



# **COMBINING TO CURE®**

Arcus is at the forefront of designing precision combinations in the pursuit of cures for patients living with cancer.

CORPORATE PRESENTATION

January 2024





### **Forward-looking Statements/Safe Harbor**

This presentation contains forward-looking statements about Arcus Biosciences, Inc. ("we," "Arcus" or the "Company") made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements regarding events or results to occur in the future contained in this presentation are forward-looking statements, including statements about: our strategy, advantages, and expectations, including regarding our productivity and competitiveness; expectation that our cash and investments are sufficient to fund operations into 2027; potential of our investigational products and portfolic; anticipated benefits of our collaborations with Gilead, Taiho and AstraZeneca; achievement and expected timing of clinical and developmental milestones, including statements are subject to a number of risks, uncertainties and assumptions that may cause actual results to differ materially from those contained in any forward-looking statements we may make, including, but not limited to: risks associated with preliminary or interim clinical data or preclinical data not being guarantees that future data will be similar; the unexpected emergence of adverse events or other undesirable side effects; difficulties or delays in initiating, conducting or completing our clinical trials due to difficulties or delays in the regulatory process, enrolling subjects or manufacturing or supplying product for such clinical trials, all of which may be exacerbated by unfavorable global economic, political and trade conditions; risks associated with our collaboration arrangement with Gilead including our dependence on Gilead for the successful development and commercialization of our investigational products; changes in the competitive landscape; our limited operating history and our ability to manage our growth; risks regarding our clinese and collaboration agreements and our ability to obtain and maintain intellectual property protection for our product candidates; and the inherent uncertainty associated with pharmaceutica

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### All of Arcus's molecules are investigational and Arcus (and Gilead for all of the molecules in each optioned program) has not received approval from any regulatory authority for any use globally, nor established the safety and efficacy of these investigational molecules.

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### **Arcus Has Created a Late-stage Portfolio of Differentiated** Assets, Fueled by a Highly Productive R&D Engine

#### **FUNDING INTO** 2027

~\$1.2B in pro forma cash, cash equivalents & marketable securities\*

#### **LATE-STAGE COMPANY**

Line of sight to first product approval (dom/zim)

2 new programs entering Phase 3 development by early 2025 (quemli, AB521)

**TOP TIER PARTNERS** 

Provides funding and

resources enabling a

#### **MULTIPLE DATASETS IN 2024**

#### Dom (TIGIT)

 EDGE-Gastric ASCO oral presentation

#### AB521 (HIF-2α)

- Dose escalation data
- Dose expansion • data (2L+ ccRCC)

#### Quemli (CD73)/ Etruma (A2R)

- ✓ ARC-8 (quemli) mature OS data at ASCO GI
- ARC-9 (etruma in CRC) PFS & OS results in 1H24

diversified pipeline GILEAD







### **MULTIPLE PHASE 3 STUDIES FOR DOM IN** LUNG & UPPER GI

STAR-121 🚽 STAR-221



full enrollment expected in '24



#### WORLD CLASS DRUG DISCOVERY

1-2 new development candidates a year

#### **AB801**

Initiated Phase 1/1b for potential best-in-class small molecule AXL inhibitor in Jan-24



2L: second-line; B: billion; ccRCC: clear cell renal cell carcinoma; dom: domv analimab; etruma: etrumadenant; GI: gastrointestinal; OS: ov erall survival; PFS: progression-free survival; gueml quemliclustat; R&D: research and dev elopment; zim: zimberelimab

### **Gilead Equity Investment and Portfolio Prioritization Enables Funding of Multiple Phase 3 Programs**

EQUITY INVESTMENT	<ul> <li>\$320mm investment at \$21.00 per share</li> <li>Increases Gilead's ownership to 33%, further aligning the two companies</li> <li>Funds Arcus into 2027, through multiple late-stage datasets</li> </ul>
DOMVANALIMAB PRIORITIZATION	<ul> <li>Closure of ARC-10 enables Arcus/Gilead to focus on studies targeting the largest market opportunities and unmet need</li> <li>6 Phase 2 and 3 studies are ongoing in NSCLC and Upper GI cancers</li> <li>New Phase 3 (STAR-131) and a Phase 2 study to be initiated in settings where we have the potential to be 1st to market</li> </ul>
ADVANCEMENT OF QUEMLI AND AB521	<ul> <li>AB521 advancing rapidly with datasets in 2024 and a planned Phase 3 initiation by early 2025</li> <li>Phase 3 planning underway for quemli in 1L pancreatic cancer</li> </ul>



### Arcus Has a Broad Portfolio of Investigational Molecules with Bestin-Class Potential Targeting Huge Market Opportunities

#### DIFFERENTIATED ANTI-TIGIT + ANTI-PD-1 BACKBONE

<u>dom</u>vanalimab: Potential best-inclass, Fc-silent anti-TIGIT antibody – multiple ongoing Phase 2 and 3 studies in NSCLC and Upper GI cancers

**<u>zim</u>berelimab**: Anti-PD-1 antibody; approved in China for classical Hodgkin Lymphoma (cHL) and cervical cancer\*

#### DIFFERENTIATED SMALL MOLECULES

**AB521:** Potential best-in-class HIF-2 $\alpha$  inhibitor; Phase 1/1b and Phase 2 studies in cancer patients are ongoing

**<u>quemli</u>clustat**: First-in-class smallmolecule CD73 inhibitor; generated evidence of survival advantage in pancreatic cancer; cohort enrolling in NSCLC

<u>etruma</u>denant: First-in-class dual A<sub>2a</sub>R / A<sub>2b</sub>R antagonist; generated evidence of clinical activity in colorectal cancer

#### **NEXT-GENERATION PROGRAMS**

AB801: Potential best-in-class small molecule AXL inhibitor; Phase 1/1b study in cancer patients is ongoing

AB598: Anti-CD39 antibody; Phase 1/1b study in cancer patients ongoing

**KIT inhibitor:** In preclinical evaluation

Four additional research programs in oncology and inflammation as part of the research collaboration with Gilead

### WORLD-CLASS DRUG DISCOVERY

NSCLC: non-small cell lung cancer \*Gloria Biosciences secured China approvals; it holds commercial rights to zimberelimab in China and conducts its activities independently from Arcus



### Three Late-Stage Programs with Multiple Upcoming Milestones; Earlier-Stage Portfolio Maturing

Program	Disease	Study	Line & Regimen	Ph 1/1b	Ph 2	Ph 3	Upcoming Milestones
		STAR-121	1L, PD-L1 all-comers, metastatic dom + zim + chemo vs pembro + chemo				2024: Enrollment completion
		<b>STAR</b> -131	Lung cancer		PLANNED		YE2024 / Early 2025: Ph 3 initiation
	NSCLC	PACIFIC-8	Stage 3: durva ± dom				
Dom (Fc-silent anti-TIGIT		EDGE-Lung	1L / 2L, all-comers: dom +/- zim +/- quemli +/- chemo				
antibody)		VELOCITY-Lung	1L/2L NSCLC: dom ± zim ± etruma ± SG				• 2024: Initial data
	Upper Gl	<b>STAR</b> -221	1L Upper GI Malignancies dom + zim + chemo vs. nivo + chemo				2024: Enrollment completion
		EDGE-Gastric	1L / 2L Upper Gl Malignancies dom +/- zim +/- quemli +/- FOLFOX				1H2024: ASCO presentation
		TBD	Not disclosed		PLANNED		Early 2025: Ph 3 initiation
AB521	500	STELLAR 009	2L ccRCC: AB521 + zanza				
(HIF2a inhibitor)	RCC	ARC-20	all-comer cancer; 3L+ ccRCC				Early 2024: Dose escalation data
		pirc-20	AB521 monotherapy				• 2H24: Dose expansion data (30 pts, 6m+ follow-up)
Quemli		TBD	1L quemli + G/nP vs. GnP		PLANNED		YE2024 / Early 2025: Ph 3 initiation
U Quemii V (CD37	PDAC						✓ Jan 2024: Mature OS
US (CD37 So inhibitor)	inhibitor)		1L: quemli + zim + G/nP vs quemli + G/nP				• 1H24: MORPHEUS-PDAC (etruma); mature PFS/OS
Etruma (A2R antag.)	CRC	ARC-9	2L: etruma + zim + FOLFOX vs FOLFOX 3L: etruma + zim + FOLFOX vs rego				• 1H24: Mature PFS/OS data in 3L
AB801 (Axl inhibitor)	STK-11m NSCLC	ARC-27	<b>2L: AB801</b> ± chemo + <b>zim</b>				

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### **Our Partnerships Greatly Expand & Accelerate Opportunities** Inherent in Arcus's Portfolio

#### **10-YEAR "ALL-IN" COLLABORATION**

- Over \$1.7b in non-dilutive payments and equity investments from Gilead
- Gilead has opted into 5 molecules to date -- shares costs for studies within the joint development plan
- Arcus retains U.S. co-commercial rights

#### **COLLABORATION FOR JAPAN AND OTHER TERRITORIES IN ASIA (EX-CHINA)**

- Up to \$275mm in development, regulatory and commercial milestones per program
- Tiered royalties from high-single digit to mid-teens on net sales

#### CLINICAL COLLABORATION FOR DOMVANALIMAB PLUS DURVALUMAB

- Companies collaborating on PACIFIC-8, a Phase 3 registrational trial sponsored by AstraZeneca
  - Leverages AstraZeneca's leadership in the curative-intent Stage 3 NSCLC setting with funding shared
  - Retained economics on respective molecules

#### **CLINICAL COLLABORATION FOR AB521 + ZANZALINTINIB**

- Companies collaborating on STELLAR-009, a Phase 1b/2 trial sponsored by Exelixis
- Potential to create a "best-in-class" TKI/HIF2α combination
- Enables cost-effective path for development

#### **ENABLES MULTIPLE "SHOTS ON GOAL" AND FUNDING INTO 2027**

AstraZeneca



GILEAD



EXELIXIS<sup>°</sup>

# Domvanalimab in Non-Small Cell Lung Cancer and Upper GI Cancers



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# Domvanalimab, an Fc-Silent anti-TIGIT

#### DOMVANALIMAB

Most clinically advanced Fc-silent anti-TIGIT antibody in development

#### ZIMBERELIMAB

Anti-PD-1 antibody; approved in China (by Gloria\*)

dom: domv analimab; etruma: etrumadenant; irAE: immune-related adv erse ev ents; NSCLC: non-small cell lung cancer; zim: zimberelimab

