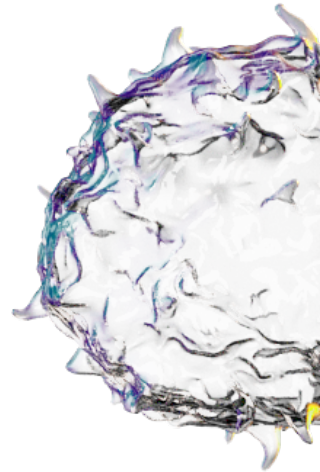
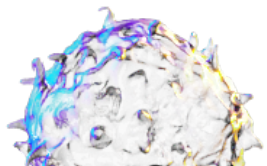
COMBINING TO CURE®

Arcus is at the forefront of designing combination therapies, with best-in-class potential, in the relentless pursuit of cures for cancer.

CORPORATE PRESENTATION

May 8, 2024





ARCUS BIOSCIENCES

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 portfolio; anticipated benefits of our collaborations with Gilead, Taiho and AstraZeneca; achievement and expected timing of clinical and developmental milestones, including the initiation of clinical trials and the timing of completion of enrollment and presentation of clinical data; and possible first to market advantage for any of our investigational products.

These forward-looking 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 license and collaboration agreements and our ability to obtain and maintain intellectual property protection for our product candidates; and the inherent uncertainty associated with pharmaceutical product development and clinical trials. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially and adversely from those anticipated or implied in the forward-looking statements. Further information on these and other factors that could affect the forward-looking statements made herein are described in our most recent Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission.

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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

~$1.1B in 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, cas)

MULTIPLE PHASE 3 STUDIES FOR DOM IN LUNG & UPPER GI in 2024+

STAR-121 STAR-221 STAR-131

full enrollment expected in ’24

PACIFIC-8

MULTIPLE DATASETS IN 2024

Dom* (TIGIT)

- EDGE-Gastric ASCO oral presentation

Cas (AB521; HIF-2α)

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

Quemli* (CD73) / Etruma* (A2R)

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

TOP TIER PARTNERS

Provides funding and resources enabling a diversified pipeline

GILEAD AstraZeneca TAIHO PHARMA EXELIXIS

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: cas: casdatifan, clear cell renal cell carcinoma; dom: domvanalimab; etruma: etrumadenant; GI: gastrointestinal; OS: overall survival; PFS: progression-free survival; quemli: quemliclustat; R&D: research and development; zim: zimberelimab

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*includes combination with zimberelimab (anti-PD1)
** as of March 31, 2024

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

DIFFERENTIATED ANTI-TIGIT + ANTI-PD-1 BACKBONE

domvanalimab: Potential best-in-class, Fc-silent anti-TIGIT antibody – multiple ongoing Phase 2 and 3 studies in NSCLC and Upper GI cancers

zimberelimab: Anti-PD-1 antibody – multiple ongoing studies in combination with Arcus and non-Arcus molecules; approved in China for classical Hodgkin Lymphoma (cHL) and cervical cancer*

DIFFERENTIATED SMALL MOLECULES

casdatifan: Potential best-in-class HIF-2α inhibitor; Phase 1/1b and Phase 2 studies in cancer patients are ongoing

quemliclustat: Potential first-in-class small-molecule CD73 inhibitor; generated evidence of survival data in pancreatic cancer in early clinical research; Phase 3 study in planning

etrumadenant: Potential first-in-class dual $A_{2a}R$ / $A_{2b}R$ 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

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

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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
Dom (Fc-silent anti-TIGIT antibody)	NSCLC	STAR-121	**1L, PD-L1 all-comers, metastatic** **dom + zim** + chemo vs pembro + chemo				• 2024: Enrollment completion
		STAR-131	**Perioperative lung cancer**	IN PLANNING			
		PACIFIC-8	**Stage 3:** durva ± **dom**				
		EDGE-Lung	**1L / 2L, all-comers: dom ± zim ± quemli** ± chemo				
		VELOCITY-Lung	**1L/2L NSCLC: dom ± zim ± etruma** ± SG				• 2024: Update expected
	Upper GI	STAR-221	**1L Upper GI Malignancies** **dom + zim +** chemo vs. nivo + chemo				• 2024: Enrollment completion
		EDGE-Gastric	**1L / 2L Upper GI Malignancies** **dom ± zim ± quemli** ± FOLFOX				• 1H24: ASCO presentation
Cas (HIF-2α inhibitor)	ccRCC	TBD	**Not disclosed**	IN PLANNING			• 1H25: Ph 3 initiation
		STELLAR-009	**2L ccRCC: cas** + zanza				
		ARC-20	**all-comer cancer; 2L+ ccRCC** **cas** monotherapy				✓ Early 2024: Dose escalation data • 2H24: Dose expansion data (30 pts, 7m+ follow-up)
ADENOSINE **Quemli (CD73 inhib.)**	PDAC	PRISM-1	**1L quemli +** G/nP vs. GnP	IN PLANNING			• Early 2025: Ph 3 initiation
		ARC-8	**1L: quemli + zim** + G/nP vs **quemli** + G/nP				✓ Jan 2024: Mature OS
ADENOSINE **Etruma (A2R antag.)**	CRC	ARC-9	**2L: etruma + zim** + FOLFOX* vs FOLFOX* **3L: etruma + zim** + FOLFOX* vs rego				✓ 1H24: MORPHEUS-PDAC (etruma); mature PFS/OS • 1H24: ASCO presentation; mature PFS/OS data in 3L
AB801 (Axl inhibitor)	NSCLC	ARC-27	**2L+: AB801** ± chemo				

1L: first line; 2L: second line; 3L: third line; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; durva: durvalumab; etruma: etrumadenant; GI: gastrointestinal; G/nP: gemcitabine/nab-paclitaxel; NSCLC: non-small cell lung cancer; PD: pharmacodynamic; pembro: pembrolizumab; PFS; progression-free survival; Ph: phase; PK: pharmacokinetic; OS: overall survival; rego: regorafenib; SG:Sacituzumab govitecan-hziy; quemli: quemliclustat zanza:zanzalintinib; zim: zimberelimab

*+/- biologic, e.g. bevacizumab or biosimilar, will be included for all patients in whom it is not contraindicated

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

GILEAD

10-YEAR COLLABORATION

- **Gilead has opted into 5 molecules to date -- shares costs for studies within the joint development plan**
- Arcus retains U.S. co-commercial rights

TAIHO PHARMA

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

AstraZeneca

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

EXELIXIS

CLINICAL COLLABORATION FOR CAS + 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

b: billion; cas: casdatifan; dom: domvanalimab; etruma: etrumadenant; mm: million; NSCLC: non-small cell lung cancer; zim: zimberelimab

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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, with best-in-class potential

ZIMBERELIMAB

Well characterized anti-PD-1 antibody; approved in China*

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

- ✓ **Peripheral T_{reg} numbers do not decrease** with dom + zim, but they do with Fc-enabled anti-TIGIT antibodies[1]
- ✓ **No increase in irAEs** reported with dom + zim in ARC-7[2]; differentiated safety and tolerability profile relative to published data for incidences of rash, pruritis and infusion site reactions with Fc-enabled anti-TIGIT antibodies

dom: domvanalimab; etruma: etrumadenant; irAE: immune-related adverse events; NSCLC: non-small cell lung cancer; zim: zimberelimab

* Gloria obtained approval for zim in China and conducts its activities independently from Arcus.

[1]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

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

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Two De-Risking Phase 2 Datasets for Domvanalimab Plus Zimberelimab Regimens Were Presented in 2023

EDGE-Gastric

1L Gastric/EAC/GEJ

dom + zim + FOLFOX (n=40)

ASCO Plenary Series — Update at 2024 ASCO ANNUAL MEETING

- PD-L1-high (TAP ≥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

dom + **zim** *vs.* **zim** *vs.* **etruma** + **dom** + **zim** (n=150)

2023 ASCO ANNUAL MEETING

- PFS HRs:
  - **0.67** for DZ vs. Z
  - **0.72** for EDZ vs. Z
- ORRs for 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: overall response rate; OS: overall 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

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

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Phase 3 Program for Dom-Based Combinations is Targeting Significant Market Opportunities

STUDY	LEAD SPONSOR	SETTING	US PATIENT POPULATION[1]
STAR-121	GILEAD	1L NSCLC, PD-L1 All comers	119k patients
PACIFIC-8	AstraZeneca	Stage 3 NSCLC, unresectable, PD-L1≥1%	21k patients
STAR-221	ARCUS BIOSCIENCES	1L Gastric/GEJ/EAC	25k patients

Multi-billion revenue opportunities

$10B+ addressable market[1]

1L: first-line; B: billion; dom: domvanalimab; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction;; k: thousand' NSCLC: non-small cell lung cancer; TBA: to be announced; zim: zimberelimab
[1]Based on expected drug treatable US patient population. Excludes patients with actionable mutations. Source: Decision Resources Group.

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

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

Updated data to be presented at ASCO 2024

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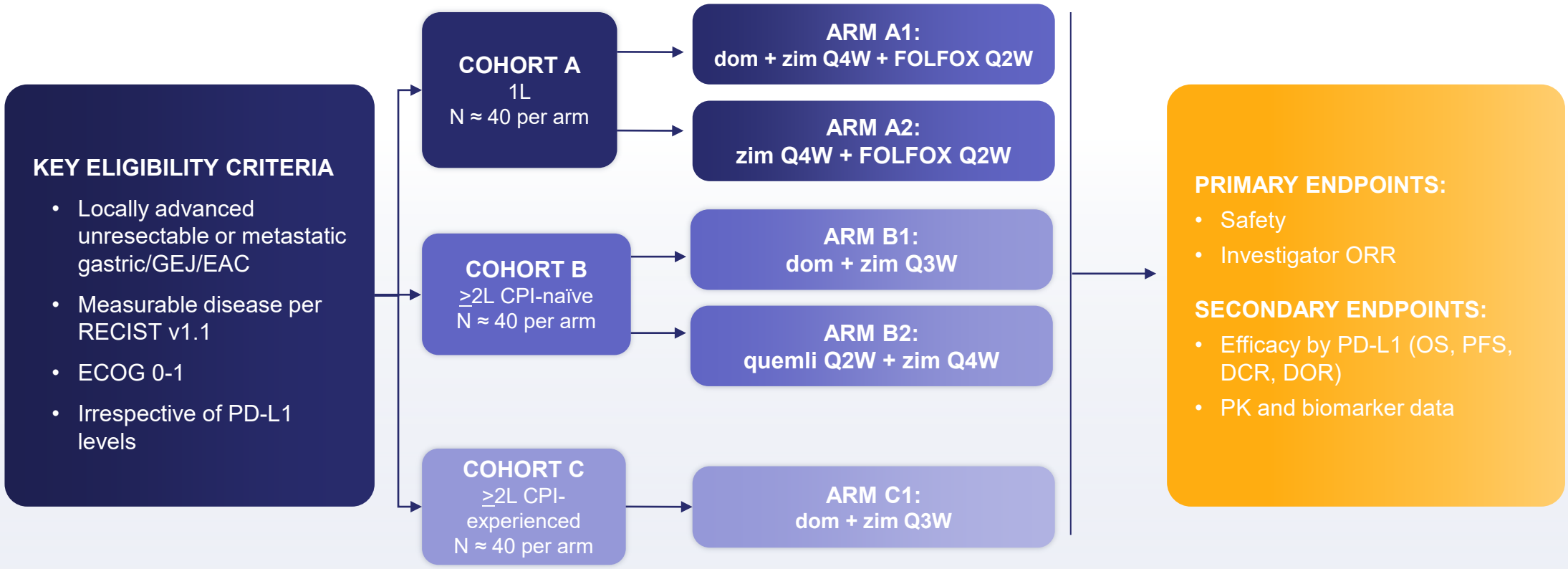
Phase 2 Trial to Evaluate Dom and Zim Combinations in Advanced Upper GI Malignancies

EDGE-Gastric

ARMS NOT RANDOMIZED, ENROLLED SEQUENTIALLY



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

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

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Results for Arm A1 in 1L Metastatic Gastric/GEJ/EAC Were Presented at ASCO Plenary in November 2023



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

1L first-line; DCR: disease control rate; dom: domvanalimab; DOR: duration of response; EAC: esophageal adenocarcinoma; ECOG: Eastern Cooperative Oncology Group; GEJ: gastroesophageal junction; ORR: objective response rate; OS: overall survival; PD: progressive disease; PFS: progression-free survival; PK: pharmacokinetics; QxW: every x weeks; RECIST: Response Evaluation Criteria in Solid Tumors; zim: zimberelimab

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

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Encouraging ORR and 6-Month PFS Results

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

	PD-L1 High* (TAP ≥5%) N=15 n (%)	PD-L1 Low* (TAP <5%) N=24 n (%)	Efficacy-Evaluable N=41 n (%)
ORR, % [95% CI]	**80** [52, 96]	**46** [26, 67]	**59** [42, 74]
Confirmed ORR, % [95% CI]	**73** [45, 92]	**46** [26, 67]	**56** [40, 72]
Confirmed Complete Response	1 (7)	0	2 (5)
Confirmed Partial Response	10 (67)	11 (46)	21 (51)
Unconfirmed Partial Response†	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.

† 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

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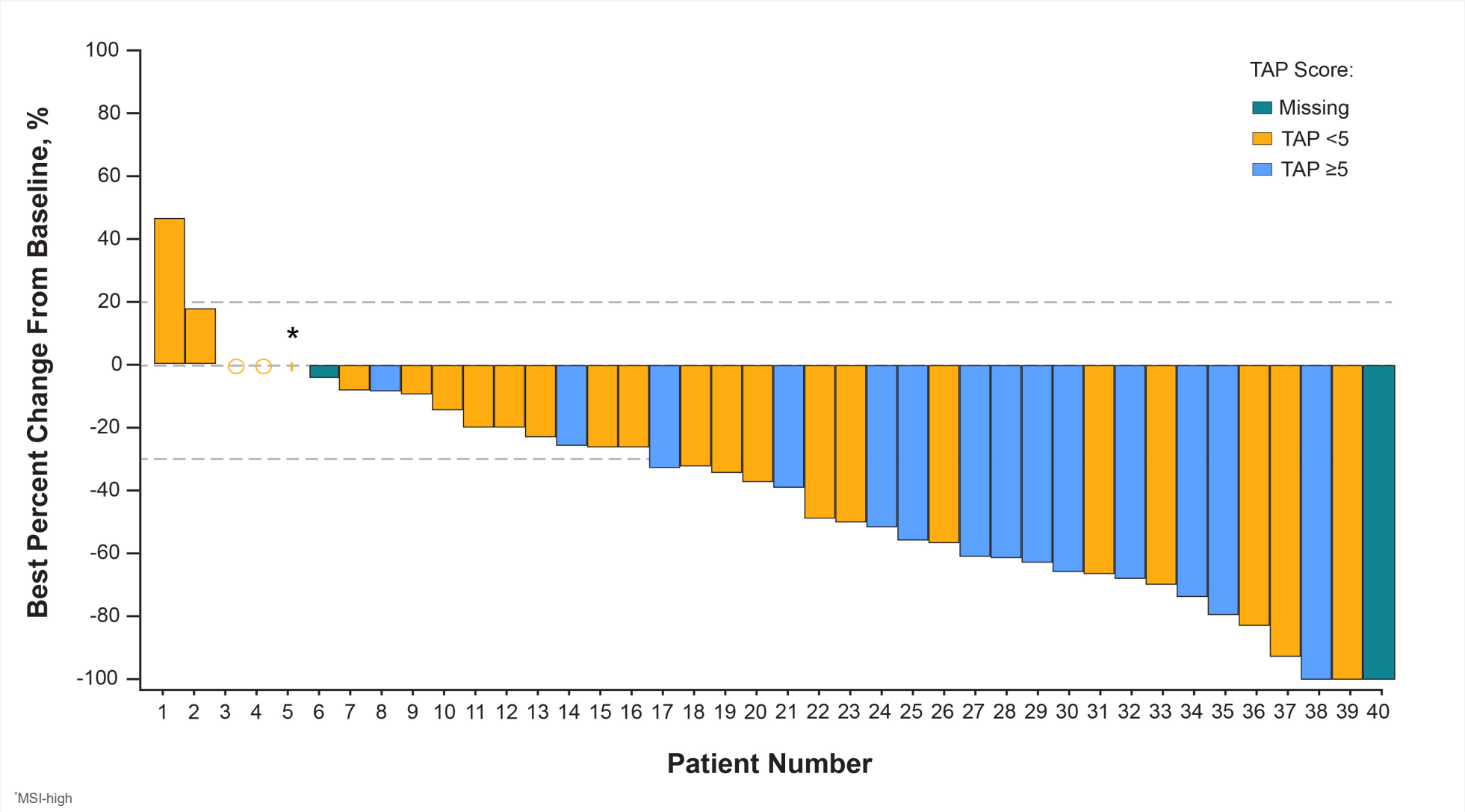
Almost All Patients Experience Some Benefit, Irrespective of PD-L1 Status



