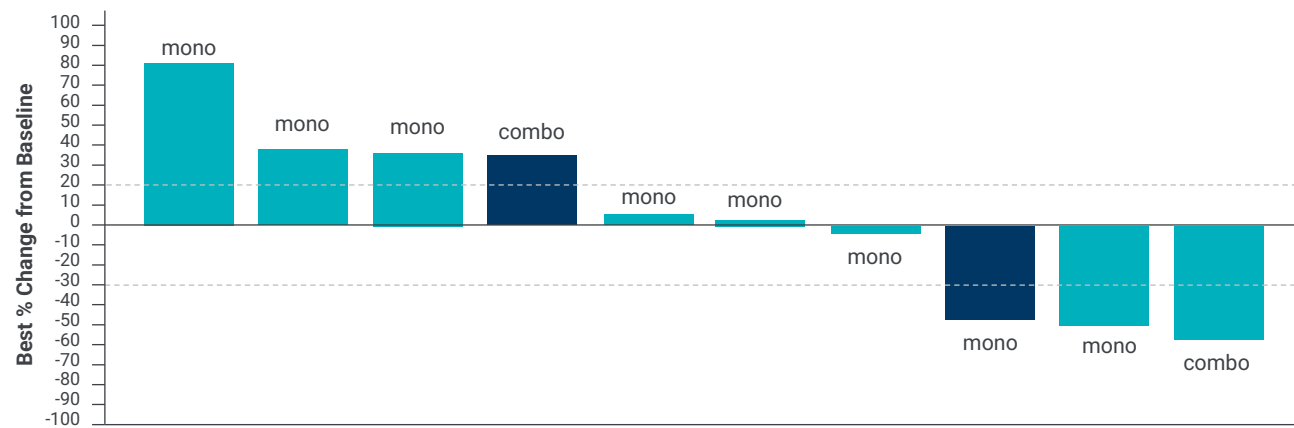
### 2L+ Melanoma

- High unmet need: no established standard of care in I-O relapsed/refractory setting
- Phase 2 results are expected in the second half of 2024, with BOT monotherapy enrollment complete and approximately 30 patients enrolled in the BOT+BAL cohort
- Currently defining strategies for the rapid enrollment of BOT in patients who are refractory to current I-O treatments

### 1L Melanoma

- Registrational study consideration: BOT+BAL vs. 1L SOC

## Cutaneous melanoma patients receiving BOT monotherapy or BOT+BAL combination



PD-1 R/R	1/2 = 50% ORR	(10-15% for ipi <sup>1</sup> )
CTLA-4/PD-1 R/R	2/8 = 25% ORR	(n/a for ipi <sup>1</sup> )