\* Gloria obtained approval for zim in China and conducts its activities independently from Arcus. <sup>1</sup>Gauthier, K. et al; Immunology 2022 (#2719): Anti-TIGIT Antibodies Promote Immune Activation Relevant to Targeting Stem-like and Tumor-specific T Cells in Combination With Anti-PD-1

<sup>2</sup>Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023

Dom may have important differences over Fc-enabled anti-TIGIT competitors

- Peripheral T<sub>reg</sub> numbers do not decrease with dom + zim, but they do with Fc-enabled anti-TIGIT antibodies<sup>1</sup>
- ✓ No increase in irAEs reported with dom + zim in ARC-7, in contrast to results from Fc-enabled anti-TIGIT antibodies which show higher incidences of rash, pruritis and infusion site reactions<sup>2</sup>



### Two De-Risking Phase 2 Datasets for Domvanalimab-Containing Regimens Were Presented in 2023



1L Gastric/EAC/GEJ dom + zim + FOLFOX (n=40)

**ASCO**<sup>•</sup> Plenary Series



- PD-L1-high (TAP  $\geq$ 5%) for DZ + FOLFOX\*:
  - ORR/cORR: 80% / 73%
  - 6-month PFS rate: 93%
- Efficacy overall for DZ + FOLFOX\*:
  - ORR/cORR: 59%
  - 6-month PFS rate: 77%
- Incidence of adverse events was similar to prior experience with anti-PD-1 + FOLFOX

ARC-7

### 1L PD-L1 high NSCLC

<u>dom</u> + zim vs. zim vs. etruma + <u>dom</u> + zim (n=150)

2023 ASCO

### • PFS HRs:

- 0.67 for DZ vs. Z
- 0.72 for EDZ vs. Z
- ORRs or DZ and EDZ vs. Z
  - Up to 14% improvement in ORR
  - Lower incidence of progressive disease
- Similar rates of immune-related adverse events observed for DZ and Z including rates of infusion-related reactions, rash and pruritis



\*STAR-221 is evaluating PD-L1 High and all-comer populations with dual primary endpoints for PFS and OS 1L: first-line; D/dom: domvanalimab; EAC: esophageal adenocarcinoma; E/etruma: etrumadenant; GEJ: gastroesophageal junction; HR: hazard ratio; ORR: ov erall response rate; OS: ov erall survival; PFS: progression-free survival; TAP: tumor area positivity; Z/zim: zimberelimab

EDGE-Gastric - Janjigian et al. ASCO Plenary Series, Nov. 7, 2023; data cut off of Sept. 4, 2023

## Phase 3 Program for Dom is Targeting Significant Market Opportunities

STUDY	LEAD SPONSOR	SETTING	US PATIENT POPULATION <sup>1</sup>
<b>STAR</b> -121	GILEAD	1L NSCLC, PD-L1 All comers	119k patients
<b>STAR</b> -131	GILEAD	NSCLC	TBA
PACIFIC-8	AstraZeneca	Stage 3 NSCLC	21k patients
STAR-221	BIOSCIENCES	1L Gastric/GEJ/EAC	25k patients
	Multi-billion revenue	\$10B+ addressable market <sup>1</sup>	

1L: first-line; B: billion; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction;; K: thousand' NSCLC: non-small cell lung cancer; TBA: to be announced <sup>1</sup>Based on expected drug treatable US patient population. Excludes patients with actionable mutations. Source: Decision Resources Group. Adenos: adenocarcinoma; dom: dom vanalimab; GEJ: gastroesophageal junction;

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ARCUS

# Summary of EDGE-Gastric Arm-A1 Results and Domvanalimab Clinical Program in Upper GI Cancers

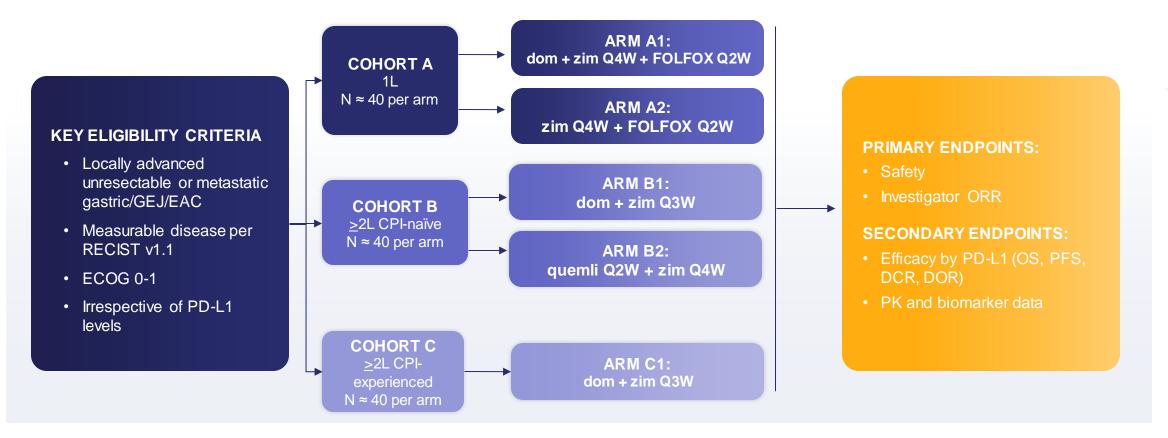
Data presented at the November 2023 ASCO Plenary Series, based on data cut off of September 4, 2023.





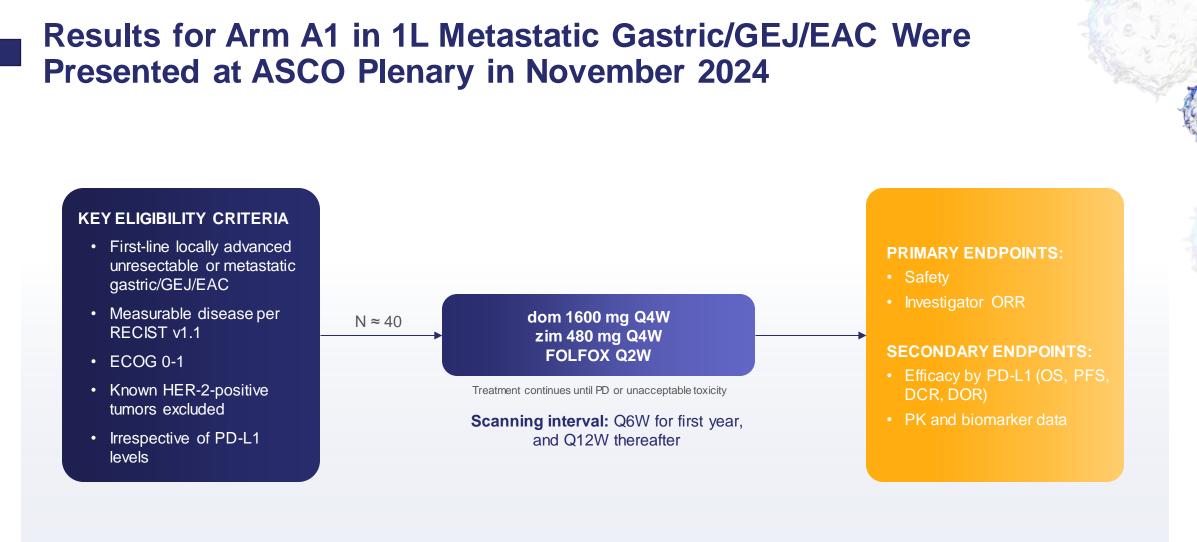
### Phase 2 Trial to Evaluate Dom- and Zim-based combos in Advanced Upper GI Malignancies

#### ARMS NOT RANDOMIZED, ENROLLED SEQUENTIALLY



1L: first-line; 2L: second-line; CPI: checkpoint inhibitor; DCR: disease control rate; dom: domv analimab; DOR: duration of response; EAC: esophageal adenocarcinoma; ECOG: Eastern Cooperative Oncology Group; GEJ: gastroesophageal junction; IV: intrav enous; ORR: objective response rate; OS: ov erall survival; PFS: progression-free survival; PK: pharmacokinetics; quemli: quemliclustat; QxW: ev ery x weeks; RECIST: Response Evaluation Criteria in Solid Tumors; zim: zimberelimab







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At the 4 September 2023 data cutoff, the minimum follow up was 6 months.

1L first-line; DCR: disease control rate; dom: domv analimab; DOR: duration of response; EAC: esophageal adenocarcinoma; ECOG: Eastern Cooperative Oncology Group; GEJ: gastroesophageal junction; ORR: objective response rate; OS: ov erall surv iv al; PD: progressive disease; PFS: progressionfree surv iv al; PK: pharmacokinetics; QxW: every x weeks; RECIST: Response Evaluation Criteria in Solid Tumors; zim: zimberelimab



# **Promising ORR and 6-Month PFS Results**

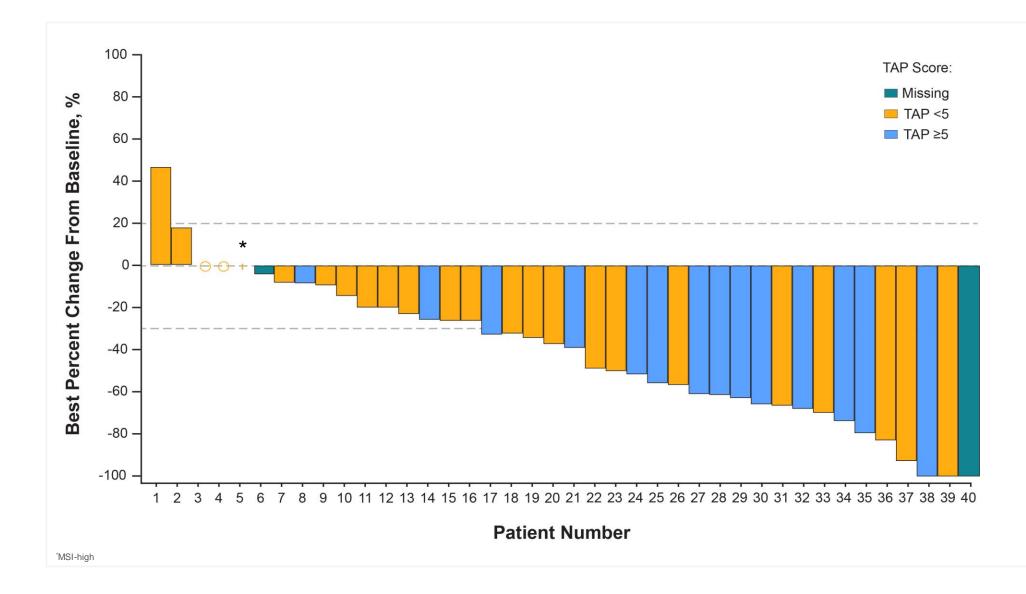
• As of the 4 September 2023 data cutoff, 24 patients (59%) continued on study treatment