*MSI-high

TAP: tumor area positivity

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

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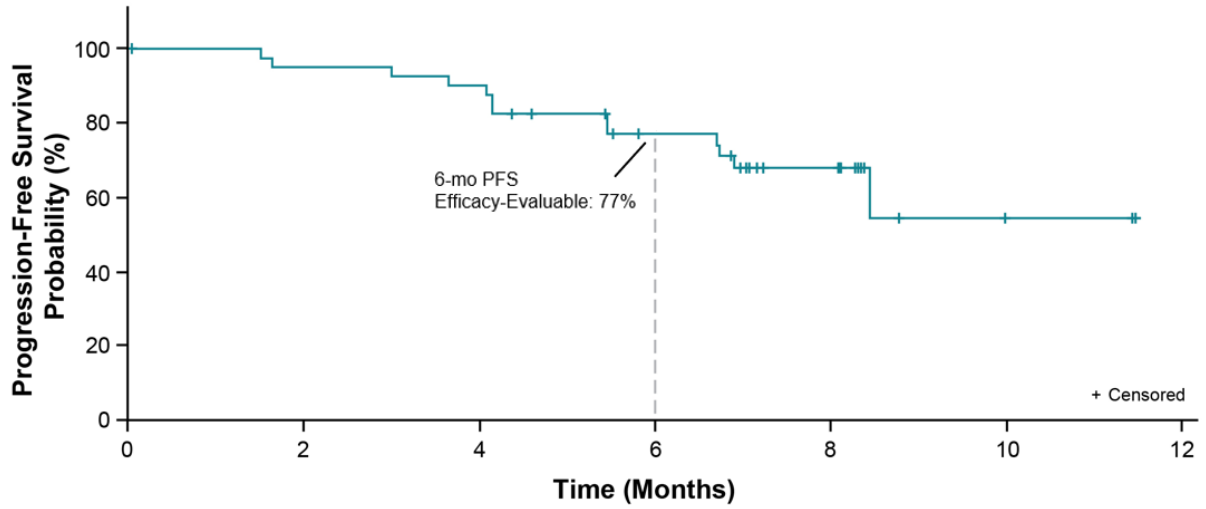
Landmark 6-Month PFS Compares Favorably to Benchmark Data of 60-65%; Median PFS Still Immature

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

Events, n (%)	Median, months (95% CI)	Month 6 Rate, % (95% CI)	Median Follow-up Time, months (95% CI)
13 (32)	NE (8, NE)	77 (64, 90)	8 (7, 8)

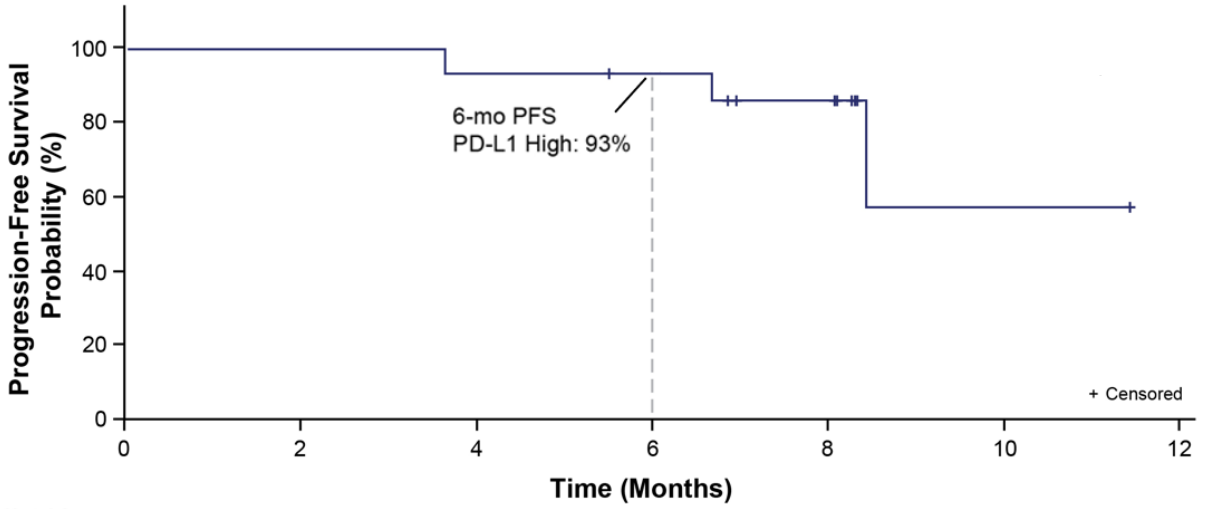


N at risk

Efficacy-Evaluable	41	38	36	26	15	2	0

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

Events, n (%)	Median, months (95% CI)	Month 6 Rate, % (95% CI)	Median Follow-up Time, months (95% CI)
3 (20)	NE (8, NE)	93 (81, 100)	8 (7, 8)



N at risk

PD-L1 High	15	15	14	13	9	2	0

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

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

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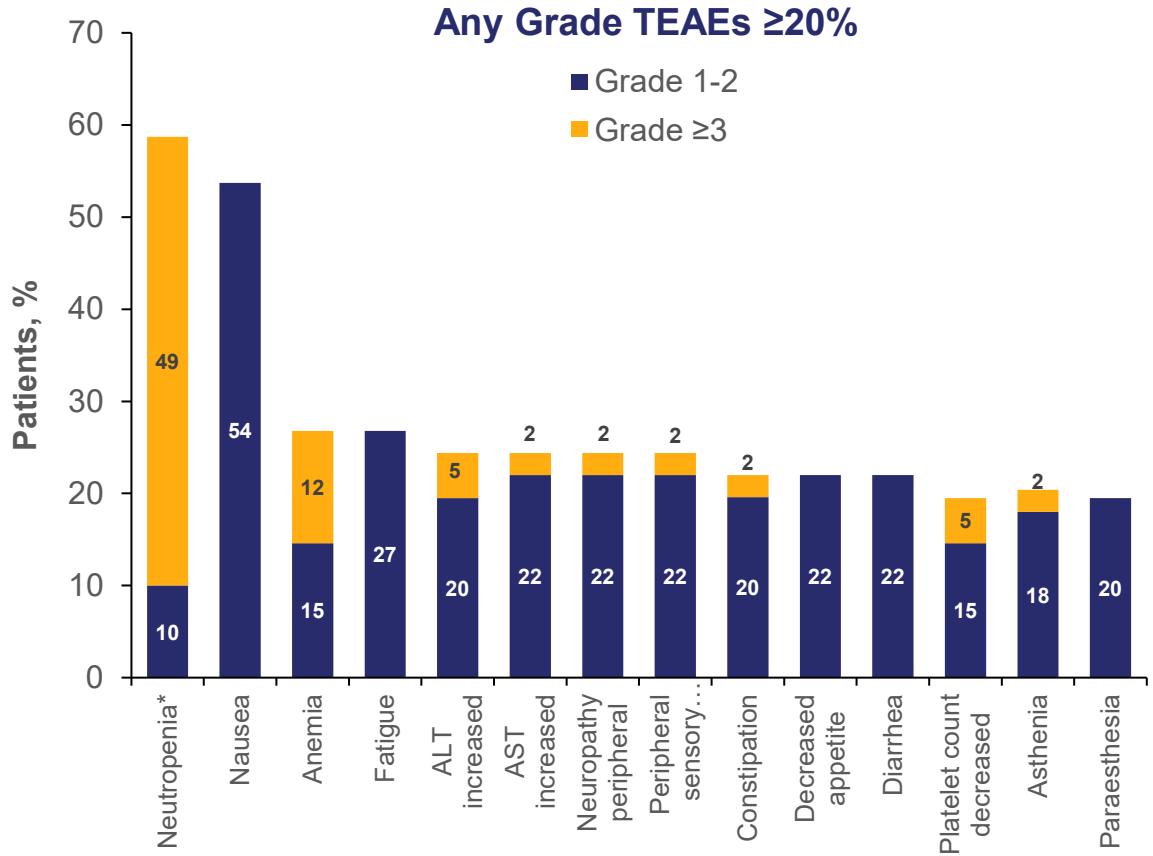
Safety Profile for Dom + Zim + FOLFOX

TEAE	Arm A1 N=41, n (%)
Any TEAE	41 (100)
TEAEs related to any study drug	40 (98)
Grade ≥3 TEAEs	28 (68)
Grade ≥3 TEAEs related to any study drug	23 (56)
Serious TEAEs	10 (24)
Serious TEAEs related to any study drug	2 (5)
TEAEs leading to permanent withdrawal from any study drug	20 (49)
TEAEs leading to dose modification/interruption of any study drug	33 (81)
TEAEs resulting in death	0



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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STAR-221

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

N=970

R 1:1

domvanalimab + zimberelimab + PI choice of chemo*

nivolumab + PI choice of chemo*

No crossover or change of chemotherapy allowed

DUAL PRIMARY ENDPOINTS:

- OS ITT
- OS in TAP ≥5%

KEY SECONDARY ENDPOINTS:

- PFS ITT
- PFS in TAP ≥5%

Initiated in 3Q22

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: domvanalimab; ECOG: Eastern Cooperative Oncology Group; GEJ: gastroesophageal junction; nivo: nivolumab; ITT: intent to treat; OS: overall survival; PFS: progression-free survival; PI: principal investigator; RECIST: Response Evaluation Criteria in Solid Tumors; TAP: tumor area positivity (revised nomenclature for vCPS [visually-estimated composite positive score]); R: randomized; zim: zimberelimab

*PI choice of chemo: FOLFOX or CAPOX.

NCT #: NCT05568095

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

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Summary of ARC-7 Results and Domvanalimab Plus Zimberelimab 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.

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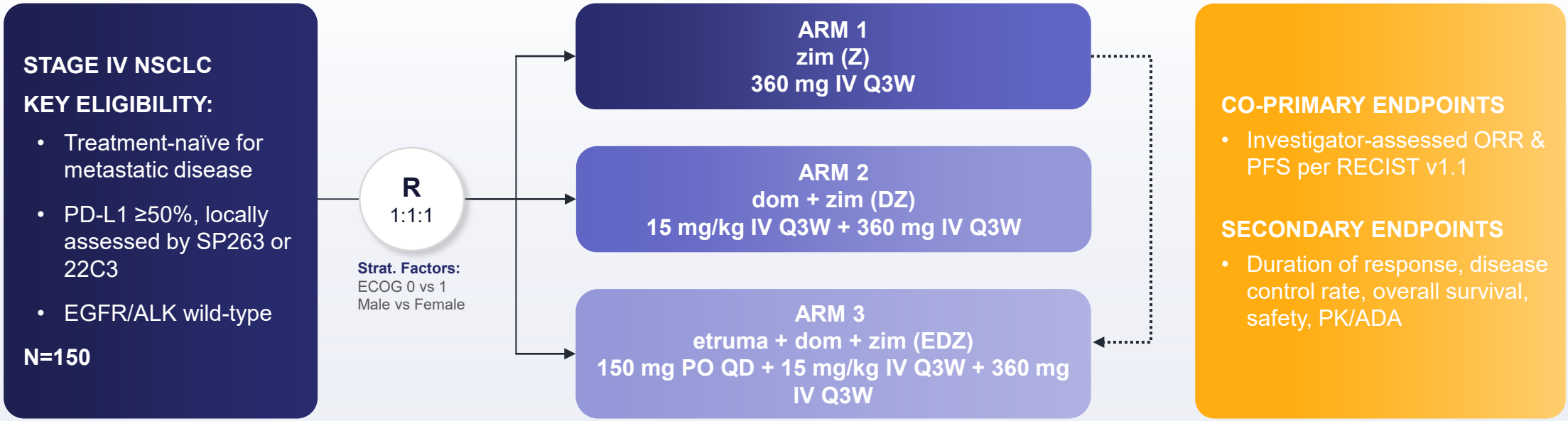
Randomized, Open-label, Ph2 Study in First-Line, Metastatic, PD-L1-High NSCLC



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: domvanalimab; ECOG: Eastern Cooperative Oncology Group; E/etruma: etrumadenant; IV: intravenous; NSCLC: non-small cell lung cancer; ORR: overall response rate; Ph: phase; PFS: progression-free survival; PK: pharmacokinetics; PO: orally; R: randomized; RECIST: Response Evaluation Criteria in Solid Tumors; Z/zim: zimberelimab; Q3W: every 3 weeks; QD: once-daily

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

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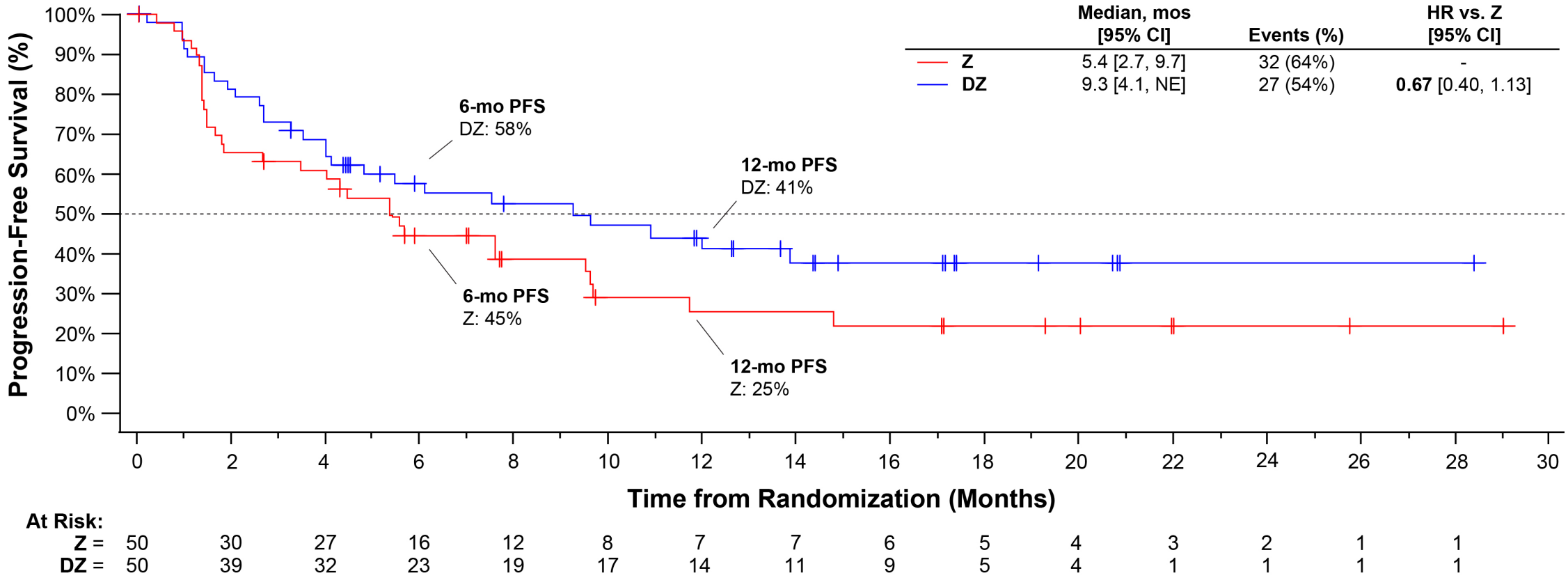
Addition of Dom to Zim Resulted in a 33% Reduction in Risk of Progression or Death, Compared to Zim Monotherapy