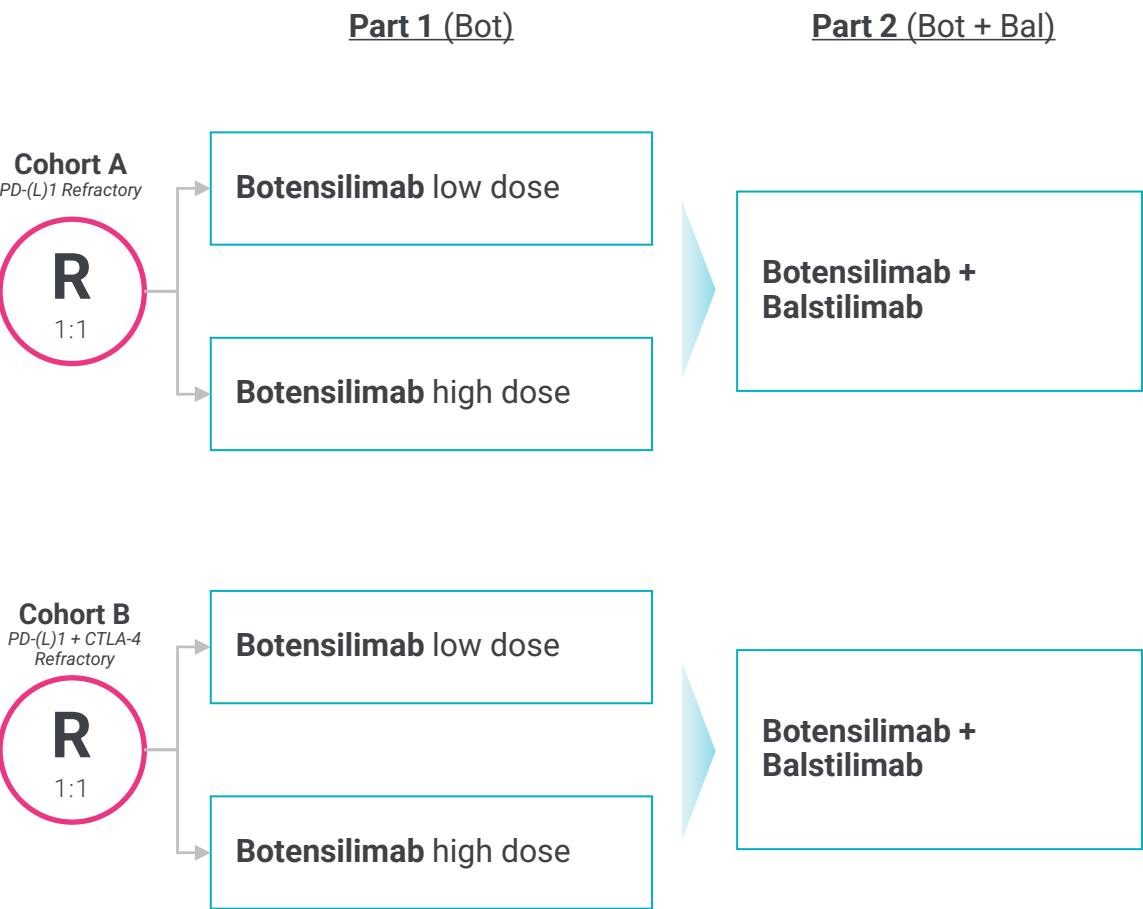
# BOT MONOTHERAPY RESPONSES IN CTLA-4/PD-1 R/R (2L+) MELANOMA

Demonstration of BOT differentiated profile

	Dose	BRAF	Prior Tx	BORR	BORR%	Sites
Phase 1 C800-01	High Dose	Mutant	1. <b>BRAF + MEK inhibitor</b> 2. anti-PD-1 3. anti-CTLA-4 + anti-PD-1	PR	-50%	Adrenal, Inguinal, Oral/ Cervical
	High Dose	Mutant	1. anti-PD-1 2. anti-CTLA-4 + anti-PD-1 3. <b>BRAF + MEK inhibitor</b>	PR*	-65%	<b>Liver</b> , Lungs, Soft Tissue
Phase 2 C800-23	High Dose	WT	1. anti-PD-1 2. anti-CTLA-4 + anti-PD-1	PR	-48%	<b>Liver</b> , Soft Tissue
	High Dose	WT	1. anti-PD-1 2. anti-CTLA-4 3. <b>anti-PD-1 + anti-LAG3</b>	PR*	-60%	Skin only
	Low Dose	WT	1. anti-PD-1 2. anti-CTLA-4	PR*	-39%	Lungs, Thoracic Nodes