	PD-L1 High <sup>*</sup> (TAP ≥5%) N=15 n (%)	PD-L1 Low <sup>*</sup> (TAP <5%) N=24 n (%)	Efficacy-Evaluable N=41 n (%)
ORR, % [95% CI]	<b>80</b> [52, 96]	<b>46</b> [26, 67]	<b>59</b> [42, 74]
Confirmed ORR, % [95% CI]	<b>73</b> [45, 92]	<b>46</b> [26, 67]	<b>56</b> [40, 72]
Confirmed Complete Response	1 (7)	0	2 (5)
Confirmed Partial Response	10 (67)	11 (46)	21 (51)
Unconfirmed Partial Response <sup>†</sup>	1 (7)	0	1 (2)
Stable Disease	3 (20)	10 (42)	14 (34)
Progressive Disease	0	2 (8)	2 (5)
No Post-Baseline Scan	0	1 (4)	1 (2)

CI: confidence interval; ITT: intent to treat; ORR: objective response rate; TAP: tumor area positivity 'Tumor samples from 39 patients were available for central PD-L1 testing. <sup>†</sup> One partial response was not confirmed and the patient has discontinued study treatment as of the data cutoff.

Janjigian et al. ASCO Plenary Series, Nov. 7, 2023; data cut off of Sept. 4, 2023

### Almost All Patients Experience Some Benefit, Irrespective of PD-L1 Status





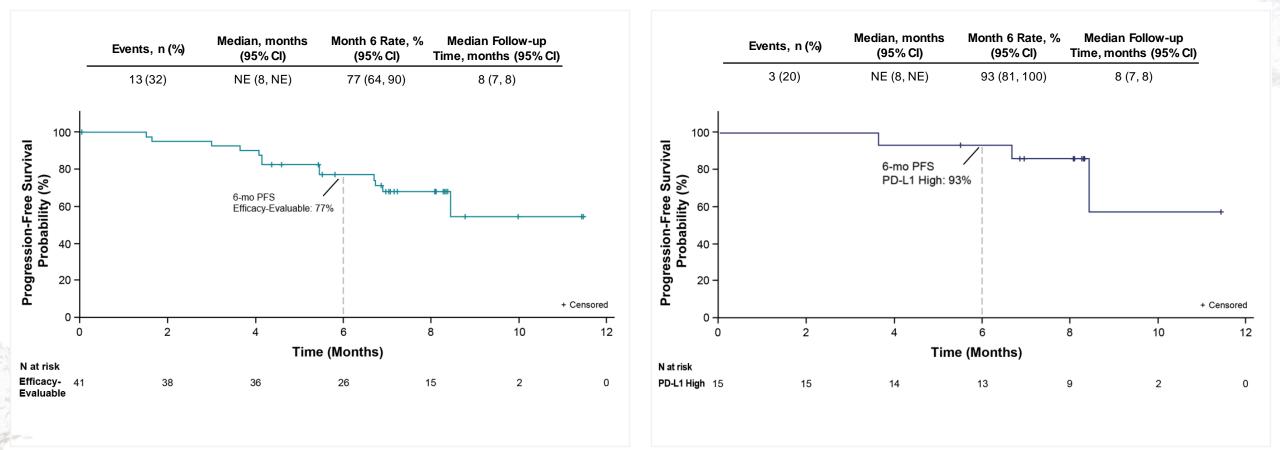
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### Landmark 6-Month PFS Compares Favorably to Benchmark Data of 60-65%; Median PFS Still Immature

#### Efficacy-Evaluable (N=41) 6-month PFS = 77%

#### PD-L1 High (TAP ≥5%, N=15) 6-month PFS = 93%

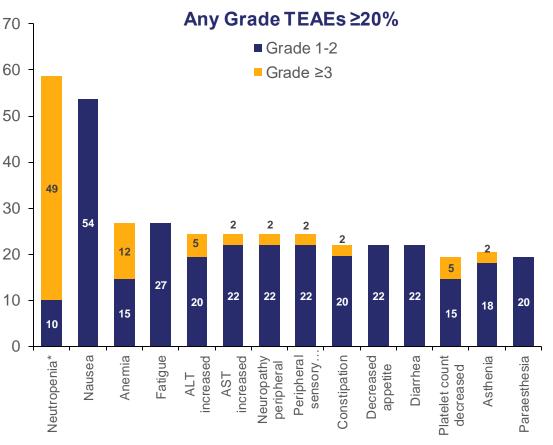




CI: confidence interval; NE: not estimable; PFS: progression-free survival; TAP: tumor area positivity

# Safety Profile is Similar to FOLFOX Alone

TEAE	Arm A1 N=41, n (%)	70 г
Any TEAE	41 (100)	60 -
TEAEs related to any study drug	40 (98)	50 -
Grade ≥3 TEAEs	28 (68)	× 40
Grade ≥3 TEAEs related to any study drug	23 (56)	49 Batients, 30 - 54
Serious TEAEs	10 (24)	20 - 54
Serious TEAEs related to any study drug	2 (5)	10 -
TEAEs leading to permanent withdrawal from any study drug	20 (49)	0 <b>10</b>
TEAEs leading to dose modification/interruption of any study drug	33 (81)	Neutropenia* Nausea
TEAEs resulting in death	0	υZ



ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; TEAE: treatment-emergent adverse event

\*'Neutrophil count decreased', 'Neutropenia', and 'Febrile neutropenia' were coded to separate Preferred Terms and combined post-hoc.

Janjigian et al. ASCO Plenary Series, Nov. 7, 2023; data cut off of Sept. 4, 2023

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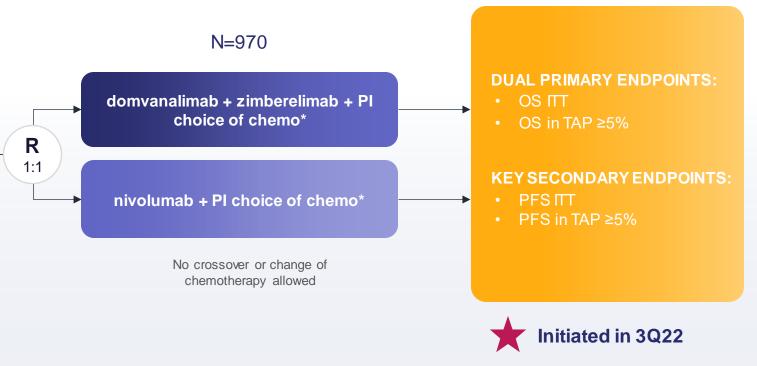




# Phase 3 Evaluating Dom + Zim + Chemo vs Nivo + Chemo in 1L Gastric, GEJ and Esophageal Adenocarcinoma

#### KEY ELIGIBILITY CRITERIA:

- 1L locally advanced unresectable or metastatic w/o prior systemic treatment
- Measurable disease (RECIST 1.1)
- PD-L1 all comers
- Known HER-2 positive tumors excluded



#### **Stratification Factors:**

- PD-L1 expression (TAP ≥5% or TAP <5%)
- ECOG PS (0 or 1)
- Region (US/Canada/EU5 vs. Asia vs. rest of world)

1L: first-line; dom: domv analimab; ECOG: Eastern Cooperative Oncology Group; GEJ: gastroesophageal junction; nivo: nivolumab; ITT: intent to treat; OS: ov erall survival; PFS: progression-free survival; PI: principal investigator; RECIST: Response Ev aluation Criteria in Solid Tumors; TAP: tumor area positivity (revised nomenclature for v CPS [v isually-estimated composite positive score]); R: randomized; zim: zimberelimab

\*PI choice of chemo: FOLFOX or CAPOX. NCT #: NCT05568095

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Janjigian et al. ASCO Plenary Series, Nov. 7, 2023; data cut off of Sept. 4, 2023

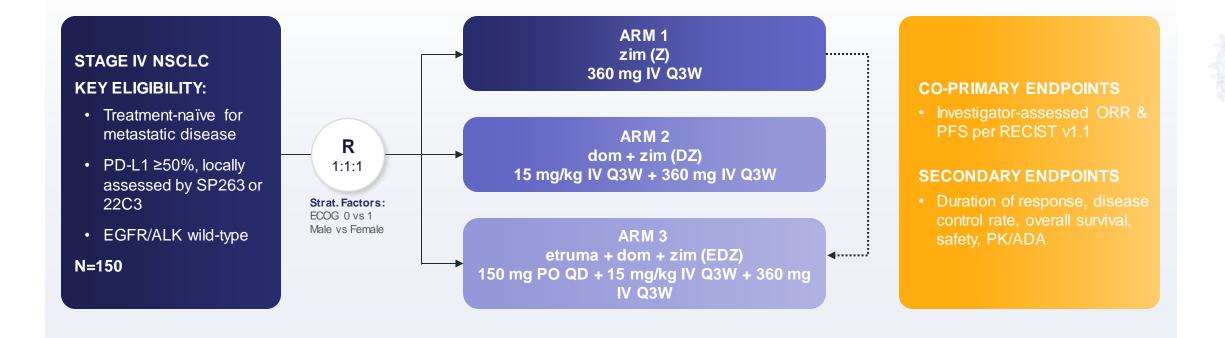


# Summary of ARC-7 Results and Domvanalimab Clinical Program in Non-Small Cell Lung Cancer

Data presented at the 2023 ASCO Annual Meeting, based on data cut off of Feb. 7, 2023.