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

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

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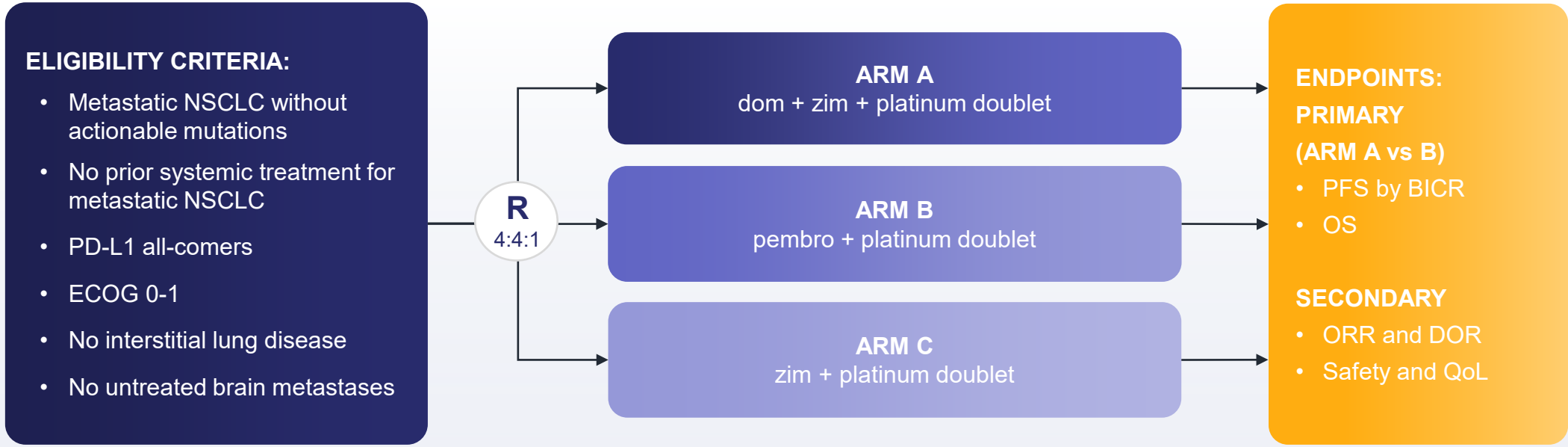
Phase 3 Evaluating Dom + Zim + Chemo vs. Pembro + Chemo in 1L NSCLC (All PD-L1 Subgroups)

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



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

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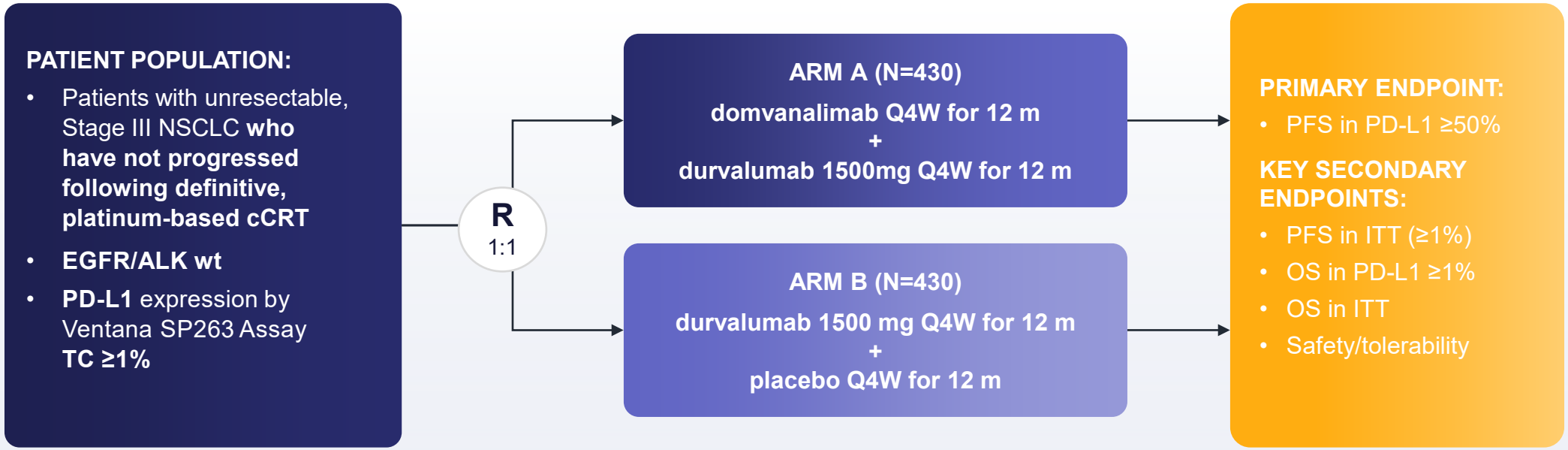
Phase 3 Evaluating Dom + Durva vs Placebo + Durva in Unresectable, Stage III NSCLC

- 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:

- 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: overall survival; PFS: progression free survival; Q4W: every 4 weeks; TC: tumor count

NCT #: NCT05211895

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HIF-2α Program

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Value Proposition for Casdatifan (AB521), a Potential Best-in-Class HIF-2α Inhibitor

Efficacy

Opportunity to reach greater intra-tumoral 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 best-in-class and first-in-class combinations

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

Cas: casdatifan; PD: pharmacodynamics; PK: pharmacokinetics; TKI: tyrosine kinase inhibitor

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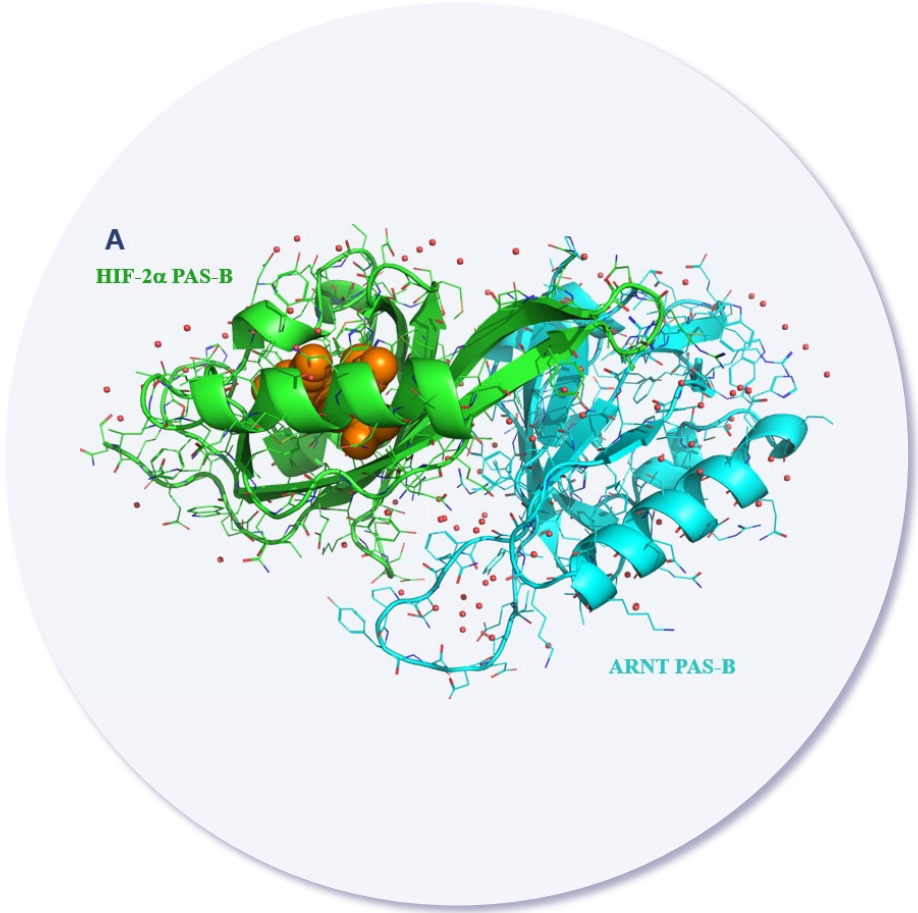
Extensive Preclinical Characterization Confirms Greater Potency of Casdatifan (AB521) Relative to that of Belzutifan

	ASSAY	Casdatifan	Belzutifan[a]
CELLULAR	HIF-2α 786-O Luc Reporter IC_{50} (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)**
CELLULAR	HIF-2α 786-O Luc Reporter IC_{50} (nM) [in 100% Serum]	**46.5 ± 14.2 (n=24)**	**61.8 ± 6.6 (n=4)**
CELLULAR	786-O VEGF AlphaLISA IC_{50} (nM)	**28.9 ± 3.6 (n=11)**	**47.7 ± 30.8 (n=4)**
BIOCHEMICAL	HIF-2α $TSAT_m\Delta$ (°C)	**14.7 ± 0.6 (n=14)**	**12.1 ± 0.3 (n=4)**
BIOCHEMICAL	HIF-2α MST K_D (nM)	**2.4 ± 0.8 (n=3)**	**15.4 ± 2.7 (n=3)**
BIOCHEMICAL	HIF-2α ITC K_D (nM)	**53.6 ± 17.9 (n=3)**	**53.8 ± 19.3 (n=3)**
BIOCHEMICAL	HIF-2α SPA IC_{50} (nM)	**16.6 ± 5.0 (n=8)**	**22.3 ± 5.6 (n=5)**



[A] Belzutifan was synthesized according to Xu *et al.* 2019 J Med Chem; DOI: 10.1021/acs.jmedchem.9b00719

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Casdatifan (AB521) Monotherapy Dose Escalation/ Expansion in ccRCC is Ongoing

PH 1 DOSE ESCALATION

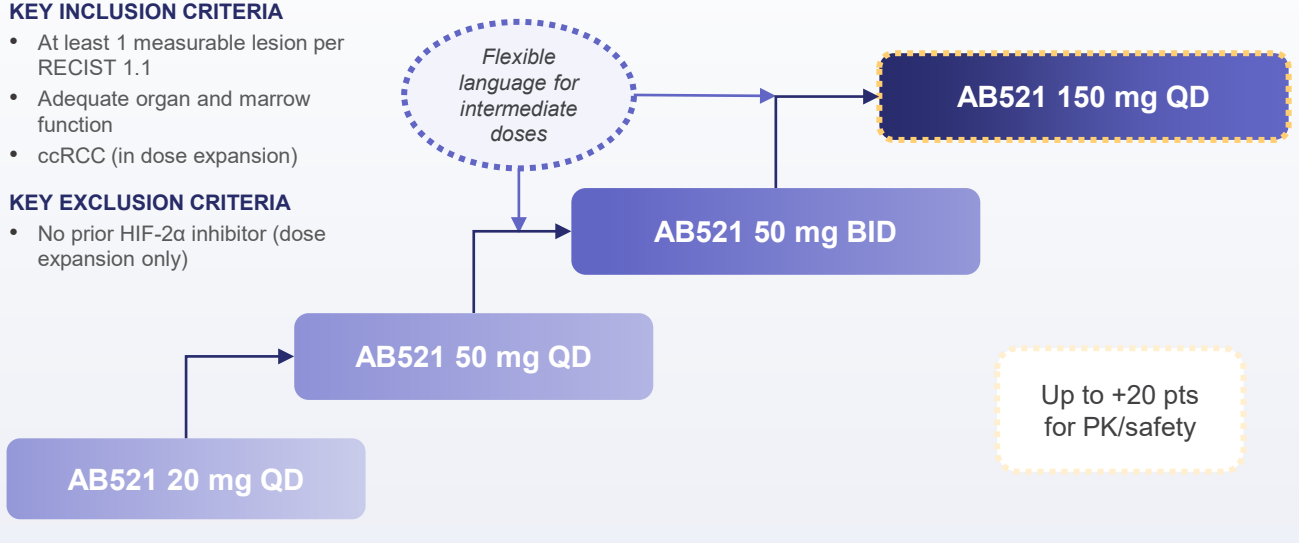
3+3 design with 21-day DLT window **Solid-tumor patients w/o SOC**

KEY INCLUSION CRITERIA

- At least 1 measurable lesion per RECIST 1.1
- Adequate organ and marrow function
- ccRCC (in dose expansion)

KEY EXCLUSION CRITERIA

- No prior HIF-2α inhibitor (dose expansion only)



EXPANSION COHORTS (2L+ ccRCC)

- **50mg (n=30) COMPLETED ENROLLMENT**
- **100mg (n=30) COMPLETED ENROLLMENT**
- **150mg (n=30) ENROLLING**
- **cas + cabo (n=30) PLANNED**

CURRENT STATUS:

- Dose escalation enrolled 12 patients at the 20mg QD, 50mg QD and 50mg BID doses, 4 of whom had ccRCC (across all three doses) as of Dec. 15, 2023 (see slide 31)
- **Data from the dose expansion cohort evaluating the 100 mg daily dose (n=30) to be shared 2H:24**

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

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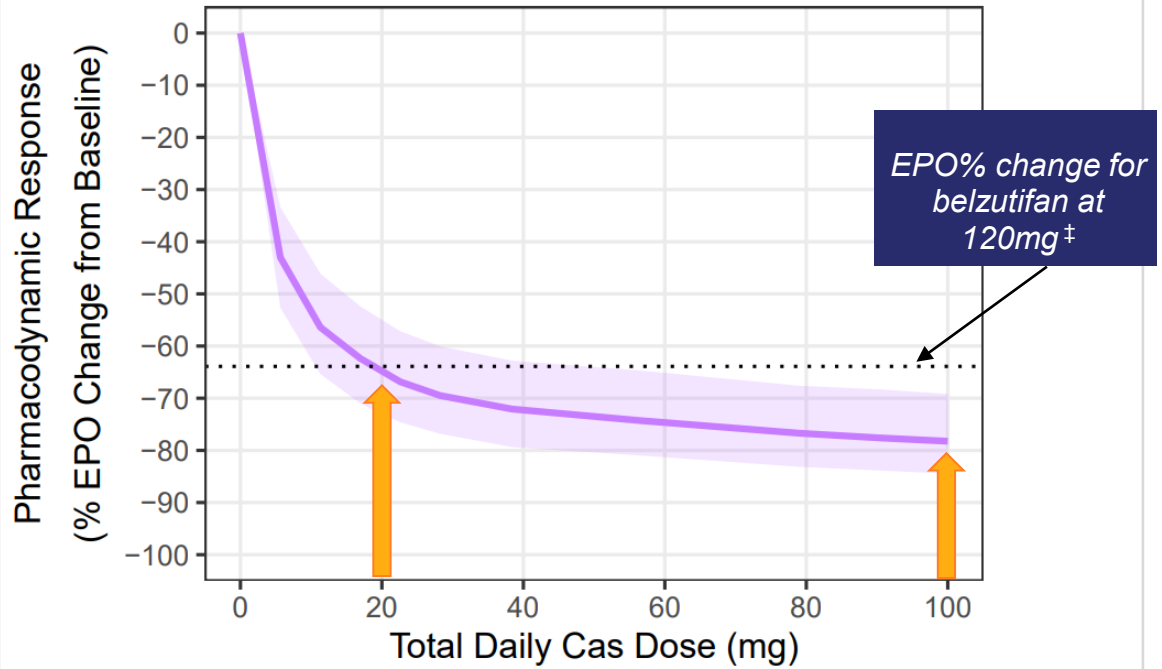
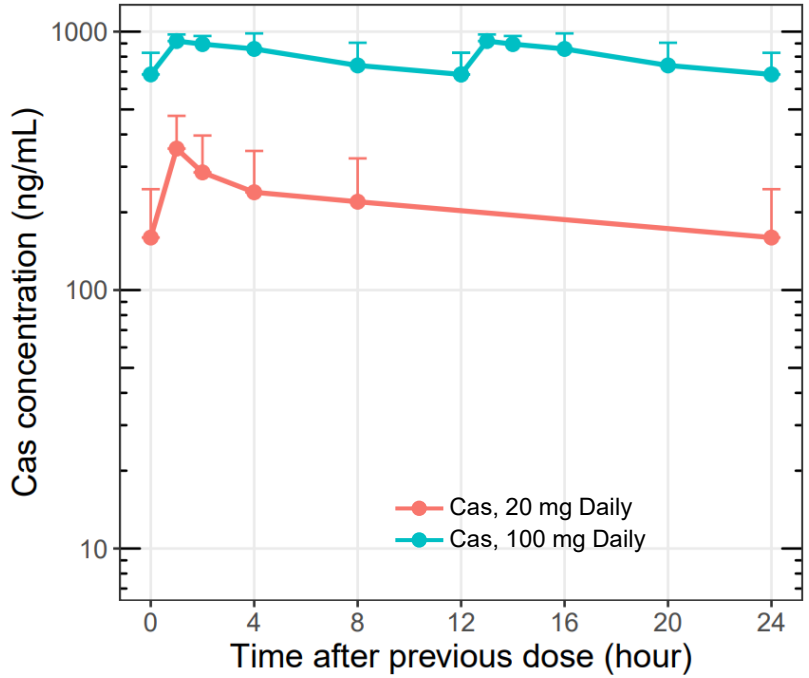
Casdatifan (AB521) 20mg Achieves Similar PD Effect as belzutifan at 120mg

20 mg of cas achieves near-complete suppression of HIF-2α-dependent EPO (peripheral PD marker); 120mg of belzutifan (the approved dose) is required for this level of EPO suppression



Human PK profile of cas is dose-linear; Daily 100mg cas dose expected to provide ~5x more drug to the tumor than the 20mg dose



cas: casdatifan; EPO: erythropoietin; PD: pharmacodynamics; PK: pharmacokinetics
§ AB521: median (solid line) and inter-quartile range (shaded area) of population PK/PD simulations using model developed from data
‡ Source: belzutifan NDA - FDA review document
casdatifan (AB521) is an investigational molecule and its safety and efficacy have not been established.
PK/PD data are from both escalation and expansion cohorts