# PHASE 2 ONGOING IN CTLA-4/PD-1 R/R (2L+) MELANOMA

Designed to address key regulatory requirements



## Objective

- Dose optimization
- Contribution of components

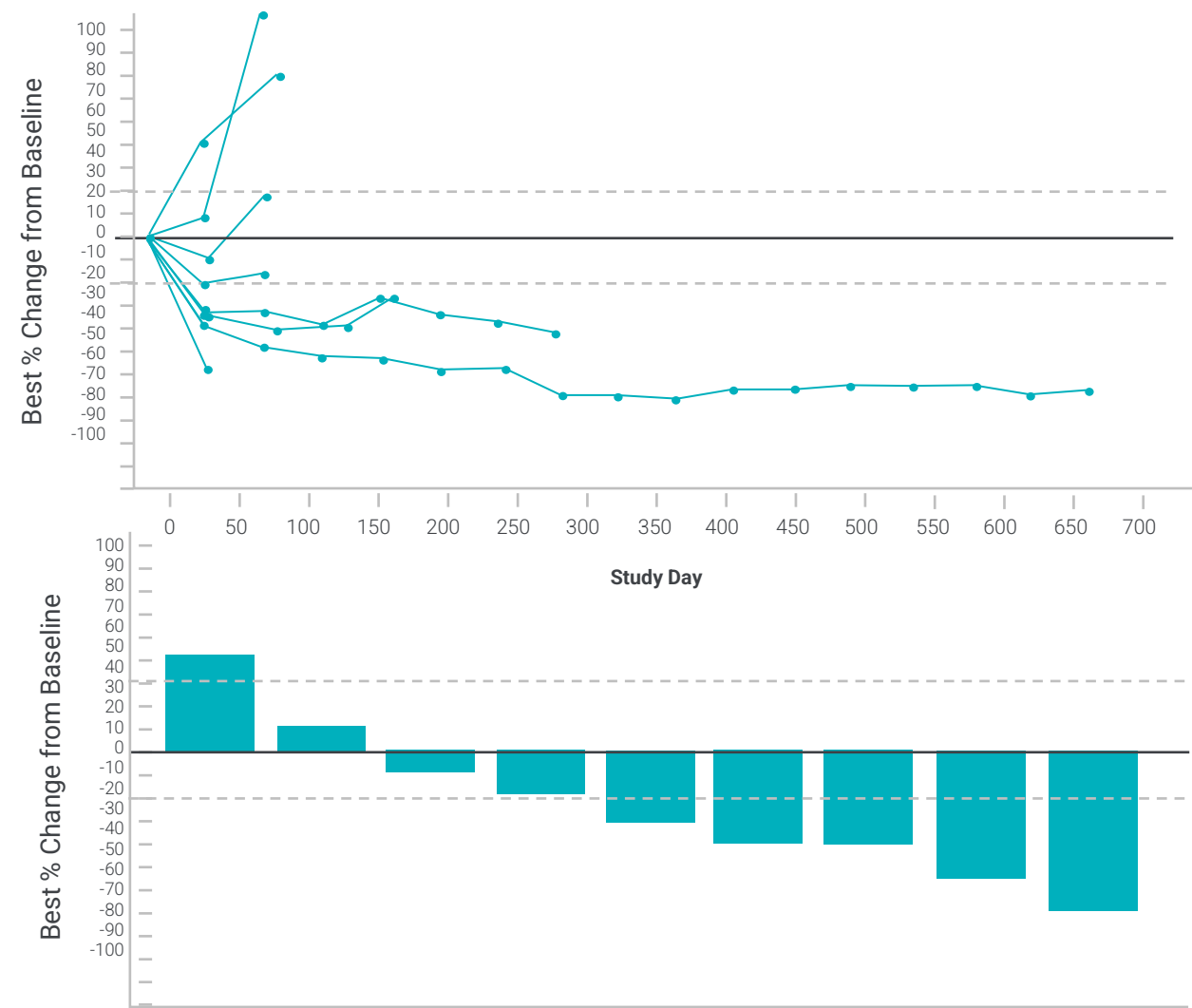
## Patient Population

- PD-1 relapsed/refractory melanoma
- PD-1/CTLA-4 relapsed/refractory melanoma

## Target Endpoints

- Primary: ORR
- Secondary: DOR, PFS, OS, Safety, PK/Immunogenicity

# BOT+BAL: RESPONSES FROM PHASE 1 IN 2L+ NSCLC



Efficacy Evaluable (n=9)	
ORR, %	56%
BOR, n (%)	
CR	0 (0)
PR	5 (56)
SD	3 (33)
PD	1 (11)
DCR (CR + PR + SD), %	89%

Reported standard of care: 14% ORR<sup>1</sup>

## Current Status & Go-forward Plan

- With 46 patients enrolled in the Phase 1b expansion, initial readout expected mid 2024
- In the process of designing trials to support rapid approval in patients who are refractory to PD-1, as well as patients with mutations

# BOT+BAL: POTENTIAL BLA FILINGS

Based on promising clinical signal across treatment settings

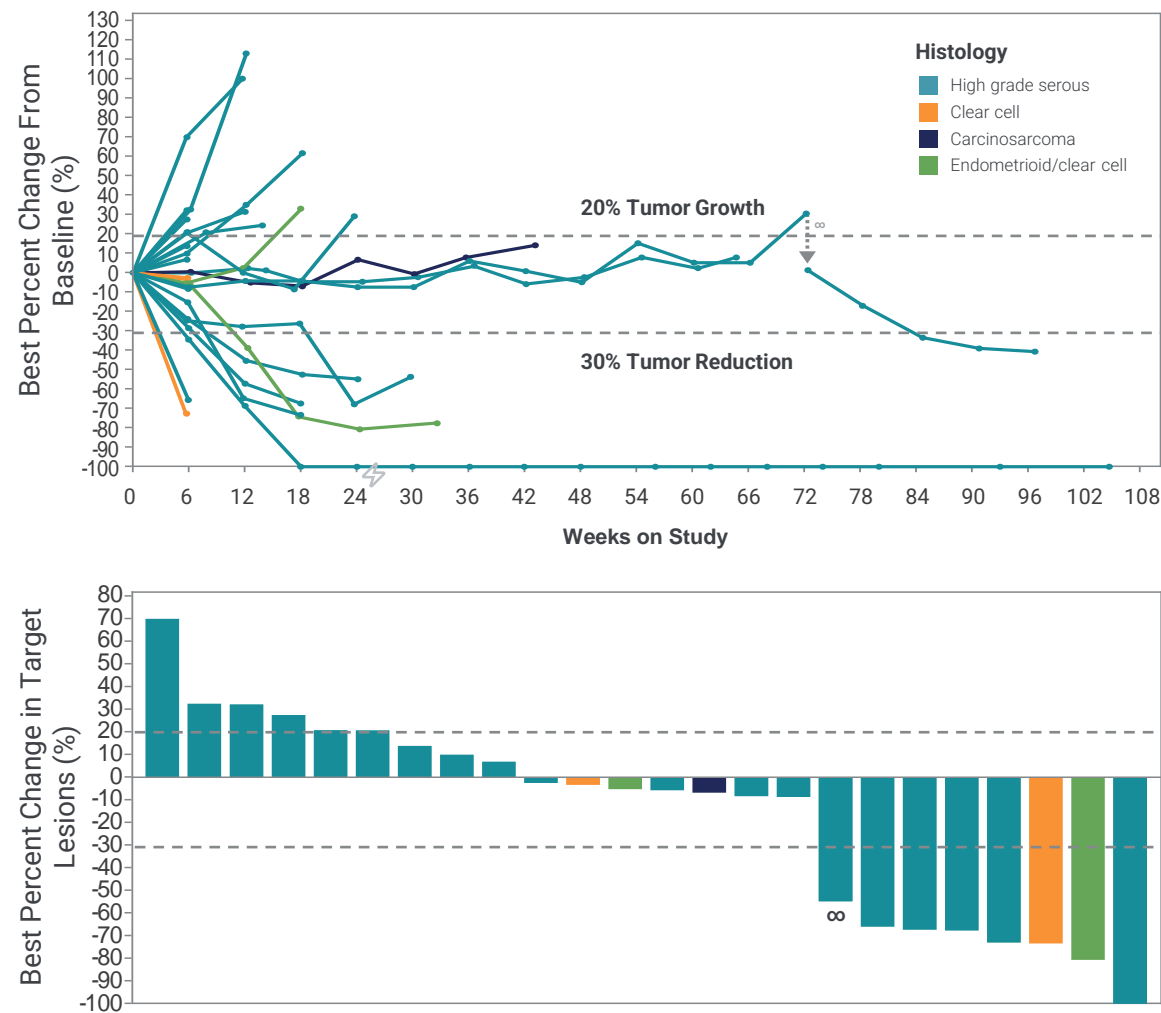
Treatment Setting	BOT/BAL Highlights	Development Plan	US + EU5 Patients <sup>1</sup>
2/3L+ MSS CRC NLM	Data in >300 Patients Fast Track Designation Granted	<ul style="list-style-type: none"> <li>U.S. and EU Regulatory interactions ongoing</li> <li>Planned U.S. BLA filing mid 2024</li> <li>Planned EU Marketing Authorization filing 2025</li> </ul>	13,000
2L Pancreatic	Tumor and Biomarker Reduction in Majority of Patients	<ul style="list-style-type: none"> <li>Anticipated 1H 2024 Phase 2 data update</li> <li>Potential path to accelerated filing in 2025</li> </ul>	22,000
2L+ Melanoma	Confirmed Responses in PD-1/CTLA-4 Failures	<ul style="list-style-type: none"> <li>Anticipated 2H 2024 Phase 2 data update</li> <li>Potential path to accelerated filing in 2025</li> </ul>	6,000
2L+ NSCLC	Responses in PD(L)-1 Refractory Patients	<ul style="list-style-type: none"> <li>Anticipated mid 2024 data update</li> </ul>	103,000
Neoadjuvant MSS CRC	Significant Pathologic Responses	<ul style="list-style-type: none"> <li>Evaluating study designs for potential registration</li> </ul>	142,000
TOTAL			286,000