## ARC-7 Randomized, Open-label, Ph2 Study in First-Line, Metastatic, PD-L1-High NSCLC



Participants randomized to Arm 1 had the option to crossover to separate, 2L EDZ cohort upon radiographically confirmed disease progression (PD))

• As of the clinical cut-off date (Feb. 7, 2023), a total of 150 patients were randomized, with a median follow-up of 18.5 months

ADA: anti-drug antibody; D/dom: domv analimab; ECOG: Eastern Cooperative Oncology Group; E/etruma: etrumadenant; IV: intrav enous; NSCLC: non-small cell lung cancer; ORR: ov erall response rate; Ph: phase; PFS: progression-f ree survival; PK: pharmacokinetics; PO: orally; R: randomized; RECIST: Response Evaluation Criteria in Solid Tumors; Z/zim: zimberelimab; Q3W: every 3 weeks; QD: once-daily

21 Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023



# **Dom-containing Arms Improved ORRs vs Zim Monotherapy**

- Across all arms, one patient in the DZ arm had a pending partial response that was confirmed after data cut-off date
- Subjects ongoing treatment with stable disease have potential to contribute to objective response rate with further data maturity

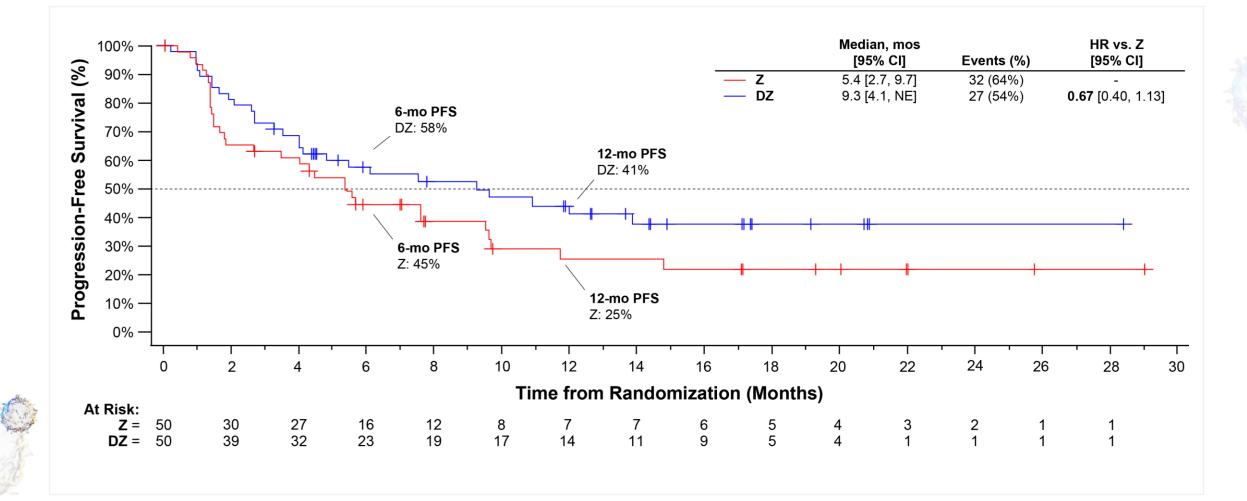
ITT, % (n)	Z (n=50)	DZ (n=50)	EDZ (n=50)
ORR, confirmed + pending [95% CI]	<b>30% (15)</b> [18, 45]	<b>40% (20)</b> [26, 55]	<b>44% (22)</b> [30, 59]
Complete Response	2% (1)	2% (1)	0% (0)
Partial Response – confirmed	28% (14)	36% (18)	44% (22)
Partial Response – pending	0% (0)	2% (1)	0% (0)
Stable Disease	32% (16)	36% (18)	32% (16)
Progressive Disease	24% (12)	8% (4)	14% (7)
Not evaluable	14% (7)	16% (8)	10% (5)

CI: Confidence Interval; D/dom: domvanalimab; E: etrumadenant; ITT: intent to treat; ORR: Objective Response Rate; Z/zim: zimberelimab

22 Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023



# Addition of Dom to Zim Resulted in a 33% Reduction in Risk of Progression or Death, Compared to Zim Monotherapy



CI: confidence interval; D/dom: domvanalimab; HR: hazard ratio; NE: not evaluable; PFS: progression-free survival; Z/zim: zimberelimab

23 Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023



## **Overall Safety Profile**

ITT, % (n)	ARM 1 (Z) (n=50)	ARM 2 (DZ) (n=50)	ARM 3 (EDZ) (n=50)
Any TEAEs	100% (50)	98% (49)	98% (49)
Grade≥3 TEAE	64% (32)	46% (23)	60% (30)
Grade 5, Related to Study Treatment*	2% (1)	2% (1)	4% (2)
SeriousTEAE	56% (28)	34% (17)	52% (26)
TEAEs leading to study drug discontinuation	28% (14)	18% (9)	18% (9)
Immune-related TEAE	48% (24)	50% (25)	66% (33)
Infusion-related Reactions	4% (2)	4% (2)	12% (6)
Median Treatment Duration, weeks (range)	16.9 (0, 103)	26.2 (0, 130)	36.1 (2, 130)

- Most common TEAEs (≥15% overall): nausea, fatigue, constipation, dyspnea, pneumonia, decreased appetite and diarrhea
- Grade  $\geq$ 3 events occurring in  $\geq$ 5% of patients: pneumonia (12%) and anemia (7%)
- \*Related Grade 5 TEAEs: interstitial lung disease (Arm 1), myocarditis (Arm 2), pneumonitis (Arm 3), and congestive heart failure (Arm 3)

D: domv analimab; E: etrumadenant; ITT: intent to treat; TEAEs: treatment emergent adverse events; Z: zimberelimab

Johnson et al. Abstract 397600, ASCO 2023; data cut-off of Feb. 7, 2023

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# Phase 3 Evaluating Dom + Zim + Chemo vs. Pembro + Chemo in 1L NSCLC (All PD-L1 Subgroups)

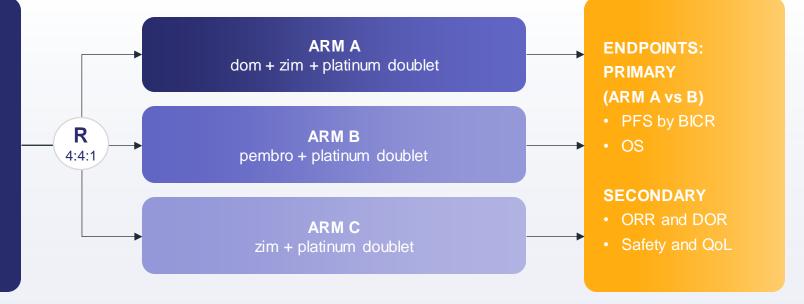
• Uses standard of care, pembrolizumab, in the comparator arm



- Metastatic NSCLC without actionable mutations
- No prior systemic treatment for metastatic NSCLC
- PD-L1 all-comers
- ECOG 0-1
- No interstitial lung disease
- No untreated brain metastases

#### **Strat Factors:**

- Baseline PDL1 PD-L1 status (≥50% vs. 1-49%)
- Geography (east Asia vs non-east Asia)
- Histology (Sq vs Non-sq)





1L: first-line; BICR: blinded independent central review; dom: domvanalimab; DOR: duration of response; ECOG: Eastern Clinical Oncology Group; NSCLC: non-small cell lung cancer; ORR: objective response rate; OS: overall survival; pembro: pembrolizumab; PFS: progression-free survival; QoL: quality of life; R: randomized; sq: squamous; zim: zimberelimab

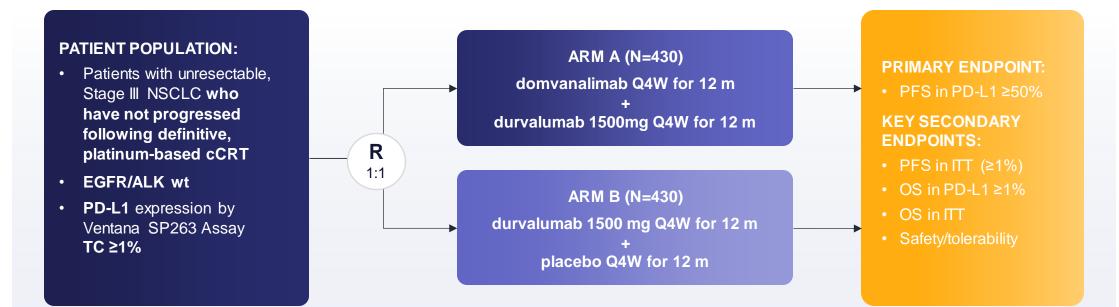
Gilead Sciences is operationalizing STAR-121

NCT #: NCT05502237



## Phase 3 Evaluating Dom + Durva vs Placebo + Durva in Unresectable, Stage III NSCLC

- Combines domvanalimab (dom) with durvalumab (durva) standard-of-care in Stage III NSCLC
- Potential to be first anti-TIGIT combination in this curative intent setting



#### **Strat Factors:**

NCT #: NCT05211895

- Disease stage prior to cCRT (IIIA vs. IIIB/IIIC)
- PD-L1 status (TC ≥ 50% vs. TC 1-49%), as assessed by a central reference laboratory using the VENTANA PD-L1 (SP263) IHC assay
- Histology (Sq vs Non-sq)

cCRT: concurrent chemoradiotherapy; IHC: immunohistochemistry; ITT: intent to treat; m: months; NSCLC: non-small cell lung cancer; OS: ov erall survival; PFS: progression f ree survival; Q4W: ev ery 4 weeks; TC: tumor count

PACIFIC-8

# **CD73-Adenosine Axis Programs**



# Quemliclustat in Pancreatic Cancer



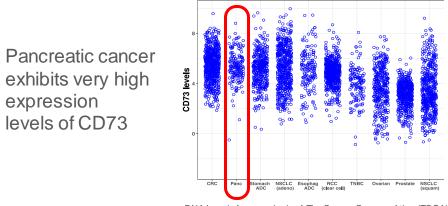
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## Quemliclustat (quemli): A Unique, Highly Potent and Selective Small Molecule CD73 Inhibitor with Several Key Advantages

### QUEMLICLUSTAT

- Highly potent molecule
- Target coverage achieved at doses as low as 25 mg every two weeks
- Extremely long (4+ days) half-life, enabling Q2W dosing by IV infusion

#### **Biological rationale for CD73** inhibition in pancreatic cancer



#### mRNA Levels from analysis of The Cancer Genome Atlas (TCGA)

# Potential advantages over CD73 antibodies<sup>1</sup>

- Highly potent and selective inhibition of both tumor cell-bound and soluble CD73
- ✓ Greater inhibition of enzymatic production of adenosine
- ✓ Orders of magnitude more potent
- ✓ Greater permeability of tumor tissue



Q2W: every 2 weeks quemliclustat is an investigational molecule and its safety and efficacy have not been established

# Final Overall Suvival Analysis for Quemli in Pancreatic Cancer (ARC-8)

Data presented at ASCO GI, January 19, 2024, based on a data cutoff of June 19, 2023.