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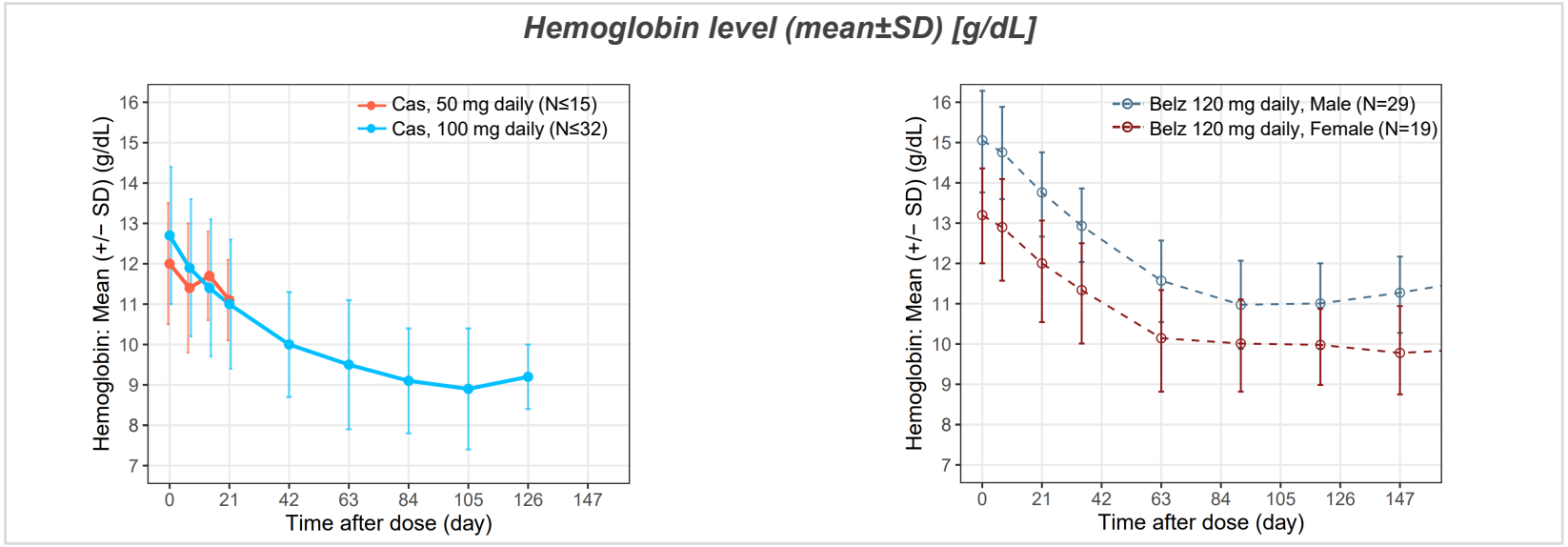
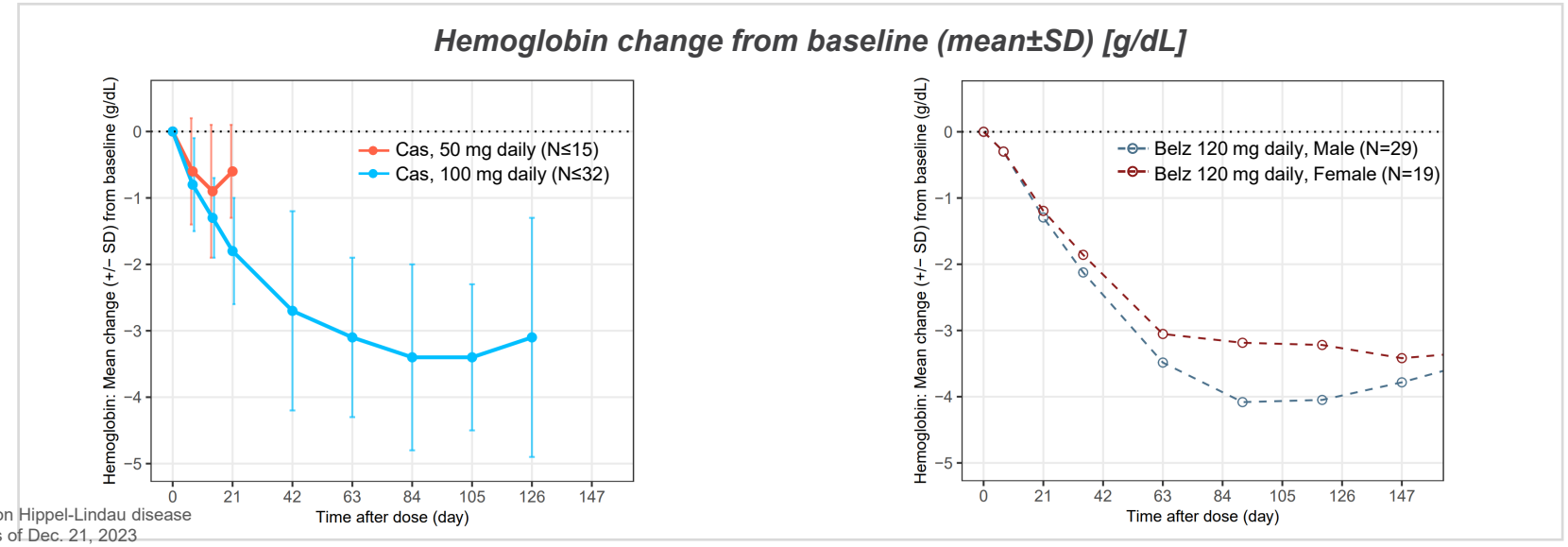
Hemoglobin Changes After Casdatifan (AB521) 100 mg Administration are Similar to that of Belzutifan at 120 mg





belz: belzutifan; cas: casdatifan; VHL:Von Hippel-Lindau disease
Casdatifan data from ccRCC patients as of Dec. 21, 2023
Belzutifan hemoglobin data from VHL patients: Source: *Nature medicine, 2021, 385(22), 2036-2048.*

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Treatment-Emergent Adverse Events (as of Dec. 15, 2023)

To date, rates of adverse events, including anemia and hypoxia, appear consistent with observations from historical trials of belzutifan.

TEAEs Reported in ≥2 Patients

Preferred Term	Dose Escalation Cohorts (N=12)
Subjects with ≥1 TEAE, n (%)	**10 (83.3)**
Anemia	7 (58.3)
Dehydration	3 (25.0)
Hypoxia	3 (25.0)
Nausea	3 (25.0)
Diarrhea	2 (16.7)
Fatigue	2 (16.7)
Headache	1 (8.3)
Vomiting	1 (8.3)
Pollakiuria	1 (8.3)

Grade ≥3 TEAEs

Preferred Term	Dose Escalation Cohorts (N=12)
Subjects with ≥1 TEAE Grade ≥3, n (%)	**4 (33.3)**
Anemia	1 (8.3)
Hypoxia	1 (8.3)
Dyspnea	1 (8.3)
Gamma-glutamyltransferase increased	1 (8.3)
Lumbar vertebral fracture	0
Lymphocyte count decreased	1 (8.3)
Pathological fracture	1 (8.3)

Data on File, Arcus Biosciences.

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Early Efficacy Signals in ccRCC Patients

Dose Escalation (n=4)

- Meaningful clinical activity observed in 3 of the 4 ccRCC patients who had 2+ prior lines of therapy
  - 2 ccRCC patients, one still on treatment, have experienced tumor reductions just short of 30%
  - 1 patient experienced almost no tumor growth for more than 14 months and remains on treatment
- Impressive durability, with time on treatment ranging from 8.5+ to 14.5+ months in these patients
  - 2 of the 3 patients remain on treatment

Dose Expansion 100mg Cohort (n=30)

- Completed enrollment in Nov. 2023
- Majority of patients have had one or 2 scans, equivalent to 1.5-3 months of radiographic follow up*
  - Belzutifan median time-to-response is 3.8 months[1]
- Despite limited follow-up, cas has already achieved a similar ORR* to what was shown in LITESPARK-005
  - Multiple patients have experienced tumor reduction with limited follow-up, and could achieved a response at future scans
- Low primary progression rate which may indicate that cas can stabilize tumor growth early in treatment

ccRCC: clear cell renal cell carcinoma; ORR: overall response rate

Data from ARC-20 study. Formal data cut-off date of December 15, 2023. Unless otherwise noted, efficacy observations are made as of February 21, 2024. Scans frequency for ARC-20 is every 6 weeks

*confirmed and unconfirmed ORR

1 Albiges L. et al. Abstract LBA88, ESMO 2023

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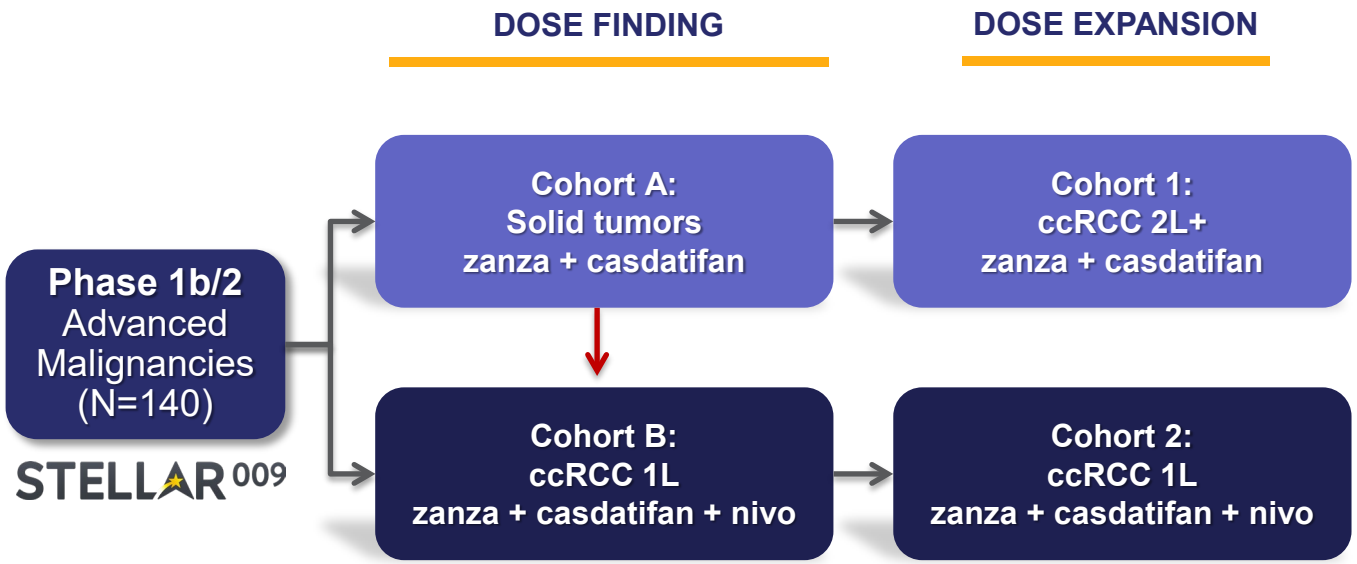
Phase 1b/2 Study of Casdatifan + Zanzalintinib +/- Nivolumab in Advanced Solid Tumors Including ccRCC*

Inclusion:
- ≥18 years
- Unresectable advanced or metastatic disease or 1L or 2L+ ccRCC
- Non-measurable or Measurable disease per RECIST v1.1
- KPS ≥70%
- SpO2 ≥92%

Exclusion:
- Prior treatment with HIF-2α targeted therapy and/or zanza
- Radiation therapy within 4 weeks before first dose
- Known brain metastases or cranial epidural disease



Primary Outcomes:
Dose-Finding Stage:
DLTs
Expansion Stage:
ORR

Secondary Outcomes:
Dose-Finding Stage:
AEs/SAEs
PK
ORR
Expansion Stage:
AEs/SAEs
DOR
PFS
OS
PK

1L: first-line; 2L: second-line; ccRCC: clear cell renal cell carcinoma; DLT: dose-limiting toxicity; DOR: duration of response; KPS=Karnofsky Performance; nivo: nivolumab; ORR: objective response rate; OS: overall survival; PFS: progression-free survival; PK: pharmacokinetics; RECIST=Response Evaluation Criteria In Solid Tumors Version 1.1. SAE=Serious Adverse Event. SpO2=Oxygen Saturation Q4W, every 4 weeks; RD: recommended dose; zanza: zanzalintinib

ClinicalTrials.gov. NCT06191796

*STELLAR-009 is being operationalized by Exelixis

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CD73-Adenosine Axis Programs

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Etrumadenant in Pancreatic and Colorectal Cancers

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

ETRUMADENANT

- Highly potent small molecule that inhibits both the A_{2a} and A_{2b} receptors
- Excellent penetration of tumor tissue and drug properties (PK, etc.)
- **MORPHEUS-PDAC (operationalized by Roche) data presented at AACR 2024 (Abstract CT212)**
- **Data from ARC-9 evaluating etruma + zim + chemo* vs. regorafenib in 3L CRC; mature PFS and OS will be an oral presentation at ASCO 2024 (Abstract 3508)**

Etrumadenant has an ideal profile

- ✓ 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

1H: first half; 3L third-line; CNS: central nervous system; CRC: colorectal cancer; etruma: etrumadenant; PFS: progression-free survival; PK: pharmacokinetics; OS: overall survival; zim: zimberelimab

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

*+/- biologic, e.g. bevacizumab or biosimilar, will be included for all patients in whom it is not contraindicated

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Summary of Results from Phase Ib/II, Global, Open-Label, Randomized Evaluation of Atezolizumab (atezo) + Etrumadenant (etruma) + Chemotherapy (chemo) vs Chemo Alone in MORPHEUS-PDAC

Data presented at AACR 2024, based on a data cutoff of January 12, 2023.

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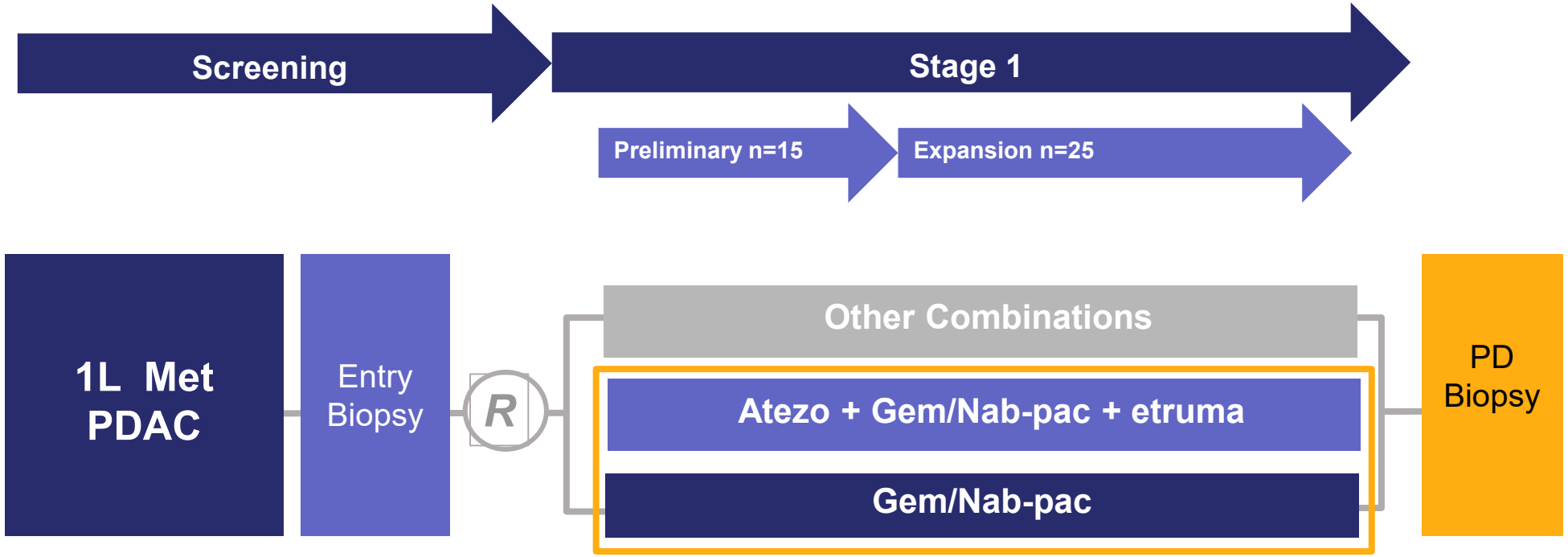
MORPHEUS-PDAC