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# BOT+BAL: ROBUST RESPONSE IN PLATINUM REFRACTORY OVARIAN CANCER

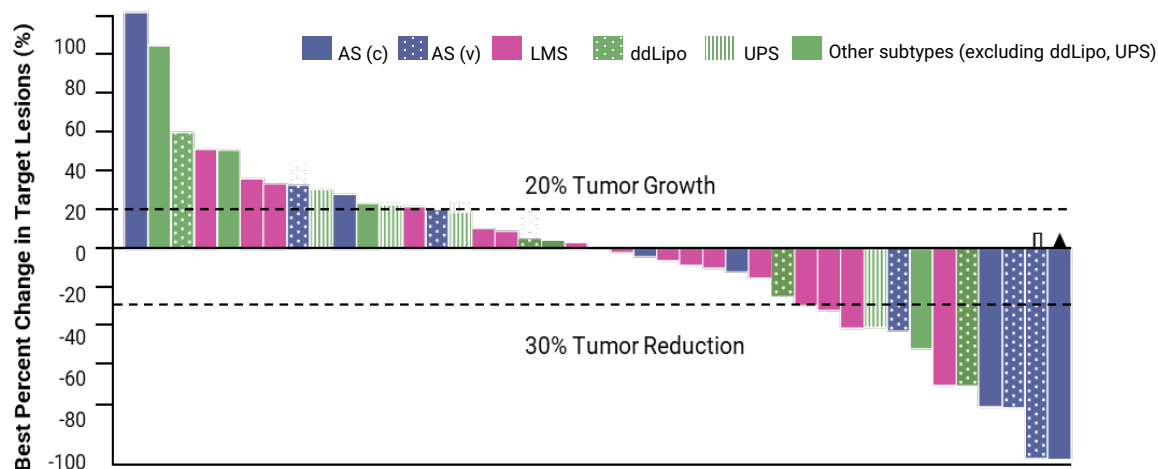
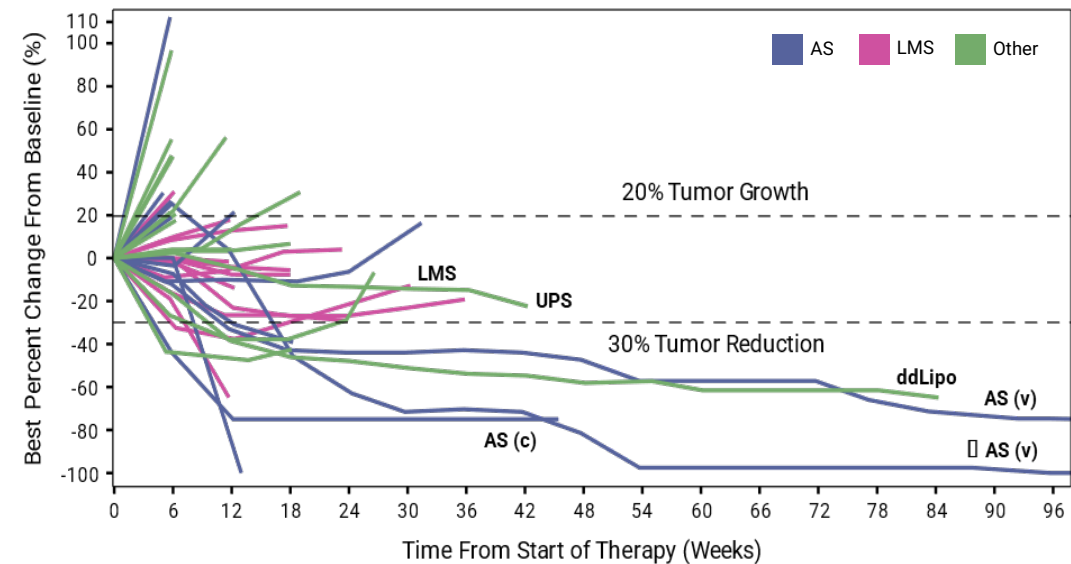


Efficacy Evaluable (n=24)	
ORR, %*	33% (95% CI, 15.6-55.3%)
BOR, n (%)	
CR	1* (4)
PR	7* (29)
SD	8 (33)
PD	8 (33)
DCR (CR + PR + SD), %	67% (95% CI, 44.7-84.4%)
Median DOR, months	NR (4.2-NR)
Median F/U, months	6.9 (Range, 1.7-29.2)

31 \*Includes unconfirmed responses, uCR is a confirmed PR, 3 uPR (1 uPR will not confirm); ∞ Patient crossed over from monotherapy BOT to combination BOT/BAL, new RECIST baseline; ⚡ Received radiation, no evidence of disease