# Highlights from the ARC-8 Study in 1L PDAC

**Median overall survival (mOS) was 15.7 months** for patients treated with a quemliclustatbased regimen, which exceeds the historical benchmark data for chemotherapy alone  $(8.5 - 11.7 \text{ months})^{1,2}$ 

A 37% reduction in risk of death and a 5.9-month improvement in mOS was observed for patients treated with the quemli-based regimen when compared to a synthetic control arm of patients treated with G/nP alone<sup>1</sup>

The quemli-based regimen was well-tolerated, with no new safety signals or significant added toxicity compared to chemotherapy alone<sup>1</sup>



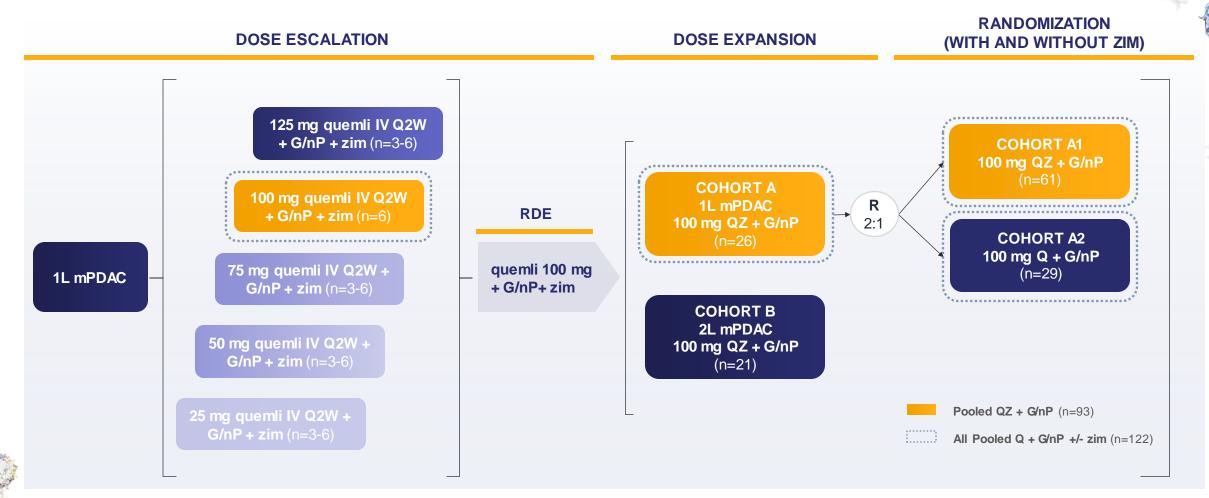
#### Phase 3 planning is underway

1L first-line; G/nP: gemcitabine/nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma; quemli: quemliclustat 1. Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023 2. Abraxane USPI. 2020 and Wainberg ZA. Melisi D. Macarulla T. et al. NALIRIFOX versus nab-paclitaxel and

2. Abravane OSPI, 2020 and Wainberg ZA, Meins D, Macardina T, et al. NALTHER Versus hab-pacintaxer and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial, Lancet, 2023;402(10409):1272-1281, doi:10.1016/S0140-6736(23)01366-1



# ARC-8 Study Design Included Dose Escalation, Expansion and Randomized Portions



# Safety monitoring throughout treatment period; radiographic disease evaluation every 8 weeks. Study treatment continued to disease progression, unacceptable toxicity, consent withdrawal, or investigator decision.

1L: first-line; 2L: second-line; IV: intrav enously; G/nP: gemcitabine/nab-paclitaxel; mPDAC: metastatic pancreatic ductal adenocarcinoma; PDAC: pancreatic ductal adenocarcinoma; Q2W: every 2 weeks; Q/quemli: quemliclustat; R: randomization; RDE: recommended dose for expansion; Z/zim: zimberelimab NCT #: NCT04104672

32 Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023



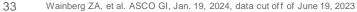
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### Dataset Includes Four Groups of Patients Treated with 100 mg of Quemli

Cohort	Quemli Dose	Combination	Partic	cipants Dose	d	>18m OS f/u?	Population
Dose escalation	25 mg	Q + Z + G/nP (quad)	4			Yes	1LmPDAC
Dose escalation	50 mg	Q + Z + G/nP (quad)	6			Yes	1LmPDAC
Dose escalation	75 mg	Q + Z + G/nP (quad)	3		Yes	1LmPDAC	
<b>Dose escalation</b>	100 mg	Q + Z + G/nP (quad)	6			Yes	1LmPDAC
Cohort A	100 mg	Q + Z + G/nP (quad)	26*	- <b>93</b>	-100	Yes (except for 3)*	1LmPDAC
Cohort A1 (randomized)	100 mg	Q + Z + G/nP (quad)	61	Pooled Q100 quad	- <b>122</b> Pooled Q100 All	Yes	1LmPDAC
Cohort A2 (randomized)	100 mg	Q + G/nP (triplet)	29			Yes	1LmPDAC
Dose escalation	125 mg	Q + Z + G/nP (quad)	3			Yes	1LmPDAC



1L: first-line; f/u: follow up; G/nP: gemcitabine/nab-paclitaxel; mPDAC: metastatic pancreatic ductal adenocarcinoma; OS: ov erall surv iv al; Q/quemli: quemliclustat; Z/zim: zimberelimab 3 additional patients enrolled as contemporaneous control for Cohort C





# **Demographics And Baseline Characteristics Are Well Balanced Across Arms & Efficacy-evaluated Populations**

% ECOG 1 (65%-69%) Was Higher than Historical G/nP Studies (42-57%); % Liver Mets (59%-69%) Was Slightly Lower than Historical G/nP Studies (78-85%) – See Slide 36 for OS Results

% (n)		A2: Q + G/nP (n=29)	A1: QZ + G/nP (n=61)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q ±Z)+G/nP (n=122)
Median Age (IQR)		65.0 (61, 70)	66.0 (58, 72)	66.0 (58, 72)	65.5 (59, 72)
Age ≥65		55 (16)	59 (36)	58.1 (54)	57.4 (70)
Female		48 (14)	49 (30)	47 (44)	48 (58)
	White	83 (24)	74 (45)	74 (69)	76 (93)
Race	Asian	6.9 (2)	8.2 (5)	8.6 (8)	8.2 (10)
Race	Black	3.4 (1)	6.6 (4)	5.4 (5)	4.9 (6)
	Other/NR	6.9 (2)	11 (7)	12 (11)	11 (13)
ECOG 0		31 (9)	30 (18)	34 (32)	34 (41)
ECOG 1		<b>69</b> (20)	<b>69</b> (42)	<b>65</b> (60)	<b>66</b> (80)
ECOG Missing		-	1.6 (1)	1.1 (1)	0.8 (1)
Liver Metasta	sis at Baseline <sup>1</sup>	<b>58.6</b> (17)	<b>68.9</b> (42)	<b>66.7</b> (62)	<b>64.8</b> (79)

ECOG: Eastern Cooperative Oncology Group; G/nP: gemcitabine/nab-paclitaxel; IQR: interquartile range; NR: not reported; Q: quemliclustat; Z: zimberelimab 1. Deriv ed f rom baseline tumor assessment data

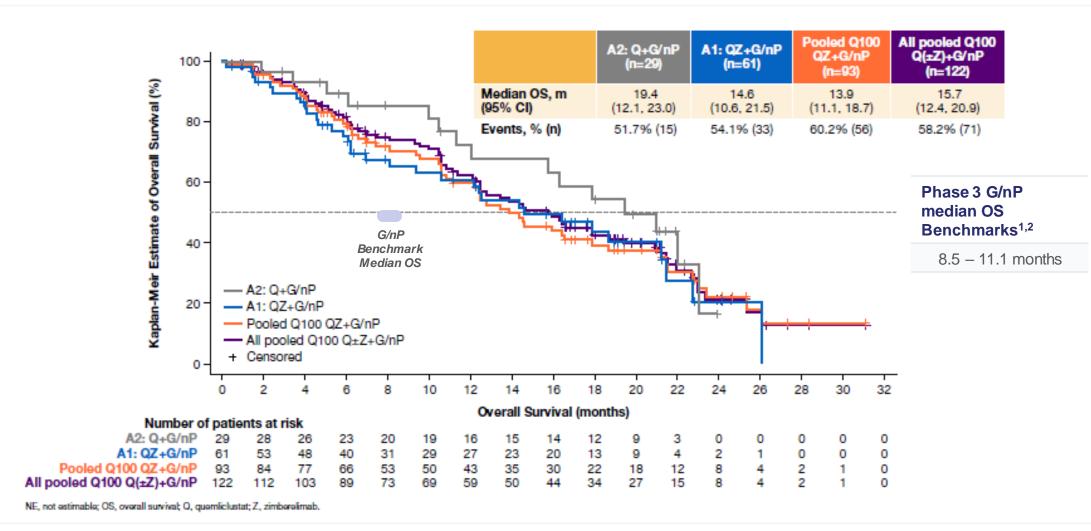
Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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### With 21-month Median Follow-up, OS Results Exceed Ph3 Benchmarks for G/nP



CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; Ph3: Phase 3

1. Abraxane USPI, 2020 and Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet. 2023;402(10409):1272-1281. doi:10.1016/S0140-6736(23)01366-1

2. Von Hoff et al. N Engl J Med 2013;369:1691-703.

35 Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023



## **Favorable OS for Patients With & Without Liver Metastasis**

- Because ARC-8 had a lower incidence of liver mets than historical studies, we analyzed the OS for ARC-8 patients with and without liver mets as shown below
- When adjusting for the lower incidence of liver mets in the triplet arm, mOS for the triplet and quad arms looked almost identical at approx. 12 months
- When evaluating just those patients <u>with</u> liver mets, median OS still exceeded historical benchmarks AND meaningfully outperformed the OS for patients with liver mets in NAPOLI-3 (the most contemporary phase 3 in 1L pancreatic) -- 12.1 mos for ARC-8 vs. 8.6 mos for NAPOLI-3