Study Design –1L Cohort (operationalized by Roche)



* Patients with PD on 1L cohort control arm (Gem/Abraxane) will have the option to enroll to 2L cohort (if experimental treatment arms are open for enrollment and patients meet eligibility criteria and sign the appropriate ICF)

1L: first-line; atezo: atezolizumab; etruma: etrumadenant; Gem/Nab-pac: gemcitabine plus nab-paclitaxel; PD: progressive disease; PDAC: pancreatic ductal adenocarcinoma

Kim et al, AACR 2024, data cut off of Jan. 12, 2023

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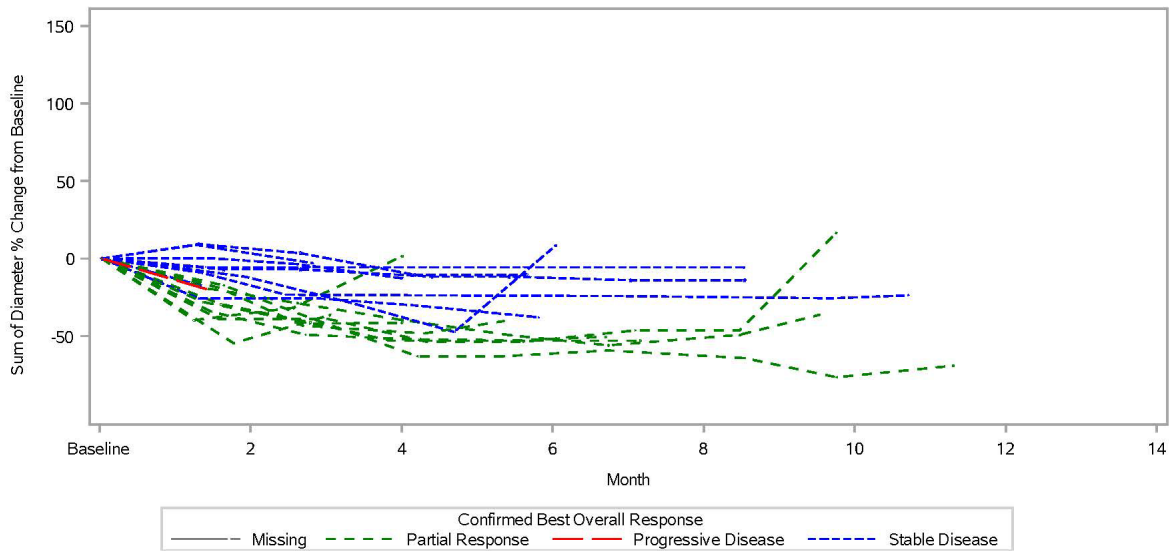
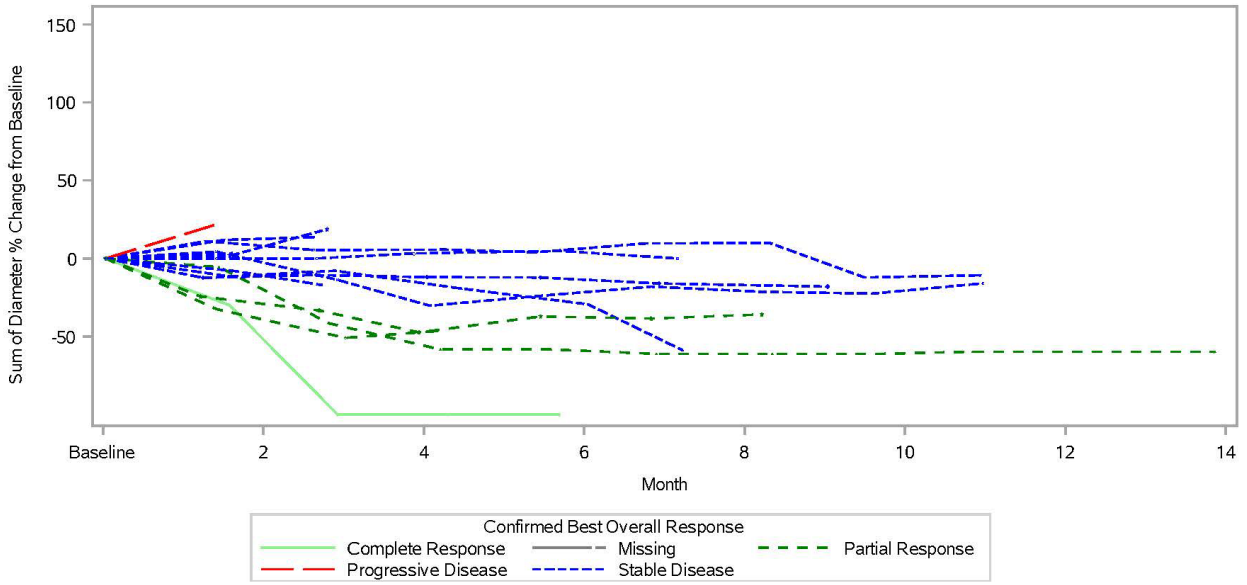
MORPHEUS-PDAC

Atezo+Gem/Nab-pac+Etruma Showed Durable Response and Stable Disease

Gem/Nab-pac



Atezo+Gem/Nab-pac+Etruma



1L: first-line; atezo: atezolizumab; etruma: etrumadenant; Gem/Nab-pac: gemcitabine plus nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma

Kim et al, AACR 2024, data cut off of Jan. 12, 2023

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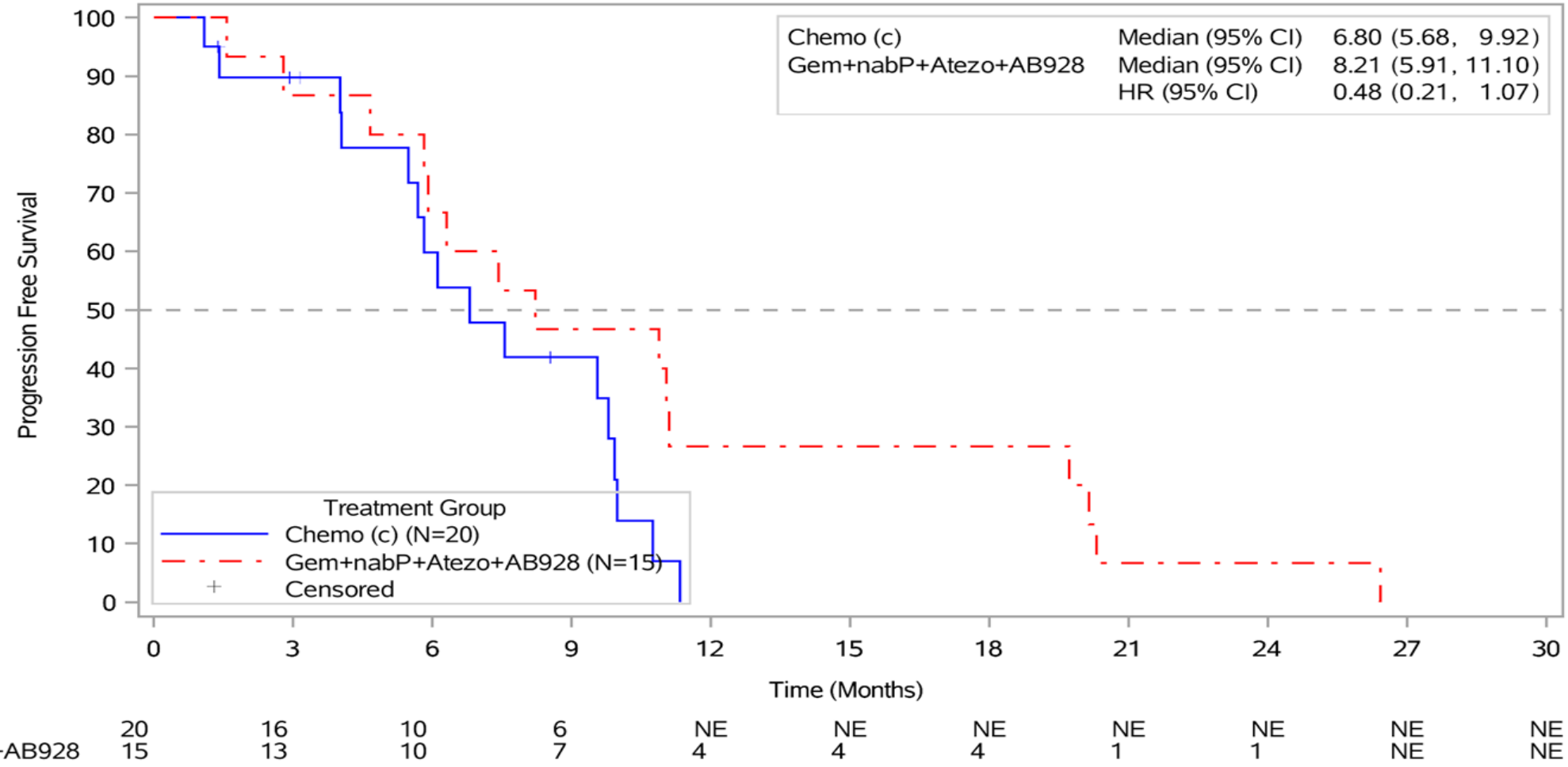
MORPHEUS-PDAC

Progression-Free Survival by Investigator per RECIST v1.1



atezo: atezolizumab; etruma/AB928: etrumadenant; Gem/Nab-pac: gemcitabine plus nab-paclitaxel; HR: hazard ratio; NE: not evaluable; PDAC: pancreatic ductal adenocarcinoma

Kim et al, AACR 2024, data cut off of Jan. 12, 2023

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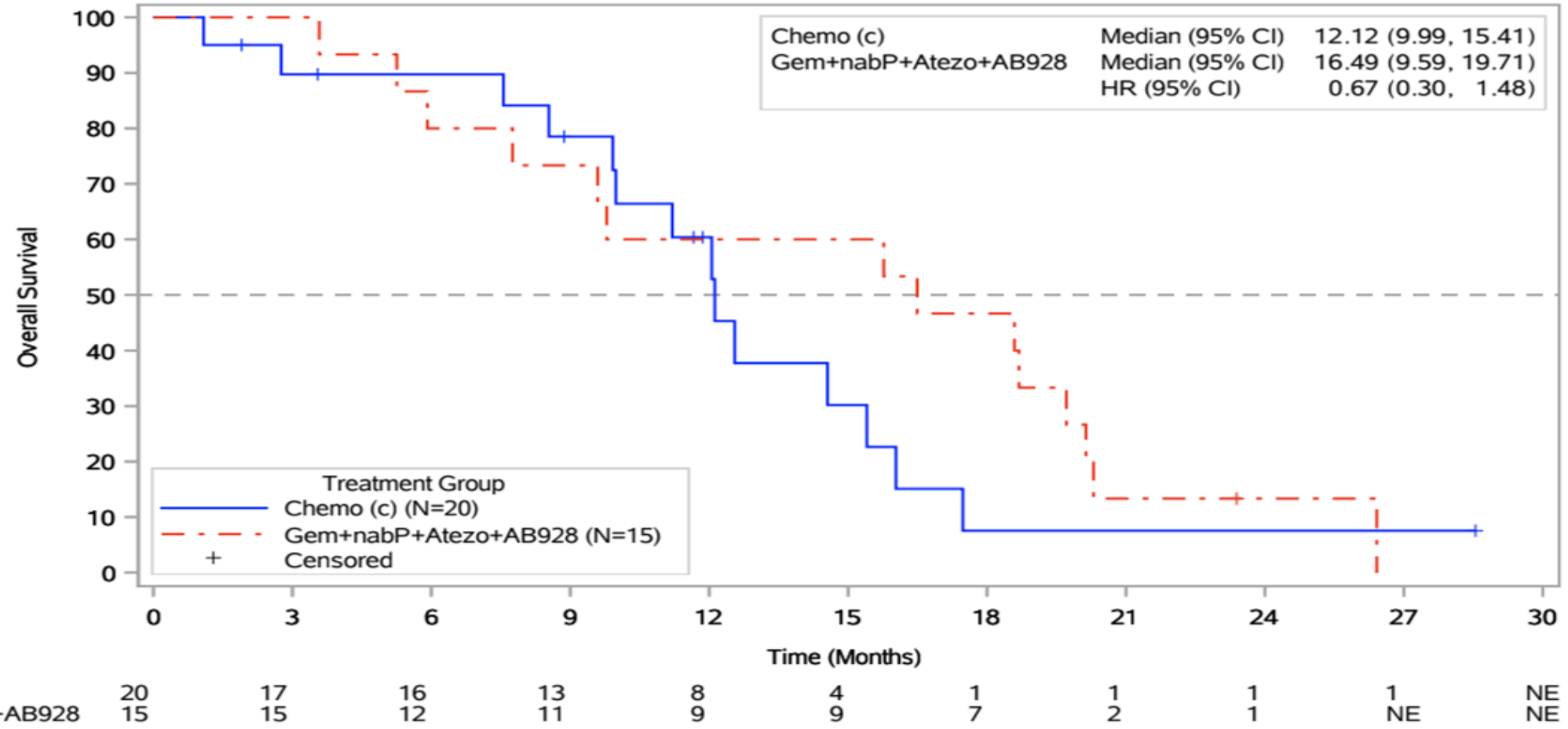
MORPHEUS-PDAC

Overall Survival by Investigator per RECIST v1.1



atezo: atezolizumab; etruma/AB928: etrumadenant; Gem/Nab-pac: gemcitabine plus nab-paclitaxel; HR: hazard ratio; NE: not evaluable; PDAC: pancreatic ductal adenocarcinoma

Kim et al, AACR 2024, data cut off of Jan. 12, 2023

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Randomized Phase 2 Study to Evaluate Etruma Plus Zim-Based Combinations in mCRC

- Randomized Phase 2 study evaluating etruma + zim + chemo combinations vs. SOC in 2L & 3L mCRC
- **Mature PFS & OS data for Cohort B (3L; n=105) to be presented in oral presentation at ASCO 2024 (Abstract 3508)**
  - Cohort A (2L) results are still immature



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

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

NCT #: NCT04660812

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Quemliclustat in Pancreatic Cancer

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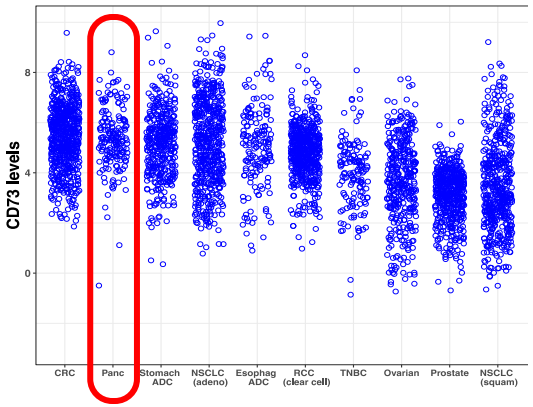
Quemliclustat (quemli): A Unique, Highly Potent and Selective Small Molecule CD73 Inhibitor with Several Key Advantages

QUEMLICLUSTAT

- Highly potent small 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

Pancreatic cancer exhibits very high expression levels of CD73



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

Potential advantages over CD73 antibodies[1]

- ✓ 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.
1) Arcus Biosciences data on file; based on preclinical studies

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Final Overall Survival Analysis for Quemliclustat and Zimberelimab in Pancreatic Cancer (ARC-8)

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

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Highlights from the ARC-8, a Phase 1b Study in 1L PDAC

Median overall survival (mOS) was 15.7 months for patients treated with a quemliclustat-based regimen, which exceeds the historical benchmark data for chemotherapy alone (8.5 – 11.7 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[1] in a post-hoc analysis

The quemli-based regimen was well-tolerated, with no new safety signals or significant added toxicity compared to chemotherapy alone[1]

Phase 3 study initiation expected by early 2025

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 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

