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

INVESTOR PRESENTATION

December 12, 2025

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Arcus is Well-Capitalized to Advance its Phase 3 Programs and Emerging I&I Portfolio

CASDATIFAN: COMMERCIALLY-VALIDATED MECHANISM AND RIGHTS RETAINED TO MOST REGIONS(1)

PEAK-1

Phase 3 in IO-experienced ccRCC

eVOLVE RCC02

Phase 1b/3 in 1L ccRCC

ARC-20

Phase 1b in early- and late-line ccRCC to support future studies

QUEMLICLUSTAT: PHASE 3 FULLY ENROLLED

PRISM-1 **1L Pancreatic**

EMERGING I&I PORTFOLIO

Five active programs, with two expected to enter clinic over next ~12 months

- **2026:** MRGPRX2
- **Late 2026 / Early 2027:** TNF

APPROX. $1 BILLION IN CASH*

Funded until at least 2H:28**

(1) Arcus owns WW rights, excluding Japan and certain other Asian territories (excluding China)

1L: first-line; 2L: second-line; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; FIH: first in human; I&I: inflammation and autoimmune; IO: immunotherapy; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; SM: small molecule; quemli: quemliclustat; R&D: research & development

- * Cash and investments balance of $841 million as of September 30, 2025, adjusted to give effect to $270 million net proceeds from the Company's November 2025 financing
- ** runway estimate based on cash, cash equivalents, marketable securities, and current planned operations

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December 2025 Updates: With the STAR-221 Discontinuation, Casdatifan and Our I&I Portfolio Are Our Top Priorities

IMPRESSIVE CASDATIFAN DATA PRESENTED AT INVESTOR EVENT

- **31% cORR and 12.2 months PFS** in a pooled analysis of all four monotherapy cohorts in late-line ccRCC (n=121)
- **35% cORR and PFS was not reached with 12+ months median follow-up** in the 100mg QD tablet cohort (going forward dose and formulation)
- In biomarker analysis, the data demonstrated that **greater EPO suppression is associated with better clinical activity of cas**

TAIHO OPT IN TO CASDATIFAN

- **Taiho exercised their option to casdatifan** for Japan and Asia (ex-China)
- **Further validates the casdatifan data and brings in additional capital** (via upfront payment + milestones) and support for cas development

DISCLOSURE OF EMERGING I&I PROGRAMS

- Arcus has had a 2+ year discovery effort focused on I&I which has now yielded **5 active programs**
- The most advanced programs are small molecules against MRGPRX2 and TNF; **initiation of first-in-human studies for MRGPRX2 and TNF expected in 2026 and late 2026 / early 2027, respectively**

STAR-221 TO BE DISCONTINUED

- STAR-221, a Phase 3 study evaluating dom + zim + chemo vs. SOC in 1L Upper GI cancers, was discontinued due to futility
- The other ongoing domvanalimab studies are now under evaluation

1L: first-line; cabo: cabozantinib; cas: casdatifan, ccRCC: clear cell renal cell carcinoma; chemo: chemotherapy; cORR: confirmed overall response rate; dom: domvanalimab; EPO: erythropoietin, GI: gastrointestinal; IA: interim analysis; I&I: inflammation and autoimmune; IDMC: Independent Data Monitoring Committee; ORR: overall response rate; OS: overall survival; PFS: progression-free survival; SOC: standard of care; zim: zimberelimab

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Multiple Upcoming Potential Catalysts

TIMING	STUDY	PRODUCT	EVENT
Early 2026	ARC-20	Casdatifan	• Additional analysis of the cas monotherapy cohorts in late-line ccRCC, including updated PFS for the 100mg QD cohort
Mid-2026	ARC-20	Casdatifan	• ORR and PFS data from the cas + cabo cohort in IO-experienced ccRCC
2026	Phase 1	MRGPRX2	• Initiation of first-in-human study
2H 2026	ARC-20 eVOLVE RCC02	Casdatifan	• Data from one or more of the early-line cohorts of ARC-20 and go / no go decision on the Phase 3 portion of eVOLVE-RCC02
Late 2026	Phase 3	Casdatifan	• Target initiation of first Phase 3 study for cas in an early-line setting of ccRCC
Late 2026 / Early 2027	Phase 1	TNF	• Initiation of first-in-human study
2027	PRISM-1	Quemliclustat	• Phase 3 data in pancreatic cancer