# BOT+BAL: CLINICAL SIGNAL ACROSS REFRACTORY SARCOMAS

Robust activity in heterogenous sarcoma population



Efficacy Evaluable (N=41)*	iRECIST	RECIST v1.1
<b>ORR<sup>†</sup>, % (95% CI)</b>	<b>20%</b> (9–35)	<b>17%</b> (7–32)
1mg/kg (n=27)	15%	11%
2mg/kg (n=14)	29%	29%
<b>BOR, n (%)</b>		
CR	0	0
PR	8 (20)	7 (17)
SD	18 (44)	18 (44)
PD	15 (37)	16 (39)
<b>Median DOR, months (95% CI)</b>	<b>19.4</b> (1.9–NR)	<b>11.8</b> (1.9–NR)
<b>DCR (CR + PR + SD), % (95% CI)</b>	<b>63%</b> (47–78)	<b>61%</b> (45–76)
<b>CBR (CR + PR + SD at 6 months), % (95% CI)</b>	<b>27%</b> (14–43)	<b>24%</b> (12–40)
<b>6-month PFS, % (95% CI)</b>	<b>40%</b> (23–57)	<b>37%</b> (20–54)

32 \* Median f/u: 5.7 months (range, 1.4–28.4); <sup>†</sup> One response confirmed after data cutoff

# BOT+BAL: MANAGEABLE TOXICITY

TRAEs of  $\geq 10\%$  related to BOT; data from expanded Phase 1b study

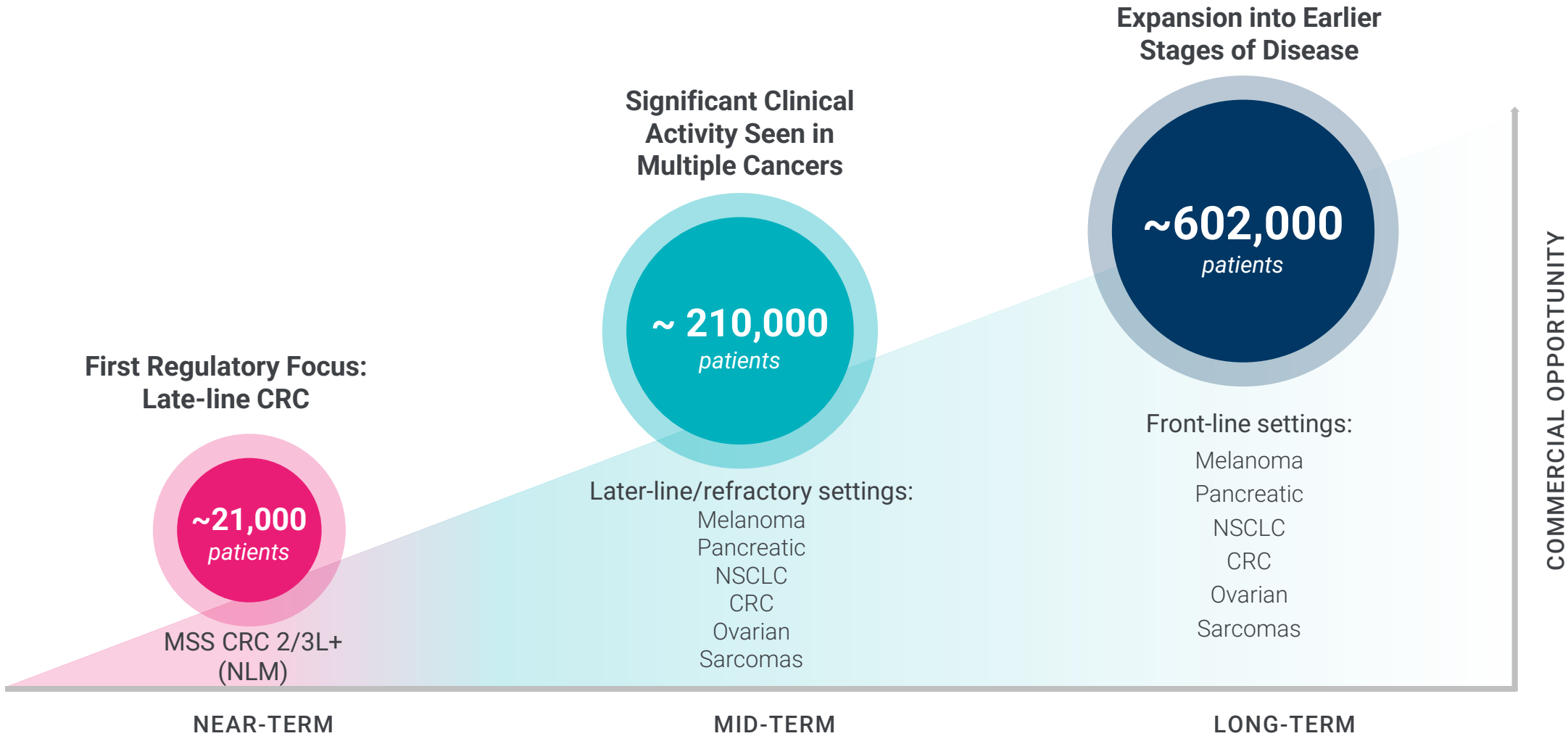
All Patients Treated with BOT+BAL Combo at 1mg/kg or 2mg/kg BOT (n = 255)			
n (%)	All Grade	Grade 3	Grade 4
Any TRAE	204 (80)	70 (27)	5 (2)
GASTROINTESTINAL			
Immune-mediated diarrhea/colitis*	84 (33)	36 (14)	1 (0)
Nausea	49 (19)	5 (2)	0 (0)
Vomiting	28 (11)	3 (1)	0 (0)
CONSTITUTIONAL			
Chills	40 (16)	0 (0)	0 (0)
Decreased appetite	45 (18)	0 (0)	0 (0)
Fatigue	73 (29)	6 (2)	0 (0)
Pyrexia	44 (17)	4 (2)	0 (0)
SKIN			
Pruritus	38 (15)	0 (0)	0 (0)
Rash Maculo-Papular	37 (15)	3 (1)	0 (0)
MUSCULOSKELETAL			
Arthralgia	29 (11)	1 (0)	0 (0)