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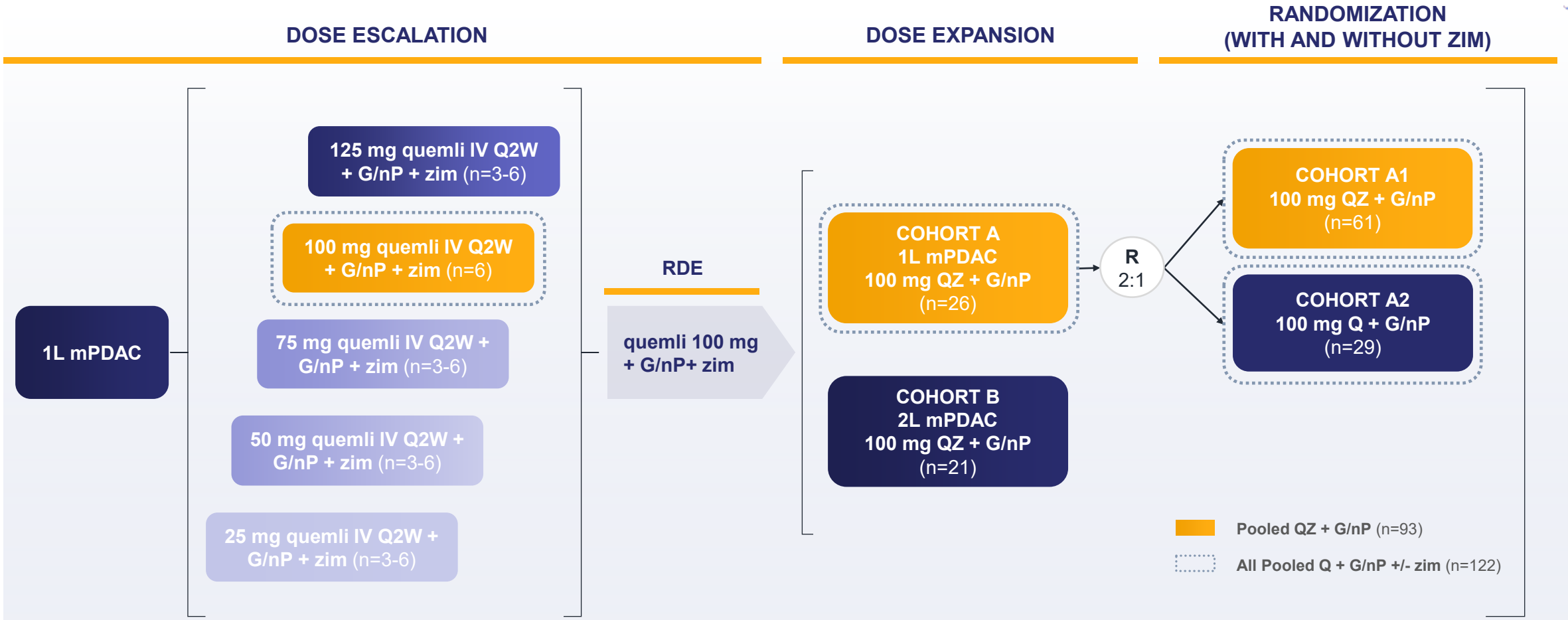
ARC-8 Study Design Included Dose Escalation, Expansion and Randomized Portions



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: intravenously; 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

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	Participants Dosed			>18m OS f/u?	Population
Dose escalation	25 mg	Q + Z + G/nP (quad)	4			Yes	1L mPDAC
Dose escalation	50 mg	Q + Z + G/nP (quad)	6			Yes	1L mPDAC
Dose escalation	75 mg	Q + Z + G/nP (quad)	3			Yes	1L mPDAC
Dose escalation	**100 mg**	**Q + Z + G/nP (quad)**	6	**93** Pooled Q100 quad	**122** Pooled Q100 All	Yes	1L mPDAC
Cohort A	**100 mg**	**Q + Z + G/nP (quad)**	26*			Yes (except for 3)*	1L mPDAC
Cohort A1 (randomized)	**100 mg**	**Q + Z + G/nP (quad)**	**61**			Yes	1L mPDAC
Cohort A2 (randomized)	**100 mg**	**Q + G/nP (triplet)**	**29**			Yes	1L mPDAC
Dose escalation	125 mg	Q + Z + G/nP (quad)	3			Yes	1L mPDAC

1L: first-line; f/u: follow up; G/nP: gemcitabine/nab-paclitaxel; mPDAC: metastatic pancreatic ductal adenocarcinoma; OS: overall survival; Q/quemli: quemliclustat; Z/zim: zimberelimab

3 additional patients enrolled as contemporaneous control for Cohort C

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

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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%)

% (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)
Race	White	83 (24)	74 (45)	74 (69)	76 (93)
	Asian	6.9 (2)	8.2 (5)	8.6 (8)	8.2 (10)
	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		**69** (20)	**69** (42)	**65** (60)	**66** (80)
ECOG Missing		-	1.6 (1)	1.1 (1)	0.8 (1)
Liver Metastasis at Baseline[1]		**58.6** (17)	**68.9** (42)	**66.7** (62)	**64.8** (79)

ECOG: Eastern Cooperative Oncology Group; G/nP: gemcitabine/nab-paclitaxel; IQR: interquartile range; NR: not reported; Q: quemliclustat; Z: zimberelimab
1. Derived from baseline tumor assessment data
Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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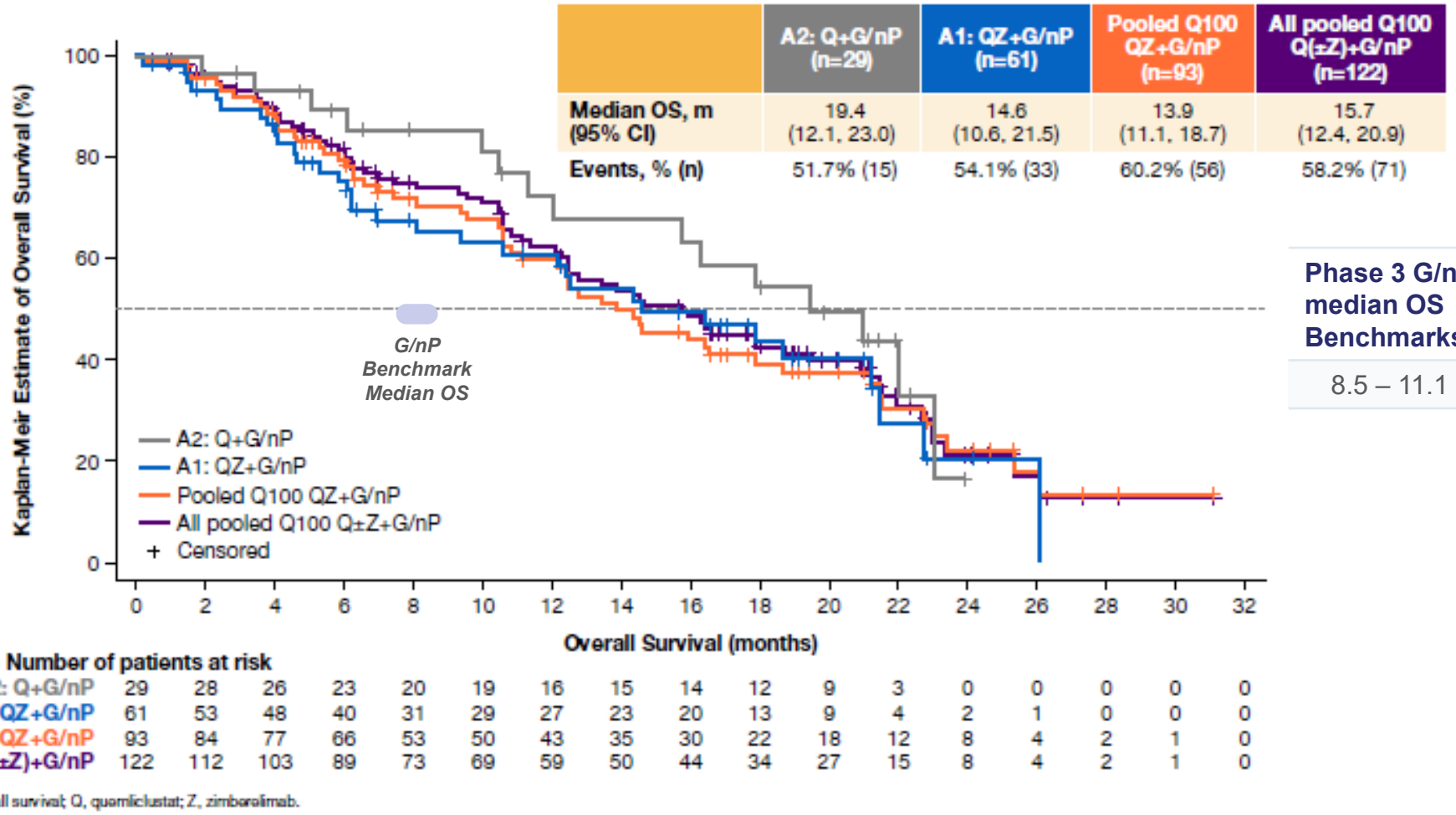
With 21-month Median Follow-up, OS Results Exceed Ph3 Benchmarks for G/nP



Phase 3 G/nP median OS Benchmarks[1,2]

8.5 – 11.1 months

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.

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

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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 *with* liver mets, median OS still exceeded historical benchmarks AND meaningfully outperformed the OS for patients with liver mets treated with G/nP 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. https://doi.org/10.1016/S0140-6736(23)01366-1.
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 Benchmark[4] (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
Serious TEAE	51.7	53.8	53.3	52
Serious TRAE	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[1]	58.6	51.6	53.3	54
AE leading to dose delay	75.9	75.3	75.4	NR
AE leading to discon[2]	24.1	22.6	23.0	23
IRR[2]	10.3	6.5	7.4	N/A
Immune related AE[3]	6.9	10.8	9.8	N/A

AE: adverse event; G/nP: gemcitabine/nab-paclitaxel; IRR: infusion-related reaction; NA: not applicable; NR: not reported; TEAE: treatment-emergent adverse event; TRAE: treatment-related adverse 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

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

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ARCUS BIOSCIENCES

Arcus & Medidata AI 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

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

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

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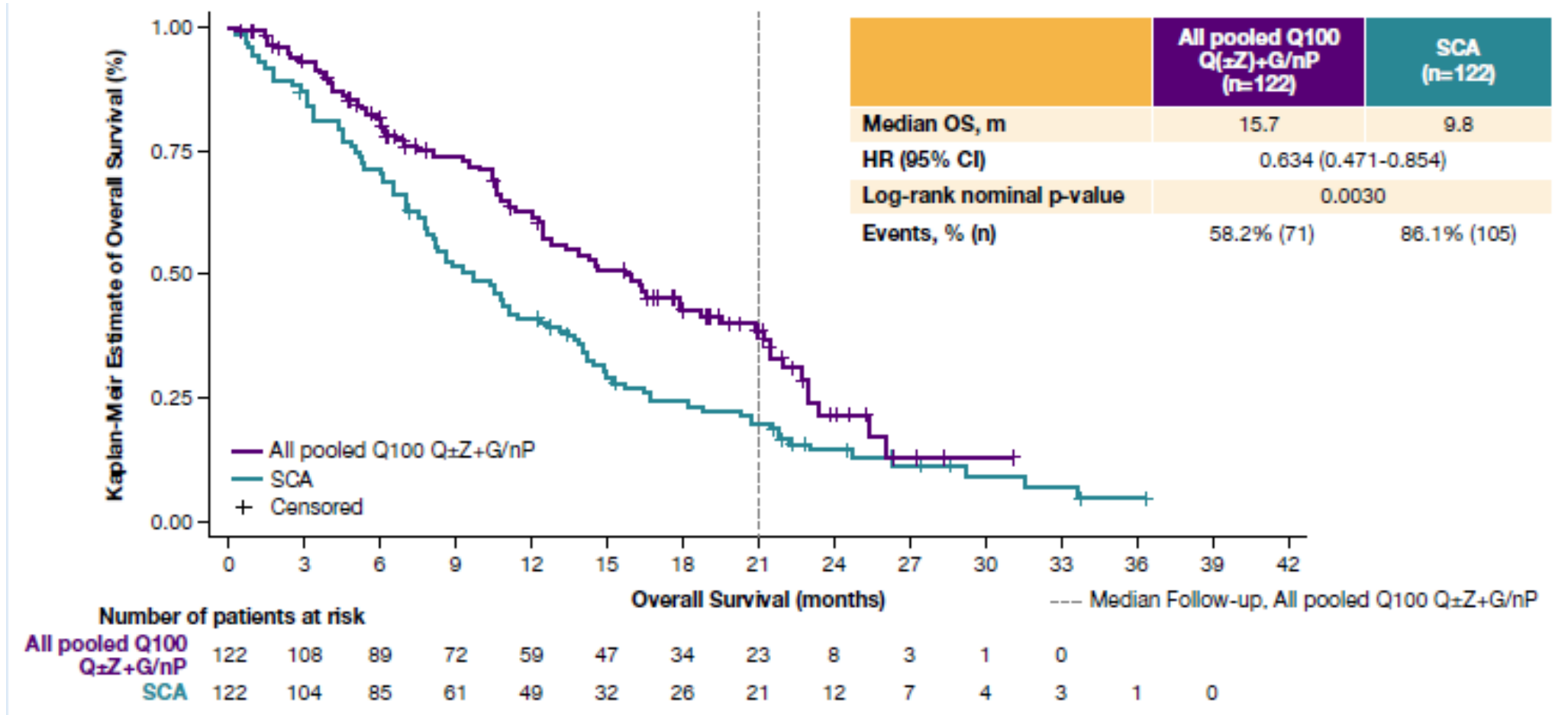
Quemli-based Regimen Reduced Risk of Death by 37% and increased mOS by 5.9 months Compared to SCA



	All pooled Q100 Q(±Z)+G/nP (n=122)	SCA (n=122)
Median OS, m	15.7	9.8
HR (95% CI)	0.634 (0.471-0.854)	
Log-rank nominal p-value	0.0030	
Events, % (n)	58.2% (71)	86.1% (105)

G/nP, gemcitabine/nab-paclitaxel; OS, overall survival; Q, quemliclustat; SCA, synthetic control arm; Z, zimberelimab.

CI: confidence interval; mOS: median overall survival; quemli: quemliclustat; SCA: Synthetic Control Arm
Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, data cut off of June 19, 2023

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AXL Program

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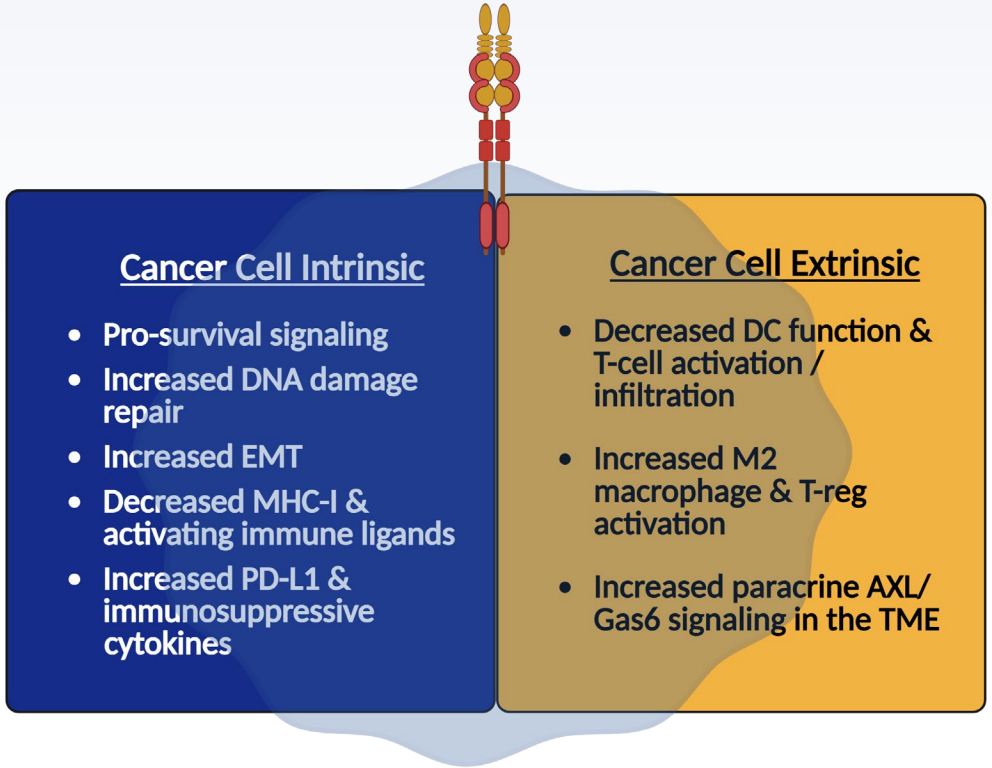
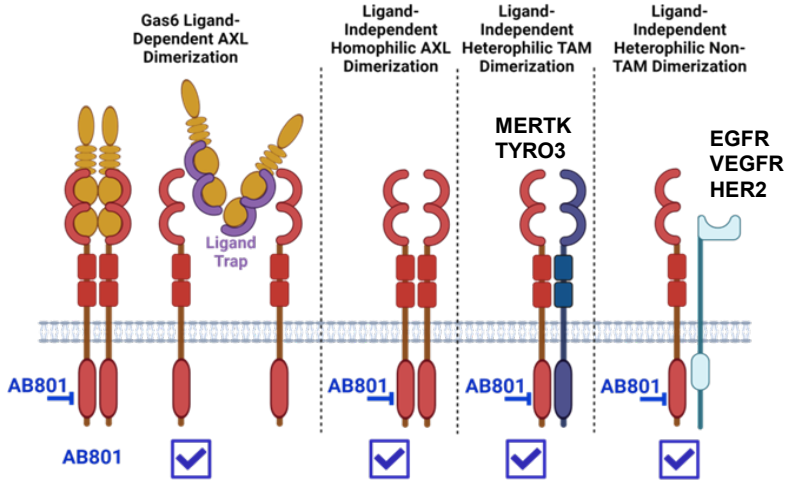
AXL Signaling is a Common Mechanism of Resistance to Chemotherapy and Immunotherapy in Tumors