1L: first-line; 2L: second-line; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; ORR: overall response rate; PFS: progression-free survival; QD: once daily

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Casdatifan (HIF-2α) in ccRCC

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Casdatifan is Poised to Become the HIF-2α Treatment of Choice

A BEST-IN-CLASS CLINICAL PROFILE

- Based on data from 121 patients, **cas has shown higher ORR, ~50% lower rate of primary progressive disease, and >2x longer median PFS** relative to published studies for belzutifan**
- Cas + cabo has shown a 46% ORR vs 31% for belzutifan + cabo**
- Similar rates of anemia and hypoxia compared to marketed dose of belzutifan**

BROAD AND DIFFERENTIATED DEVELOPMENT PLAN

- Global Phase 3 PEAK-1 study currently enrolling and evaluating cas + cabo in IO-experienced ccRCC represents a **"fast-to-market" opportunity**
- **Evaluating multiple early-line strategies** based on eVOLVE and encouraging, emerging data from "early-line" cohorts of ARC-20 (cas + anti-PD-1 in 1L ccRCC, cas mono in IO-experienced ccRCC, cas mono in 1L favorable risk ccRCC)

STRATEGIC OPTIONALITY AND EXTERNAL VALIDATION

- **Casdatifan rights are wholly-owned by Arcus in the major markets (ex-Japan*),** enabling significant strategic optionality
- Taiho's recent opt-in further validates casdatifan's best-in-class profile and market potential

*and certain other Asian territories, excluding China

** Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

1L: first-line; cas: casdatifan; cabo: cabozantinib; ccRCC: clear cell renal cell carcinoma; h: hours; IO: immunotherapy; ORR: overall response rate

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With a Differentiated Efficacy Profile and Development Plan, Cas is Well Positioned in a Two-Horse Race

EFFICACY & SAFETY DATA BASED ON ARC-20 (CAS) AND LITESPARK-005 (BELZ), MONOTHERAPY DATA IS FOR PATIENTS THAT HAVE RECEIVED BOTH PRIOR ANTI-PD-1 AND TKI

	casdatifan 100mg QD	belzutifan[1]
		
Primary PD rate for monotherapy	**16%**	34%
cORR for monotherapy	**35% (42% uORR*)**	22%
mPFS for monotherapy	**12+ months**	5.6 months
cORR in combination with cabo ("IO-experienced")	**46%**	31%
TKI partner in post-IO setting	**+ cabo**	+ lenva
1L / "Early-line" Strategy	**+ volru and / or other cas-regimen**	+ pembro/lenva
Pill burden	**1 (+1 for cabo)**	3 (+2 for lenva)

*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%. DCO for casdatifan data: August 15, 2025

1. Clinical data from LITESPARK-005. Sources: Albiges L. et al. Abstract LBA88, ESMO 2023; Choueiri et al. 2024.

Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

1L: first-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear-cell renal cell carcinoma; cORR: confirmed overall response rate; DCO: data cutoff; IO: immunotherapy; lenva: lenvatinib; mPFS: median progression free survival; m: months; pembro: pembrolizumab; QD: once daily; TKI: tyrosine kinase inhibitor; uORR: unconfirmed overall response rate; volru: volrustomig

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Strategy to Advance Casdatifan into 1L ccRCC

eVOLVE-RCC02 Ph 1b/3 Study

- Evaluating casdatifan + volrustomig, AstraZeneca's anti-PD-1/CTLA-4 bi-specific, in 1L ccRCC; sponsored and operationalized by AstraZeneca
- Following rapid recruitment into the study, new enrollment was paused following observations of potentially immune-mediated AEs
  - The AEs were Grade 3 or lower and no Grade 4 or 5 AEs have been observed to date
- Patients already enrolled will continue to be treated; longer-term follow-up data, along with any discussions with health authorities, will inform next steps for the study