Liver Mets at Baseline	A2: Q + G/nP (n=17)	A1: QZ + G/nP (n=42)	Pooled Q100 QZ + G/nP (n=62)	All Pooled Q100 Q(±Z) + G/nP (n=79)	NAPOLI-3 (n=309)
Events (%)	11 (64.7)	26 (61.9)	40 (64.5)	51 (64.6)	242 (78.3)
Median OS, months	12.1	12.2	11.1	12.1	8.6
95% CI	10.0, 20.9	6.2, 17.9	8.1, 14.5	10.0, 15.7	

No Liver Mets at Baseline	A2: Q + G/nP (n=12)	A1: QZ + G/nP (n=19)	Pooled Q100 QZ + G/nP (n=31)	All Pooled Q100 Q(±Z) + G/nP (n=43)	NAPOLI-3 (n=78)
Events (%)	4 (33.3)	7 (36.8)	16 (51.6)	20 (46.5)	43 (55.1)
Median OS, months	22.0	21.2	21.2	21.5	13.8
95% CI	17.9, NE	14.6, NE	13.9, 25.4	17.9, 25.4	

BL: Baseline; CI: confidence interval; G/nP: gemcitabine/nab-paclitaxel; mets: metastasis; mOS: median overall survival; mos: months; NE: not estimable; OS: overall survival; Q: quemliclustat

NAPOLI-3: Wainberg, et al. *The Lancet*. Sept 2023. <u>https://doi.org/10.1016/S0140-6736(23)01366-1</u>. Data shown is for the G/nP arm only

Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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## Safety Profile Similar to G/nP with Regards to Overall TEAEs

%	A2: Q + G/nP (n=29)	Pooled Q100 QZ + G/nP (n=93)	All Pooled Q100 Q ±Z)+G/nP (n=122)	NAPOLI-3 G/nP Benchmark⁴ (n=379)
Any TEAE	100	100	100	99
Any TRAE	100	98.9	99.2	93
Grade 3-5 TEAE	89.7	83.9	85.2	86
Grade 3-5 TRAE	75.9	72.0	73.0	68
SeriousTEAE	51.7	53.8	53.3	52
SeriousTRAE	34.5	25.8	27.9	19
Grade 5 TEAE	0	5.4	4.1	6
Grade 5 TRAE	0	0	0	2
AE leading to mod <sup>1</sup>	58.6	51.6	53.3	54
AE leading to dose delay	75.9	75.3	75.4	NR
AE leading to discon <sup>2</sup>	24.1	22.6	23.0	23
IRR <sup>2</sup>	10.3	6.5	7.4	N/A
Immune related AE <sup>3</sup>	6.9	10.8	9.8	N/A

AE: adv erse event; G/nP: gemcitabine/nab-paclitaxel; IRR: inf usion-related reaction; NA: not applicable; NR: not reported; TEAE: treatment-emergent adv erse event; TRAE: treatment-related adv erse event

1. AE leading to dose reduction; 2. Discontinuation of any study drug; 3. As reported by investigator; 4. Wainberg, et al. The Lancet. Sept 2023. https://doi.org/10.1016/S0140-6736(23)01366-1

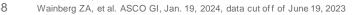




## Arcus & Medidata Al Synthetic Control Arm (SCA) Project

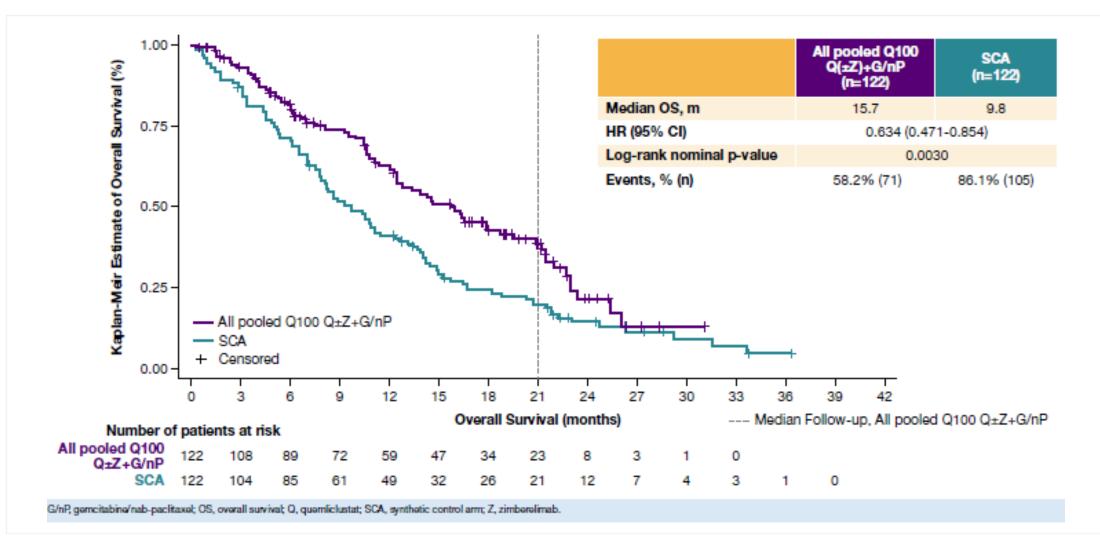
- Developed in collaboration with Medidata, the industry's leading provider of electronic data capture for clinical trials
- Constructed SCA using historical data from patients treated with G/nP alone and balanced to the patient baseline characteristics of ARC-8
  - Contemporaneous global randomized Phase 2 and 3 clinical trials that meet key ARC-8 entry criteria
  - 515 eligible external patients identified for further matching
  - SCA matched to All Pooled Q100 Q±Z+G/nP (n=122) using propensity score statistical method including exact matching on baseline liver metastasis
- Assessed the treatment effects on OS, PFS, and objective response rate in the SCA patients and compared these to the matched ARC-8 patients
- SCA analyses were conducted versus all four analysis groups and showed consistent results; for simplicity, only the SCA for the All Pooled Q100 group was reported

Al: artificial intelligence; G/nP: gemcitabine/nab-paclitaxel; OS: overall survival; PFS: progression-free survival; Q: quemliclustat; Z: zimberelimab





## Quemli-based Regimen <u>Significantly Reduced Risk of Death</u> by 37% and increased mOS by 5.9 months





CI: confidence interval; mOS: median ov erall survival; quemli: quemliclustat Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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## Etrumadenant in Colorectal Cancer



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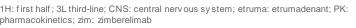
## Etrumadenant Represents a Potentially Best-in-Class Adenosine Receptor Antagonist

### **ETRUMADENANT**

- Highly potent small molecule that inhibits both the A2aR and A2bR receptors
- Excellent penetration of tumor tissue and drug properties (PK, etc.)
- Data from ARC-9 evaluating etruma + zim + chemo vs. regorafenib in 3L CRC is expected to be presented in 1H:24

## Etruma has ideal pharmacological properties

- Retains potency in physiologically relevant conditions
  - $IC_{50} = 87 nM$
- ✓ High tumor penetration
  - Tumor: Plasma ratio: >60%
- ✓ Low CNS permeability (in mouse model)
  - ~1% of the concentration found in blood
- ✓ Full engagement of target across dosing time period in humans
  - ≥90% target inhibition at trough



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Etrumadenant is an investigational molecule and its safety and efficacy have not been established.



## ARC-9 Randomized Phase 2 Study to Evaluate Etruma Combinations in 3L+ mCRC

- Randomized Phase 2 study evaluating etruma + zim + chemo combinations vs. SOC in 2L/3L mCRC
- Mature PFS / OS data for Cohort B (3L) expected to be presented in 1H24 (n=105)
- Cohort A (2L) results are still immature



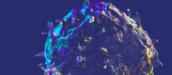
1H: first half; 2L: second-line; 3L: third-line; bev : bev acizumab; etruma: etrumadenant; irino: irinotecan; mCRC: metastatic colorectal cancer; OS: ov erall surv iv al; oxali: oxaliplatin; PFS: progression-free surv iv al; R: randomized; SOC: standard of care; zim: zimberelimab

\*bev will be included for all patients in whom it is not contraindicated

NCT #: NCT04660812









## Value Proposition for AB521, a Potential Best-in-Class, HIF-2α Inhibitor

### **Potency**

### Opportunity to reach greater intratumoral HIF-2α inhibition compared to 120 mg dose of belzutifan

- Requires a compound with greater potency and/or a better PK/PD profile than belzutifan
- Potentially without increased toxicity, which appears to be driven by peripheral (normal tissue) on-target effects that saturate at lower doses

### **Novel Combinations**

### Opportunity to create potentially bestin-class and first-in-class combinations

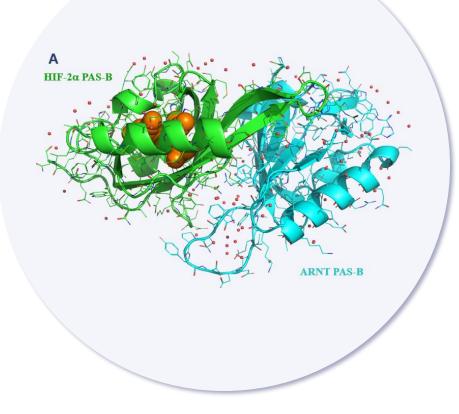
• Announced clinical collaboration with Exelixis to combine AB521 with their next-generation TKI, zanzalintinib





## **Extensive Preclinical Characterization Confirms Greater Potency of AB521 Relative to that of Belzutifan (MK-6482)**

	ASSAY	AB521	MK-6482ª
	HIF-2 $\alpha$ 786-O Luc Reporter IC <sub>50</sub> (nM)	8.2 ± 2.5 (n=24)	16.9 ± 10.1 (n=8)
CELLULAR	Control 786-O Luc Reporter $IC_{50}$ (nM)	> 10,000 (n=6)	> 10,000 (n=7)
	HIF-2 $\alpha$ 786-O Luc Reporter IC <sub>50</sub> (nM) [in 100% Serum]	46.5 ± 14.2 (n=24)	61.8 ± 6.6 (n=4)
	786-O VEGF AlphaLISA IC <sub>50</sub> (nM)	28.9 ± 3.6 (n=11)	47.7 ± 30.8 (n=4)
BIOCHEMICAL	HIF-2α TSAT <sub>m</sub> Δ (°C)	14.7 ± 0.6 (n=14)	12.1 ± 0.3 (n=4)
	HIF-2 $\alpha$ MST $K_D$ (nM)	2.4 ± 0.8 (n=3)	15.4 ± 2.7 (n=3)
	HIF-2 $\alpha$ ITC $K_D$ (nM)	53.6 ± 17.9 (n=3)	53.8 ± 19.3 (n=3)
-	HIF-2 $\alpha$ SPA IC <sub>50</sub> (nM)	16.6 ± 5.0 (n=8)	22.3 ± 5.6 (n=5)