THERAPEUTIC HYPOTHESIS:

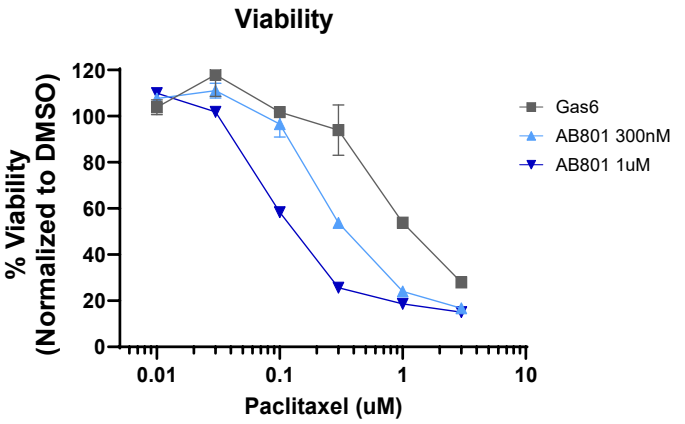
AXL inhibition will overcome multiple mechanisms of drug-resistance



AXL signals via Ligand-dependent and Ligand-independent mechanisms



AB801 sensitizes cancer cells to chemotherapy



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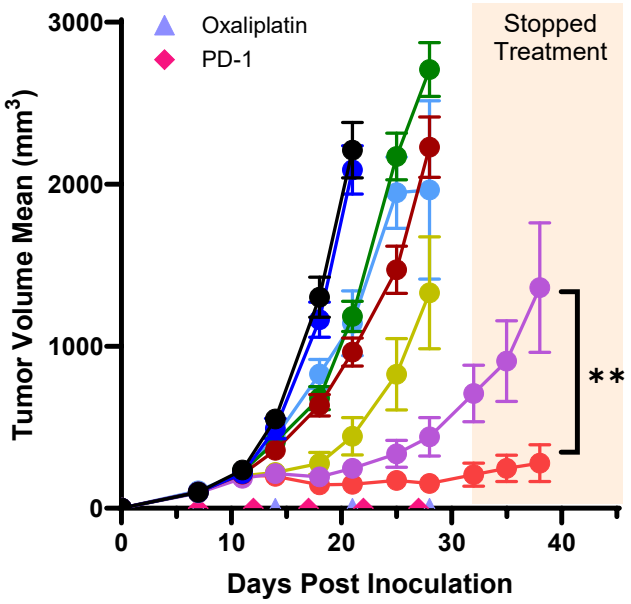
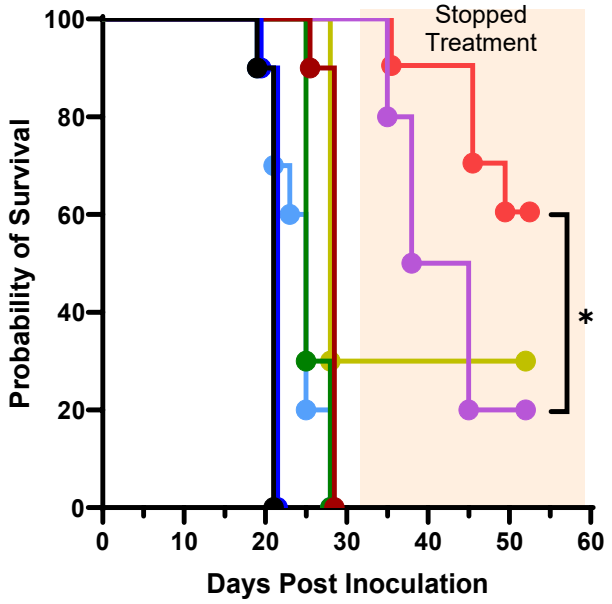
AB801 is a Potent, Selective, and Efficacious AXL Inhibitor

AB801 is a highly potent and selective AXL inhibitor

	Assay	AB801
BIOCHEMICAL	AXL K_i	**0.024 nM**
BIOCHEMICAL	Fold selectivity over hMERTK/ hTYRO3 (enzyme K_i over AXL K_i)	**860x / 1400x**
BIOCHEMICAL	Kinome Selectivity against 403 kinases at 100x IC_{50} for AXL	**Only one kinase with less that 200x fold selectivity**
CELLULAR	pAXL ELISA IC_{50} (serum-free media)	**17 nM**
CELLULAR	pAXL ELISA IC_{50} (100% serum)	**68 nM**

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





Vehicle
AB801
OXA
PD-1
OXA + PD-1
AB801 + PD-1
AB801 + OXA
AB801 + OXA + PD-1

*Syngeneic mouse MC38 tumor model; data on file at Arcus.
AB801 is an investigational molecule and its safety and efficacy have not been established.

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AB801 is Potentially 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 completed:
  - 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; **expansion cohort planned in 2L+ NSCLC**

2L: second-line; NSCLC: non-small cell lung cancer

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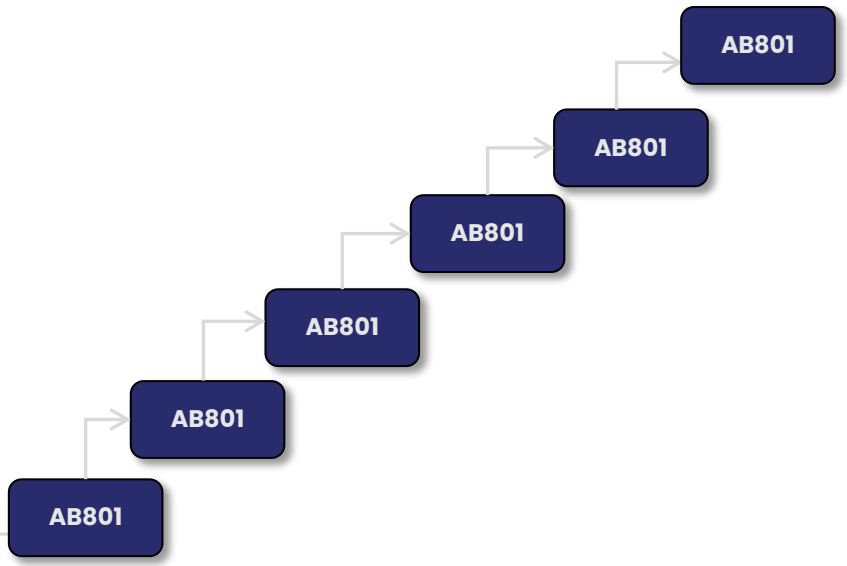
ARC-27 Phase 1 Dose-Finding Study in Patients with Advanced Solid Tumors

PRE-SCREENING / SCREENING | DOSE ESCALATION STAGE | EXPANSION STAGE

Advanced Solid Tumors

NSCLC, CRC, Breast, RCC, Ovarian, HNSCC, Bladder



Cohort 1: NSCLC adenocarcinoma

AB801 + docetaxel

Safety run-in n=6

n=40
Prior α-PD-(L)-1 and chemo

DOSE ESCALATION

PRIMARY ENDPOINT
- Safety / DLT

SECONDARY ENDPOINT
- PK
- ORR

EXPLORATORY ENDPOINTS
- Biomarkers / PD
- PFS, OS

DOSE EXPANSION

PRIMARY ENDPOINT
- Safety

SECONDARY ENDPOINT
- PK
- ORR

EXPLORATORY ENDPOINTS
- Biomarkers / PD
- PFS, OS

- Evaluate AB801 single agent tolerability and activity to inform dose in expansion stage
- Expansion cohort: all comers NSCLC adenocarcinoma designed to generate preliminary safety, PK, and activity signal (ORR), to support randomized POC Phase 2 study

CRC: colorectal cancer; DLT: dose-limiting toxicity; mg: milligram; NSCLC: non-small cell lung cancer; ORR: objective response rate; PD: pharmacodymamics; PFS: progression-free survival; PK: pharmacokinetics; OS: overall survival; RCC: renal cell carcinoma

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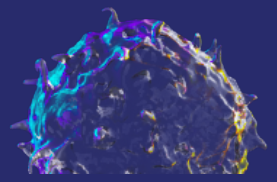
APPENDIX



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Diverse Pipeline with Multiple Molecules in Late-Stage Development

MOLECULE	INDICATION	STUDY	PHASE 1	PHASE 1B	PHASE 2	PHASE 3
DOMVANALIMAB (DOM) (Fc-silent anti-TIGIT) **ZIMBERELIMAB** (ZIM) (ANTI-PD1)	Perioperative lung cancer (in planning)	STAR-131	dom + zim + chemo → dom + zim			
	Stage III, unresectable, PD-L1≥1% NSCLC	PACIFIC-8	dom + durvalumab vs durvalumab			
	1L NSCLC, PD-L1 All Comers	STAR-121	dom + zim + chemo vs pembro + chemo vs. zim + chemo			
	1L Upper GI Malignancies	STAR-221	dom + zim + chemo vs nivo + chemo			
	1L / 2L Upper GI Malignancies	EDGE-Gastric	dom ± zim ± quemli +/- FOLFOX			
	1L / 2L NSCLC	VELOCITY-Lung	dom ± zim ± sacituzumab govitecan			
	1L / 2L NSCLC, All Comers	EDGE-Lung	dom +/- zim ± quemli ± chemo			
	1L NSCLC, PD-L1 ≥50%	ARC-7	dom + zim ± etruma vs zim			
QUEMLICLUSTAT (QUEMLI) (CD73)	1L Pancreatic cancer (in planning)	PRISM-1	quemli + gem/nab-pac vs gem/nab-pac			
	1L, 2L Pancreatic Cancer	ARC-8	quemli + zim + gem/nab-pac vs quemli + gem/nab-pac			
	1L Lung cancer	EDGE-Lung	dom + zim ± quemli ± chemo			
	1L Gastrointestinal cancer	EDGE-Gastric	dom ± zim ± quemli			
ETRUMADENANT (ETRUMA) (A2a/A2b)	2L / 3L+ mCRC	ARC-9	etruma + zim + FOLFOX/bev vs FOLFOX/bev			
			etruma + zim + FOLFOX/bev vs regorafenib			
	1L / 2L Lung Cancer	VELOCITY-Lung	dom ± zim ± etruma ± sacituzumab govitecan			
	1L, PD-L1 ≥50% NSCLC	ARC-7	dom + zim ± etruma vs zim			
CASDATIFAN (CAS) (HIF-2a)	ccRCC (in planning)	undisclosed	undisclosed			
	1L, ccRCC	STELLAR 009	cas + zanza ± nivo			
	2L+, inc. ccRCC	ARC-20	cas monotherapy; cas + cabo			
AB598 (CD39)	1L	ARC-25	AB598 ± zim + chemo			
AB801 (AXL)	2L+	ARC-27	AB801 + chemo			

Operationalized by Gilead Sciences Operationalized by AstraZeneca Operationalized by Exelixis

bev: bevacizumab, cas: casdatifan; gem/nab-pac: cabo: cabozantinib; gemcitabine/nab-paclitaxel, inc: including; nivo: nivolumab, pembro: pembrolizumab
CRC: colorectal cancer, ccRCC: clear cell renal cell carcinoma, GI: gastrointestinal cancers (gastric, gastroesophageal junction, and esophageal adenocarcinoma), NSCLC: non-small cell lung cancer, PDAC: pancreatic ductal adenocarcinoma

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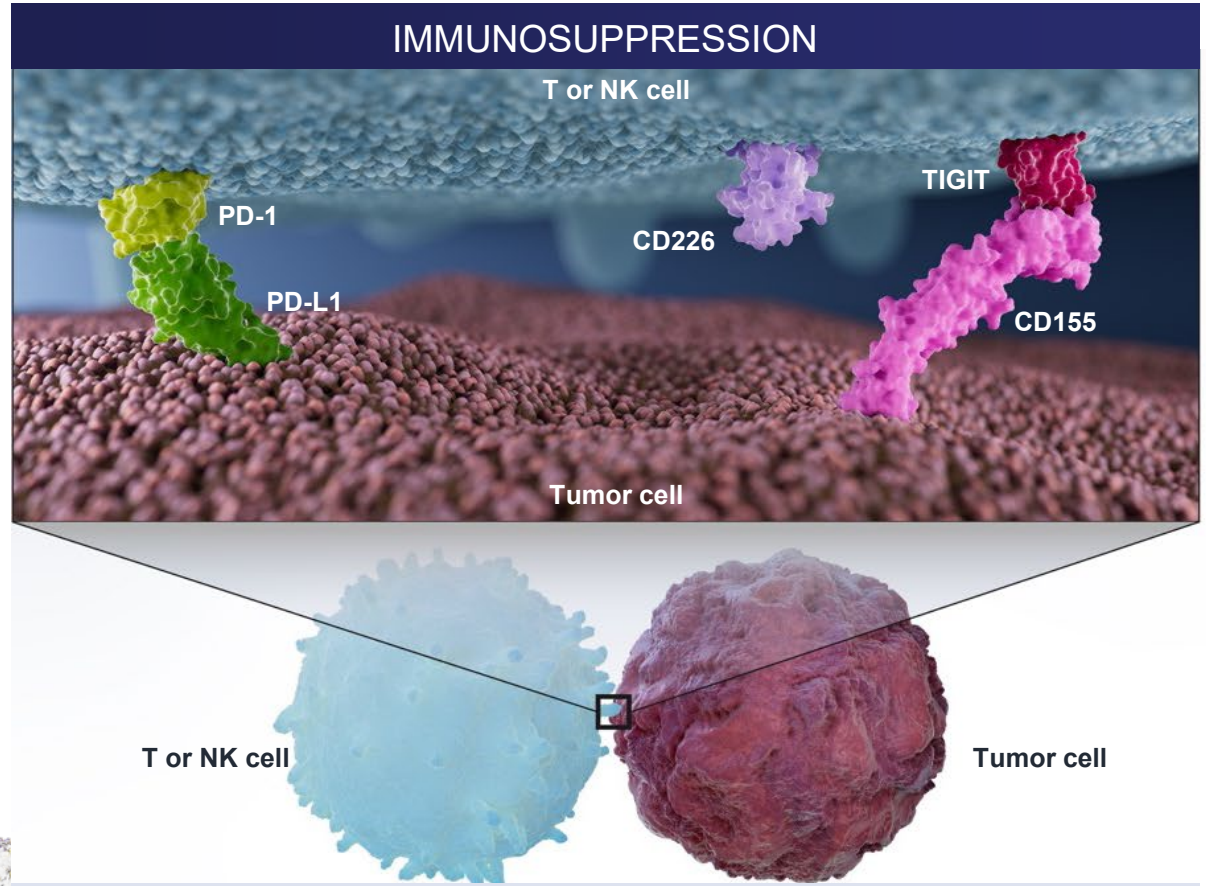
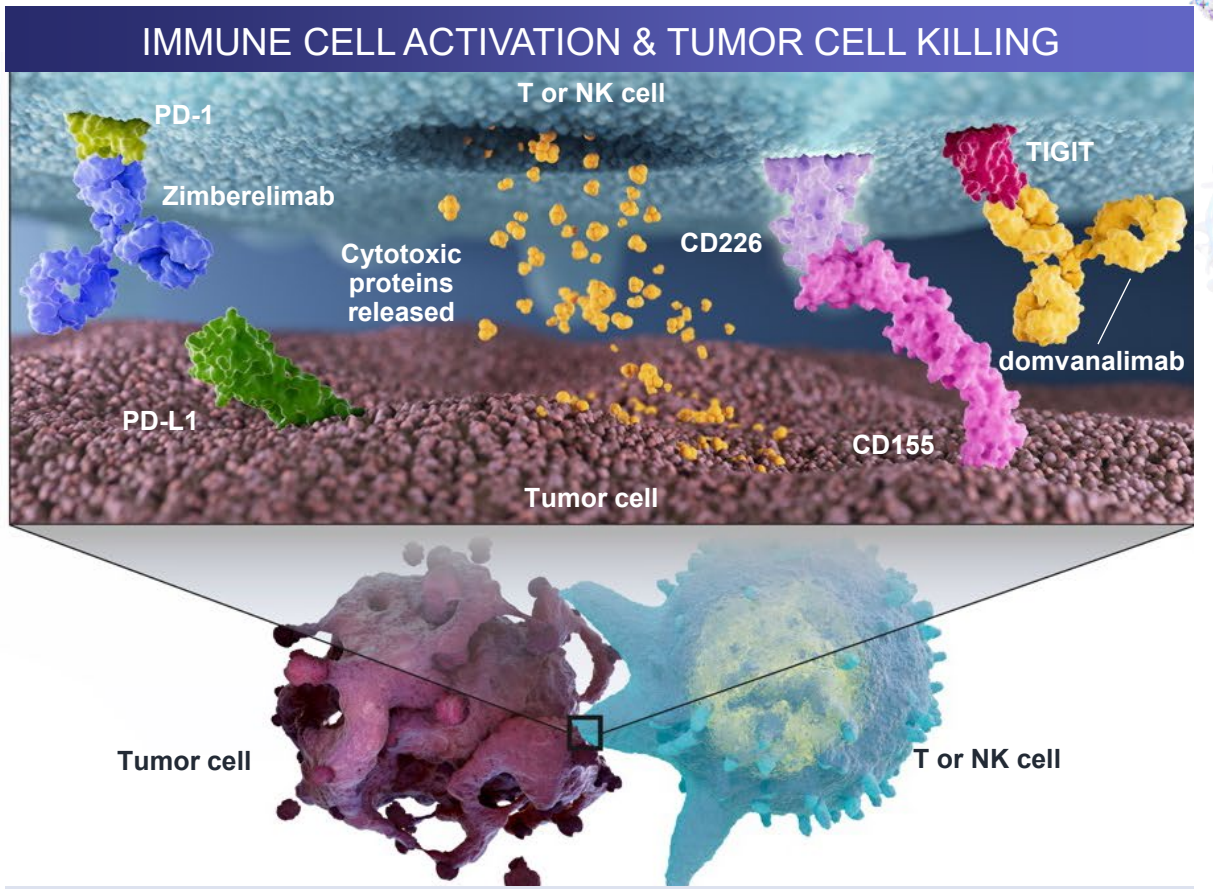
Domvanalimab (dom): Most Clinically Advanced Fc-Silent TIGIT Antibody in Clinical Development