33 Immune-mediated diarrhea/colitis includes investigator-reported cases or patients who received steroids or immunosuppressants/infliximab; Median follow-up of 5.4 months  
Note: discontinuation due to a BOT TRAE = 22%

Source: Agenus data extracted 26MAY2023

# BLOCKBUSTER MARKET POTENTIAL

Near term opportunity in late-line setting with expansion opportunities into earlier lines



# ACHIEVEMENTS & UPCOMING CATALYSTS

2023	1H 2024	Mid 2024	2H 2024	2025
<ul style="list-style-type: none"> <li>✓ Data from Phase 1b: 2/3L+ MSS CRC (ASCO GI 2023)</li> <li>✓ Data from Phase 1b: ovarian cancer (SGO 2023)</li> <li>✓ Fast Track designation from U.S. FDA for BOT/BAL in CRC (April 2023)</li> <li>✓ Data from Phase 1b: 2/3L+ MSS CRC (ESMO GI 2023)</li> <li>✓ Phase 2 CRC enrollment completed (October 2023)</li> <li>✓ Data from Phase 1b: advanced sarcomas (ESMO 2023)</li> <li>✓ Data from CRC, pancreatic, lung, melanoma studies (Corporate Event, ESMO 2023)</li> </ul>	<ul style="list-style-type: none"> <li>• Phase 2 Data: 2L Pancreatic</li> <li>• Phase 1b Data: 2/3L+ MSS CRC</li> <li>• IST Data: 1L MSS CRC</li> <li>• IST Data (Expanded): Neoadjuvant CRC</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Planned BLA filing: 2/3L+ MSS CRC</b></li> <li>• Phase 1b Data: PD-(L)1 +/- chemotherapy relapsed/refractory 2L+ NSCLC</li> </ul>	<ul style="list-style-type: none"> <li>• Phase 2 Data: 2L+ Melanoma</li> <li>• Phase 2 Data: 2/3L+ MSS CRC</li> </ul>	<ul style="list-style-type: none"> <li>• Potential sBLA filing: Pancreatic</li> <li>• Potential sBLA filing: Melanoma</li> </ul>

# BOT+BAL: REMARKABLE RESPONSES IN RESISTANT PATIENTS

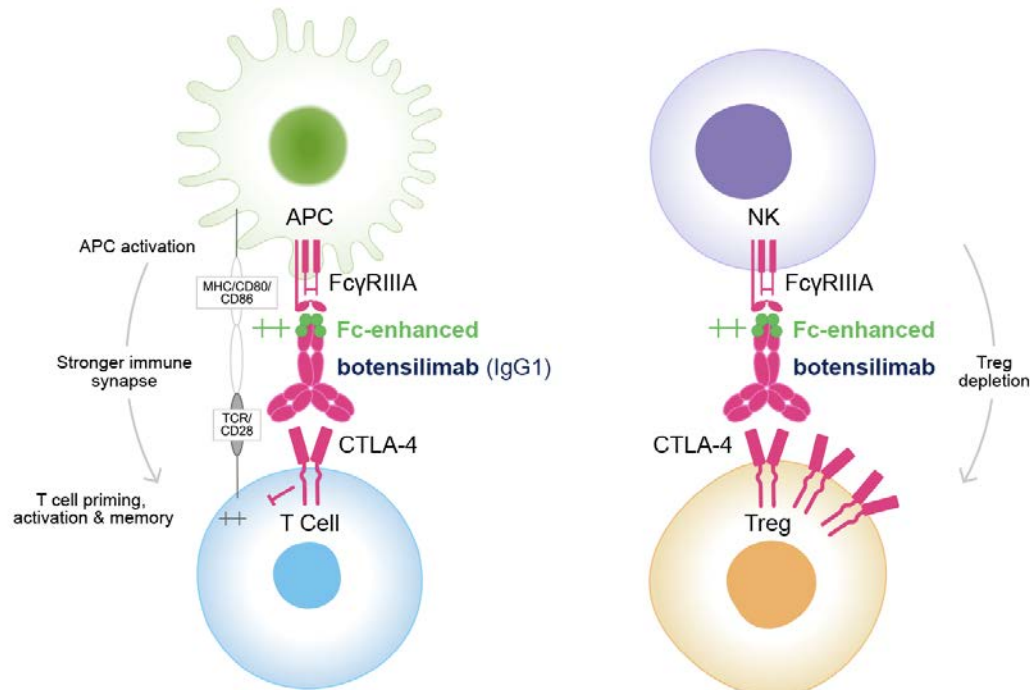
- 1 Planned BLA Filing Mid 2024 for BOT+BAL in 2/3L+ Metastatic MSS Colorectal Cancer (CRC)
- 2 Opportunity to Significantly Improve Patient Benefit in Stage 3 Neoadjuvant CRC
- 3 Potential for Multiple Supplemental BLA Filings: *Pancreatic (2025), Melanoma (2025), Lung (NSCLC)*
- 4 Compelling Clinical Responses in Advanced Metastatic Solid Tumors: *Ovarian, Sarcomas*
- 5 Novel Immune Activator to Deliver Improved Treatments