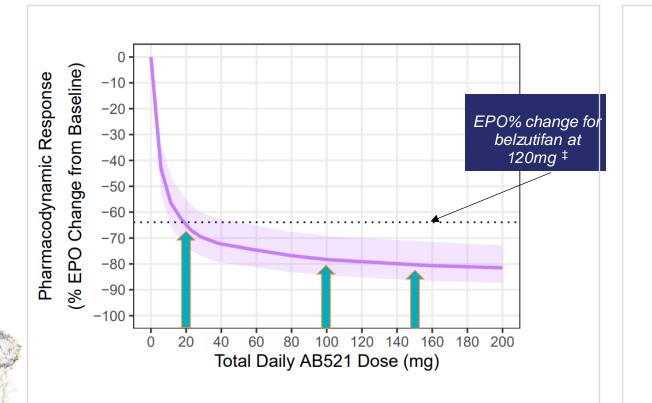
<sup>a</sup> MK-6482 was synthesized according to Xu *et al.* 2019 J Med Chem; DOI: 10.1021/acs.jmedchem.9b00719

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# AB521 is a HIF-2α Inhibitor with Best-in-Class PK-PD Properties

20 mg of AB521 achieves near-complete EPO suppression (peripheral PD marker for HIF2α inhibition) while a 120mg dose of belzutifan (the approved dose) is required for this level of EPO suppression Human PK profile of AB521 Increases in a dose-linear fashion Daily 100 mg AB521 expected to provide ~5x more drug to the tumor than the reference drug



1000 AB521 concentration (ng/mL) 100 ----- AB521, 20 mg Daily AB521, 100 mg Daily 10 12 16 20 24 Time after previous dose (hour)

EPO: ery thropoietin; PD: pharmacody namics; PK: pharmacokinetics § AB521: Observation (points) and median (solid line) and inter-quartile range (shaded area) of pop PK/PD simulations





# ARC-20 AB521 Monotherapy Dose Escalation/Expansion in ccRCC is Ongoing

#### **PH1 DOSE ESCALATION**

#### 3+3 design with 21-day DLT window Solid-tumor patients w/o SOC



#### **CURRENT STATUS:**

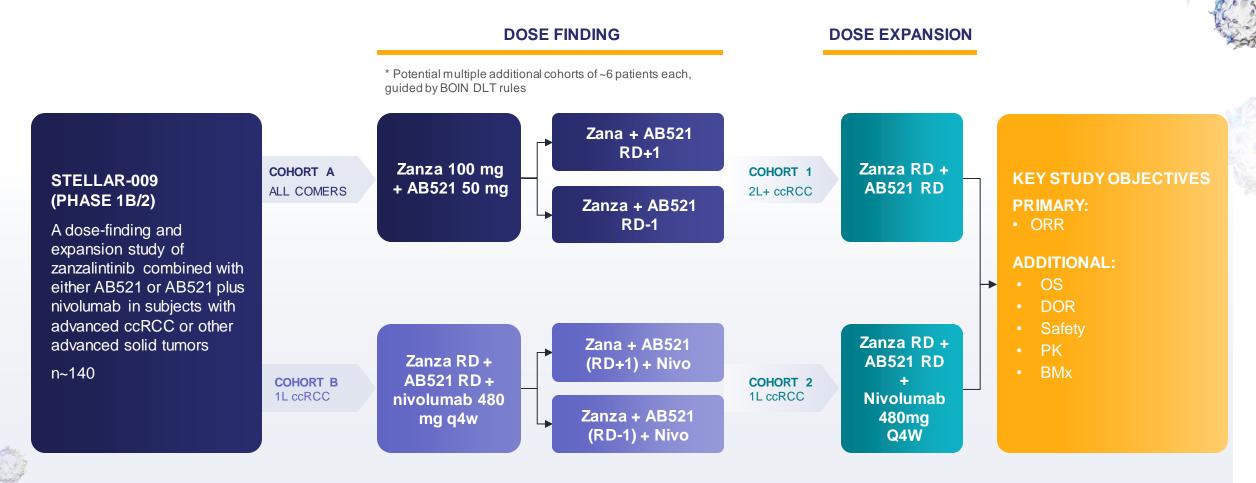
- Dose escalation enrolled 12 patients; 4 of whom had ccRCC plus 2 who had non-ccRCC and were treated at the 50mg QD or 50mg BID doses. Safety/PK/PD/anecdotal efficacy data to be presented early 2024
- Enrollment of the dose expansion cohort evaluating the 100 mg daily dose (n=30) completed in November 2023 – results to be shared 2H:24

2L: second-line; 2H: second half; BID: twice daily; ccRCC: clear cell renal cell carcinoma; PD: pharmacody namics; Ph: phase; PK: pharmacokinetics; QD: once daily; RECIST: Response Evaluation Criteria in Solid Tumors; SOC: standard of care



STELLAR<sup>009</sup>

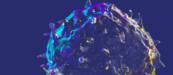
### Phase 1b/2 Study of AB521 + Zanzalintinib +/- Nivolumab in Advanced Solid Tumors Including ccRCC\*



1L: first-line; 2L: second-line; ccRCC: clear cell renal cell carcinoma; DOR: duration of response; niv o: niv olumab; ORR: objective response rate; OS: ov erall surv iv al; PK: pharmacokinetics; Q4W, ev ery 4 weeks; RD: recommended dose; zanza: zanzalintinib

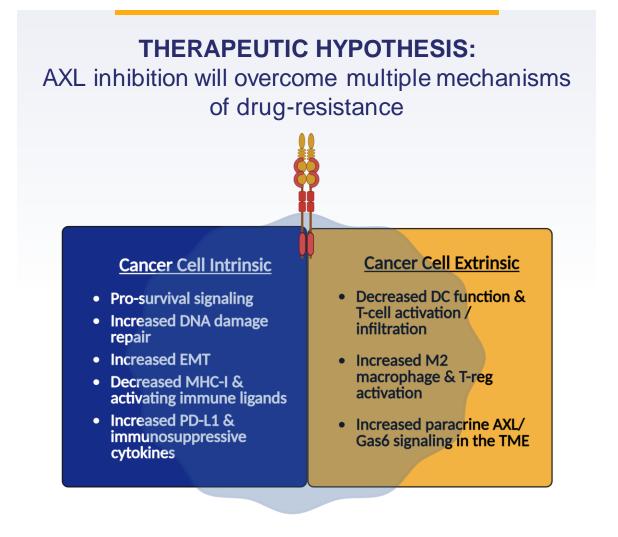




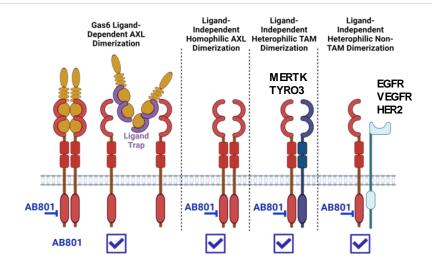




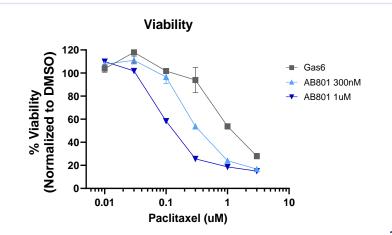
## AXL Signaling is a Common Mechanism of Resistance to Chemotherapy and Immunotherapy in Tumors



## AXL signals via Ligand-dependent and Ligand-independent mechanisms



#### AB801 sensitizes cancer cells to chemotherapy

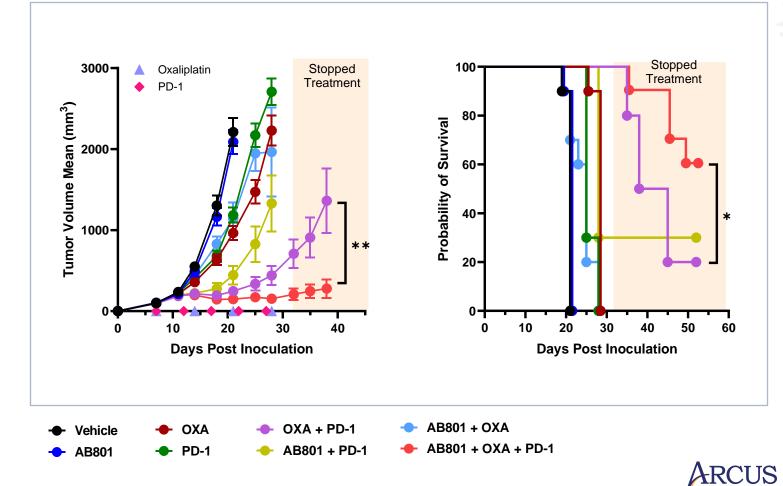


## AB801 is a Potent, Selective, and Efficacious AXL Inhibitor

#### AB801 is a highly potent and selective AXL inhibitor

	Assay	AB801
	AXL K <sub>i</sub>	0.024 nM
BIOCHEMICAL	Fold selectivity over hMERTK/ hTYRO3 (enzyme K <sub>i</sub> over AXL K <sub>i</sub> )	860x/ 1400x
	Kinome Selectivity against 403 kinases at 100x IC <sub>50</sub> for AXL	Only one kinase with less that 200x fold selectivity
CELLULAR	pAXLELISAIC <sub>50</sub> (serum-free media)	17 nM
	pAXLELISAIC <sub>50</sub> (100% serum)	68 nM

Combination of AB801 with Oxaliplatin & α-PD-1 Increases Anti-Tumor Efficacy and Survival in Preclinical Models\*





## AB801 is Believed to be the Most Potent & Selective AXL Inhibitor in Clinical Development

THERAPEUTIC HYPOTHESIS: Inhibiting AXL will overcome resistance against chemotherapy and immunotherapy in human tumors