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

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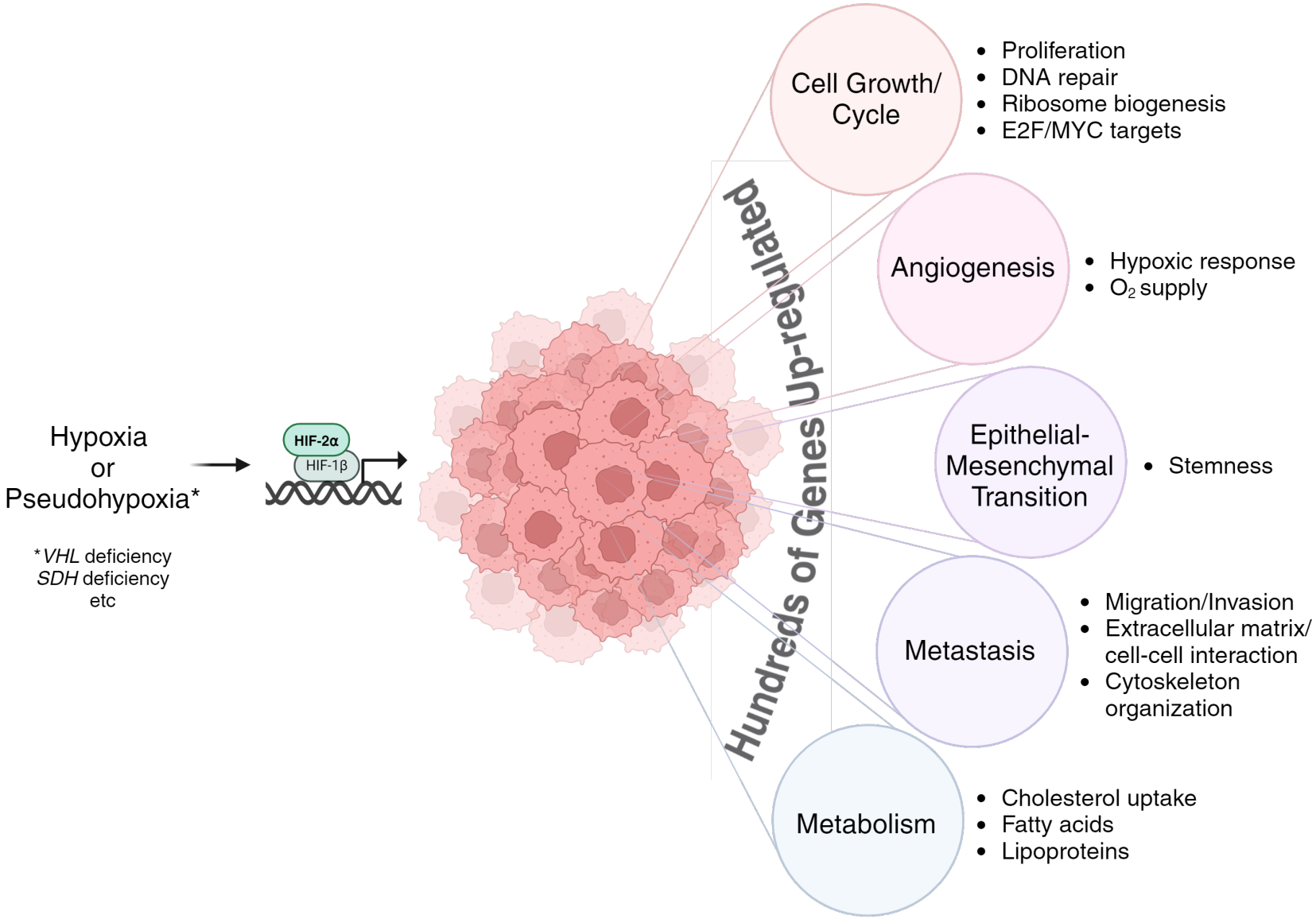
HIF-2α Regulates Multiple Facets of Cancer Cell Biology



SDH: Succinate dehydrogenase; VHL: Von Hippel-Lindau

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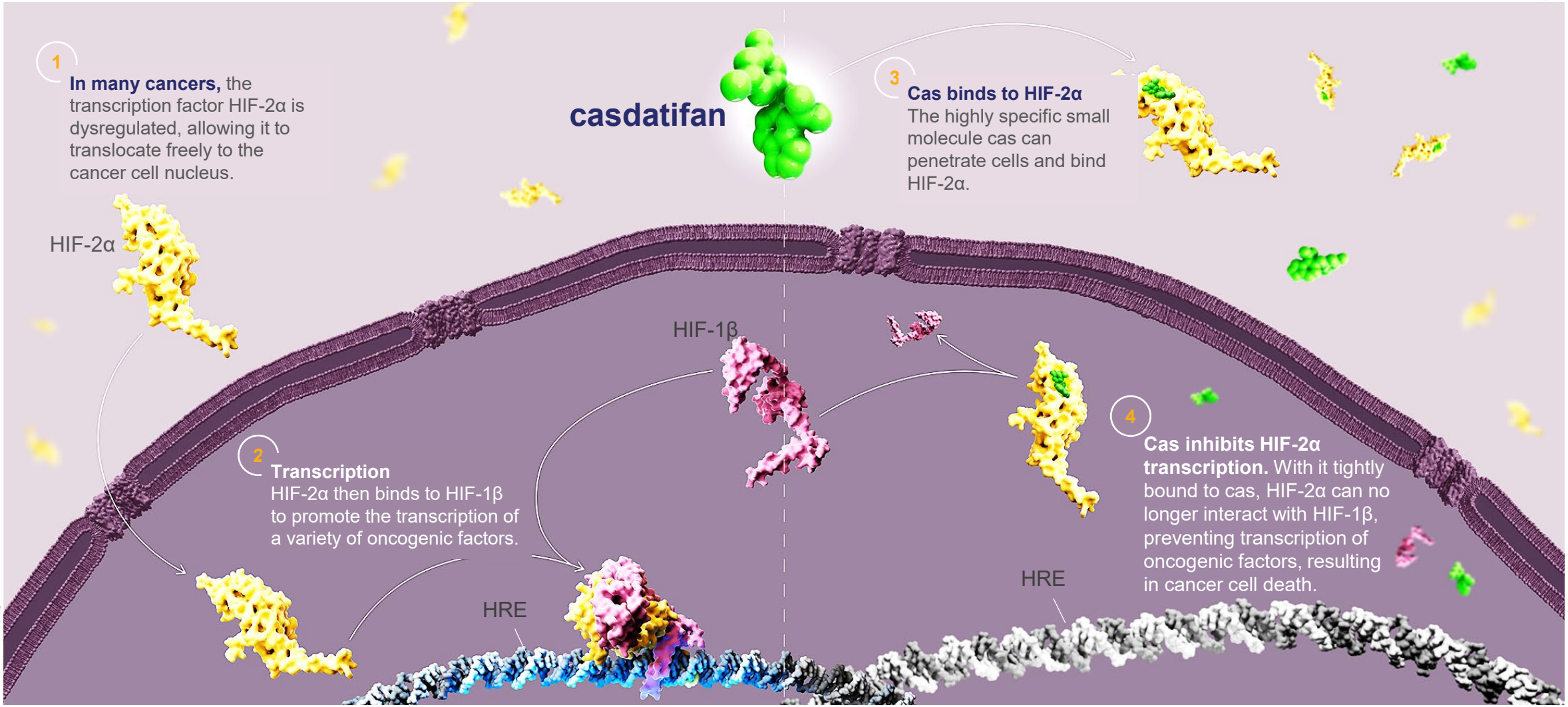
Casdatifan (HIF-2a inhibitor) in the Cancer Cell Nucleus



Casdatifan is an investigational molecule and its safety and efficacy have not been established.
Cas: casdatifan; HRE: Hypoxia Response Element.

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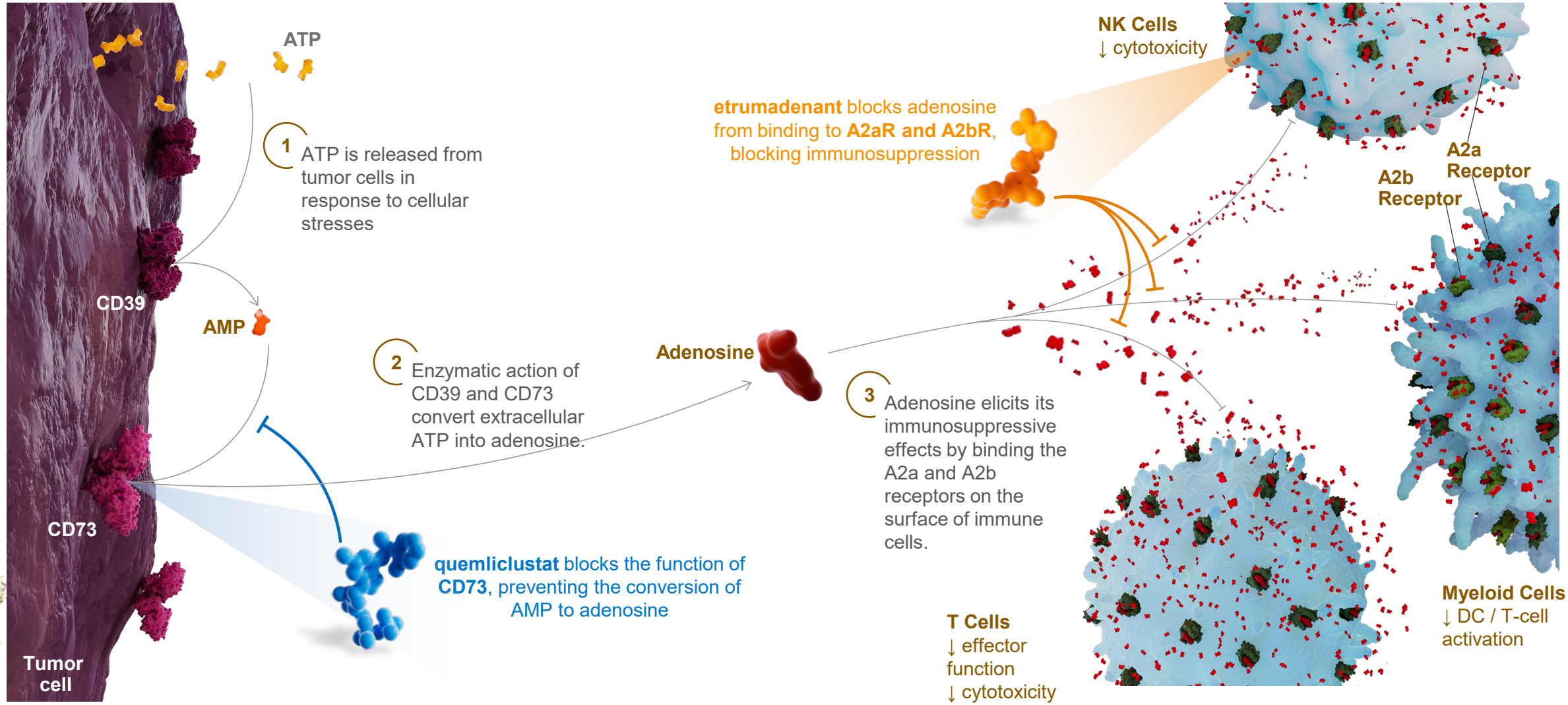
The CD73-Adenosine Axis Plays a Well-Established and Critical Role in Suppression of the Immune Response



Arcus and Gilead have not received regulatory approval from any regulatory authority for etrumadenant and quemliclustat and their uses are investigational only.

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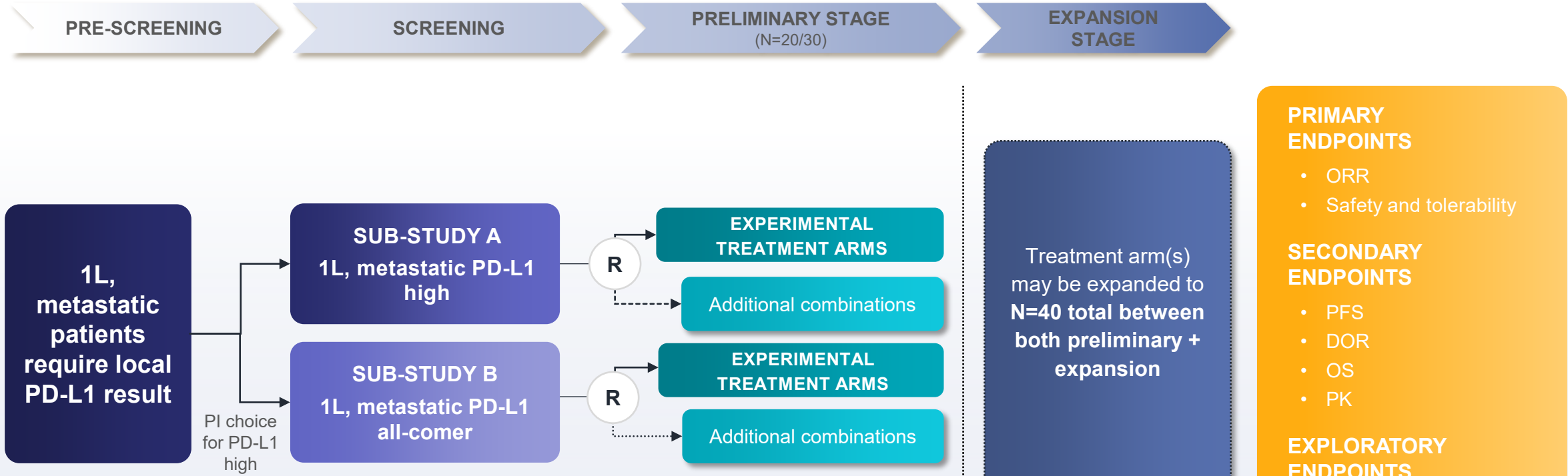
Platform Design to Rapidly Evaluate Novel Combinations for NSCLC, Including Quemli and Dom-based Regimens



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, pharmacodynamics; PD-L1,ORR programmed death-ligand 1; PK, pharmacokinetics; PI, principal investigator; R, randomized

NCT #: NCT05676931

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COMBINING TO CURE®