# BOT: MULTI-FUNCTIONAL ANTI-CTLA-4 IMMUNE ACTIVATOR

Harnesses the surveillance, killing, and memory power of the immune system to eliminate cancer

## BOT Mechanism of Action



## “Turning Cold Tumors Hot”

- **Primes and expands** T cells to eradicate tumor
- **Activates** Natural Killer (NK) cells, and antigen presenting cells (APCs) to identify and attack the cancer
- **Reduces regulatory T cells** that suppress the activity of cytotoxic (tumor killing) T cells
- **Establishes memory** with T cells and dendritic cells











# Additional Clinical Portfolio Highlights

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# CLINICAL STAGE PIPELINE

Diverse portfolio targeting complementary mechanisms of the cancer immunity cycle

	Mechanism/target	Product Candidate	Partner	Phase 1	Phase 2
Majority / fully owned pipeline	Fc-enhanced CTLA-4 +/- PD-1	Botensilimab +/- Balstilimab	 GILEAD <small>Option program</small>	Non MSI-H colorectal cancer	
	Fc-enhanced CTLA-4 +/- PD-1	Botensilimab +/- Balstilimab		PD-1 r/r melanoma	
	Fc-enhanced CTLA-4 + chemo	Botensilimab +/- Chemotherapy		Pancreatic (w/chemo)	
	CD137 + Fc-enhanced CTLA-4	AGEN2373 + Botensilimab		PD-1 r/r melanoma	
	CD137	AGEN2373		Solid tumors	
Temporarily Paused	PD-1 +/- CTLA-4	Balstilimab +/- Zalifrelimab	 Greater China	Cervical (2 <sup>nd</sup> line)	
	ILT2 +/- PD-1 +/- CTLA-4	AGEN1571 +/- Balstilimab +/- Botensilimab		Solid tumors	
Partner directed pipeline	ILT4	MK-4830	 MERCK	NSCLC, ES-SCLC, EC, melanoma, CRC, RCC, ovarian	
	TIM-3	INCAGN2390	 Incyte	PD-1 r/r melanoma, SCCHN, endometrial	
	LAG-3	INCAGN2385	 Incyte	PD-1 r/r melanoma, SCCHN, endometrial	
	TIGIT (bispecific)	BMS-986442	 Bristol Myers Squibb	NSCLC and solid tumors	
	RTGel™ + CTLA-4	UGN-301	 UroGen	NMIBC	
Clinical collaborations	EP4 + PD-1	CR6086 + Balstilimab	 ROTTAPHARM BIOTECH	Non-MSI-H-colorectal cancer	
	Hedgehog + CTLA-4	NLM001 + Zalifrelimab	 Nelum	Pancreatic cancer	
	CD205 + PD-1	OBT076 + Balstilimab	 OXFORD Biotherapeutics	Solid tumors	

# TRACK RECORD OF VALUE CREATION THROUGH STRATEGIC PARTNERHSIPS

Seven ongoing corporate collaborations with oncology industry leaders

**\$825M**

received from  
partnerships and  
transactions

**\$2.5B**

in potential future  
milestone payments, in  
addition to royalties

	 Bristol Myers Squibb™	 GILEAD	 Incyte	 UroGen™ Pharma	 BETTA PHARMACEUTICALS	 MERCK	 gsk
Programs	BMS-986442	AGEN2373	INCAGN2390 INCAGN2385	Zalifrelimab (local delivery in urinary tract)	Balstilimab & zalifrelimab (Greater China)	MK-4830	QS-21 STIMULON™
Remaining Milestones	\$1.34B	\$570M	\$315M	\$200M	\$100M	\$85M	
Royalties	Up to mid-teens	Up to mid-teens	Up to low double-digit	Up to low-twenties	Up to low-twenties	Undisclosed	

40 Xoma eligible to receive 10% of milestones and 33% of royalties from Merck and Incyte transactions. STIMULON is a trademark of Agenus Inc.

# AGEN2373: SELECTIVE CD137 TARGETING ANTIBODY

**Status:** Phase 1b combination study with botensilimab ongoing in PD-1 relapsed/refractory melanoma

## Conditionally Active Design

- CD137 is an important pathway for antitumor immunity due to its ability to enhance T cell and NK cell proliferation, cytokine secretion, and cellular cytotoxicity
- However, clinical CD137 antibodies have been limited by liver toxicity caused by systemic CD137 activation
- AGEN2373 selectively enhances tumor immunity within the tumor microenvironment to mitigate side effects associated with systemic CD137 activation

## Clinical Highlights

- Data presented at ASCO (June 2023) highlighted monotherapy responses with well tolerated safety profile
- No liver or any related high-grade toxicities reported

## Development Plans

- Phase 1b ongoing in combination with botensilimab in PD-1 relapsed / refractory melanoma

## Gilead Partnership

- Gilead has exclusive option to license AGEN2373 until receipt of data package from the Phase 1b study
- **\$177.5M** received from Gilead for upfront and achieved milestones
- **\$50M** option exercise fee
- **\$520M** in potential milestone payments
- Up to **mid-teens royalties**
- Agenus opt-in right to co-fund development and commercialization in exchange for:
  - **50:50 U.S. profit share**
  - **U.S. co-commercialization rights**