- AB801 was designed to potently and selectively inhibit AXL signaling in tumors, resulting in enhanced responses to chemotherapy and immunotherapy
  - Other "AXL inhibitors" may not be potent enough or lack selectivity (leading to toxicity) that may limit their use at doses suitable for efficient AXL inhibition
- Phase 1 study in Healthy Volunteers is ongoing:
  - No safety issues have been observed to date in the first 3 dose-escalation cohorts
  - Pharmacokinetics were dose-proportional and appear to support once-daily dosing
- Phase 1 study (ARC-27) in patients with advanced solid tumors is underway; Two expansion cohorts planned:
  - STK-11 mutant NSCLC
  - 2L NSCLC

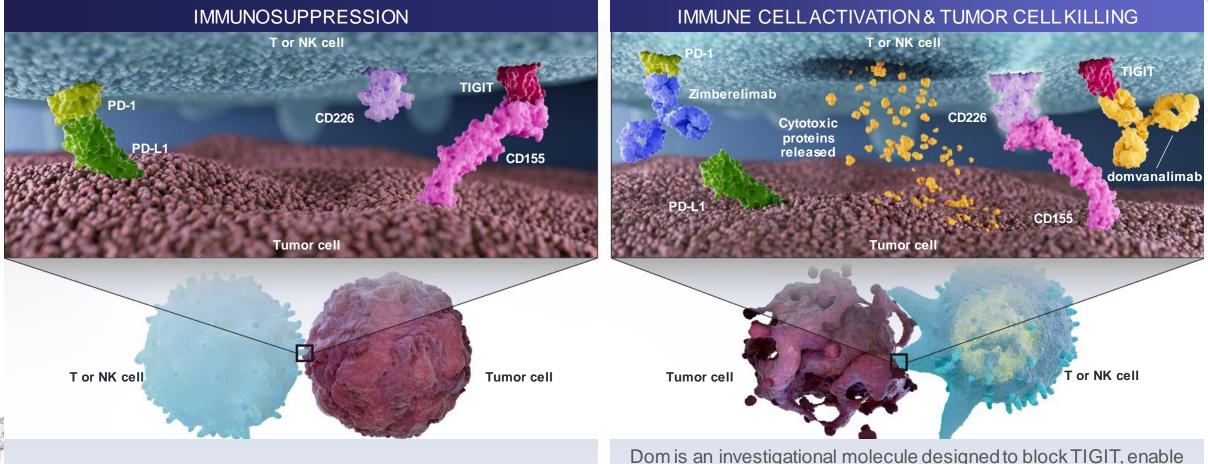








## Domvanalimab (dom): Most Advanced Fc-Silent TIGIT Antibody in Clinical Development

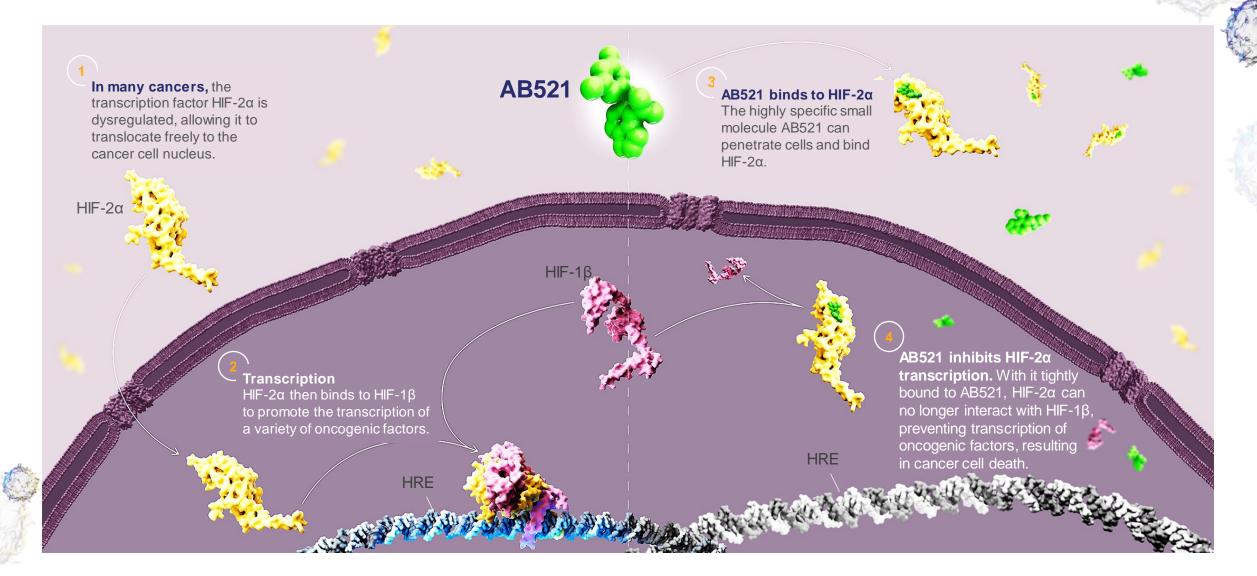


TIGIT is another checkpoint receptor expressed on immune cells that binds CD155 on tumor cells, leading to further evasion of anti-tumor immunity Dom is an investigational molecule designed to block TIGIT, enable CD155:CD226 interaction and immune cell activation

Combined inhibition of TIGIT and PD1 may have a synergistic effect, unleashing immune activity against certain tumor cells

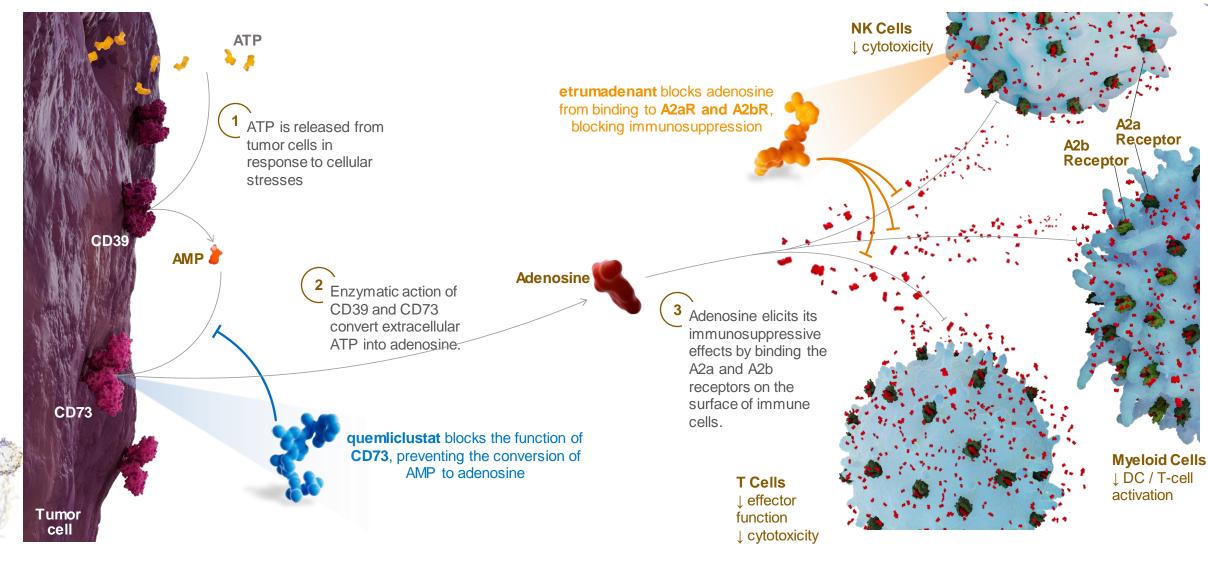


## **AB521 in the Cancer Cell Nucleus**

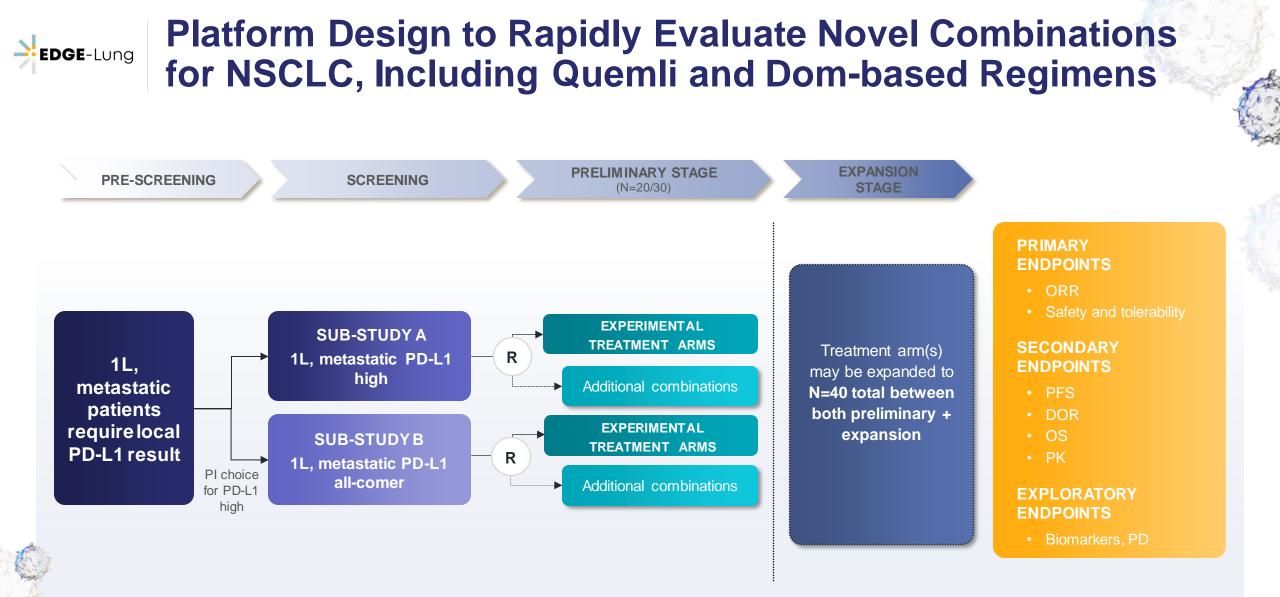




## The CD73-Adenosine Axis Plays a Well-Established and Critical Role in Suppression of the Immune Response







1L, first line; AC, all comer; DOR: duration of response; IO, immuno-oncology; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; PD, pharmacody namics; PD-L1,ORR programmed death-ligand 1; PK, pharmacokinetics; PI, principal investigator; R, randomized