# BMS-986442 (AGEN1777): FC-ENHANCED TIGIT BISPECIFIC

**Status:** Phase 1/2 combination study ongoing with nivolumab +/- chemotherapy in patients with NSCLC and gastric cancer

BMS R&D Day (Sept. 2023) highlights progress and prioritization of BMS-986442 program; disclosed second TIGIT target (CD96)

## Bispecific Design

- Targets major inhibitory receptors expressed on T and NK cells to improve anti-tumor activity
- Potential to address tumors where anti-PD-1 or anti-TIGIT monospecific antibodies alone are ineffective

## Fc Enhanced Design

- Fc engineering promotes single agent anti-tumor immunity
- Potential to expand benefit of TIGIT therapy to ~40% patients with a common genetic predisposition (low affinity FcγRIIIA)

## Development Plans

- Phase 1 dose escalation completed in solid tumors
- Phase 1/2 combination study ongoing with nivolumab +/- chemotherapy in patients with NSCLC and gastric cancer

## BMS Partnership

- BMS has exclusive worldwide license to BMS-986442
- **\$220M** received from BMS for upfront and achieved milestones
- **\$1.34B** in future milestone payments
- **Double-digit to mid-teens** royalties
- Options for co-development:
  - **Conduct clinical studies** under the development plan
  - Access BMS-986442 for certain **pipeline combination studies**
- Option to co-fund a minority of global development costs for **increased U.S. royalties up to the low-twenties percent**
- Option for **U.S. co-promotion**

# MK-4830: FIRST-IN-CLASS ILT4 ANTAGONIST ANTIBODY

**Status:** Phase 2 studies ongoing in 8 tumor types

## Design

- First-in-class human IgG4 monoclonal antibody targeting the myeloid-specific ILT4 receptor
- Catalyzes reprogramming of tumor-associated macrophages, relieving myelosuppression and enhancing T cell function

## Clinical Highlights

- MK-4830 +/- pembrolizumab confirmed responses in gastric, colorectal, head & neck, Merkel cell, ovarian, NSCLC, sarcoma, and papillary thyroid cancers
- 24% response rate observed for MK-4830 + pembrolizumab combination across tumor types in dose escalation study
- All responses maintained for  $\geq 6$  months
- Well tolerated; no DLTs or treatment-related deaths

## Development Plans

- Phase 2 studies ongoing in NSCLC, ovarian, small cell lung cancer, esophageal cancer, MSI-H CRC, renal cell carcinoma, and melanoma

## Merck Partnership

- Merck has an exclusive worldwide license to MK-4830
- **\$20M** received from Merck for upfront and achieved milestones
- **\$85M** in potential milestone payments
- **Royalties** on worldwide net sales

# **Agenus Subsidiaries: MiNK & SaponiQx**

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# MINK THERAPEUTICS (NASDAQ:INKT): ALLOGENEIC CELL THERAPY

Pioneering allogeneic iNKT cell therapies for oncology and other immune-mediated diseases

## iNKTs Bridge Adaptive and Innate Immune Systems

- Directly attack cancer cells, recruit host immunity, and reshape tumor microenvironment

## Encouraging Phase I Data in Cancer and ARDS

- Clinical benefit of iNKTs +/- anti-PD-1 in heavily pre-treated solid tumor patients refractory to standard of care.
- 70% survival in elderly mechanically ventilated patients with severe ARDS secondary to COVID-19 compared to 10% case control.

## Native and Engineered iNKT Programs

- iNKT cells engineered with CARs
- Bispecific iNKT cell engagers

## Proprietary Manufacturing at Scale

- Highly efficient isolation process from healthy donors with potential to generate >10,000 doses per year

## Access to Validated Immuno-oncology Therapies

- Combinations with Agenus’ immuno-oncology antibodies

Mechanism / Indication		Product	Preclinical	Early Clinical
Native iNKT Cells				
Oncology	Solid Tumors	AGENT-797 +/- Checkpoint Antibodies	<div></div>	<div></div>
Immune Mediated Diseases	ARDS Secondary to Viral Infections	agenT-797	<div></div>	
	Autoimmunity	agenT-797	<div></div>	
Targeted iNKT Cells				
FAP-CAR-iNKT		MiNK-215	<div></div>	
BCMA-CAR-iNKT		MiNK-413	<div></div>	
iNKT Cell Engager			<div></div>	
NY-ESO-TCR*			<div></div>	
PRAME-TCR			<div></div>	

# SAPONIQX: DESIGNED TO BE AN INTEGRATED VACCINE PLATFORM

Supplying existing demand for delivery of novel adjuvants

Discovery of novel adjuvants enabling superior vaccines

## Foundation

Tree Bark Based  
STIMULON QS21

### Generation I

- Natural product extracted from a rare tree in Chile
- Adjuvant component of SHINGRIX and MOSQUIRIX

## Enabler

Cultured Plant Cell (cpc)  
STIMULON QS21

### Generation II

- Secure supply chain with consistent quality and scalable production
- GMP material available
- FDA Master File Submitted

## Future

STIMULON Saponin  
Catalog

### Generation III

- Production of diverse saponins in partnership with Ginkgo Bioworks
- Harnessing the power of AI and Generative Molecular Design to create bespoke adjuvants to elicit tailored immune responses

## Solutions

STIMULON Integrated  
Vaccines

### Generation IV

- Modular vaccine platform integrating antigen, adjuvant and carrier
- Designed to address pandemic threats

a genus