1L Strategies for Casdatifan

- eVOLVE-RCC-002 and encouraging data from the new cohorts added to ARC-20 will inform future front-line development strategies for cas
- Data from these cohorts will inform other cas-containing regimens, including in combination with SOC, that could be advanced into Phase 3
- Data from at least one of these cohorts will be presented in 2H:26

Goal is to start one Phase 3 trial in an early-line or 1L ccRCC setting in late 2026

1L: first-line; AE: adverse event; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; PD-1: programmed cell death protein 1; SOC: standard of care

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Our Initial Focus Is on the IO-naive and Post-IO Settings, Both Multi-Billion Dollar Market Opportunities

	CURRENT SOC	POTENTIAL FUTURE TREATMENT	MARKET SIZE (MAJOR MARKETS[1,2])
1L metastatic	PD-1 + CTLA4	eVOLVE RCC02 cas + volru Other cas-containing regimens	21k patients ~$3B OPPORTUNITY
Post-IO metastatic	TKI mono	PEAK-1 cas + cabo	19k patients ~$2B OPPORTUNITY
Post-IO & Post-TKI	mTOR, TKI, HIF-2α		12k patients

3 cohorts in ARC-20 to inform future studies in early line settings:

- 1L (cas + zim)
- 1L favorable risk (cas mono)
- 1L/2L Post-IO / TKI-naive (cas mono)

1. Drug Treatable Addressable Populations (Major Markets, 2024); Decision Resources Group, Arcus analysis
2. Major Markets (US, EU5, JP) - total projected 2034

1L: first-line; 2L: second-line; B: billion; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; mTOR: mammalian target of rapamycin inhibitor; SOC: standard of care; TKI: tyrosine kinase inhibitor; volru: volrustomig; zim: zimberelimab

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Casdatifan (HIF-2α) in Late-Line ccRCC

Casdatifan Monotherapy Data Presented at October 6, 2025 Investor Event

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Data Presented at October 2025 Investor Event Support Cas's Best-in-Class Profile

- For the first time, we presented data from all four late-line monotherapy cohorts from ARC-20, including PFS – a 121-patient dataset

- Across this dataset (n=121), we have observed*:
  - ✓ **Substantially higher ORR vs. that of belzutifan**
  - ✓ **~50% lower rate of primary progressive disease**
  - ✓ **~2x longer median PFS**
  - ✓ **Faster time to response**

- Responses observed have been highly durable with the vast majority of patients still on treatment

- We believe these data substantially de-risk PEAK-1 and demonstrate the potential for casdatifan to displace TKIs in earlier line settings

*Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.
Cas: casdatifan; ORR: overall response rate; PFS: progression-free survival; TKI: tyrosine kinase inhibitor

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Patients in ARC-20 Had Greater Number of Prior Therapies Relative to the Patients in LITESPARK-005

	Dose Expansion: 2L+ ccRCC					Belzutifan[3]
Safety-Evaluable Population[1]	50mg BID (n = 33)	50mg QD (n = 31)	100mg QD (n = 32)	150mg QD (n = 31)	Pooled (n = 127)	120mg QD (n = 374)
Age, years, median (range)	62 (41–79)	65 (43–82)	60 (45–77)	65 (53–78)	62 (41–82)	66 (49–78)
Sex, Female/Male, n (%)	8 (24) / 25 (76)	10 (32) / 21 (68)	5 (16) / 27 (84)	8 (26) / 23 (74)	31 (24) / 96 (76)	77 (21) / 297 (79)
ECOG PS 0/1, n (%)	16 (48) / 17 (52)	18 (58) / 13 (42)	15 (47) / 17 (53)	13 (42) / 18 (58)	62 (49) / 65 (51)	NA
IMDC Risk Score, n (%)[2]						
Favorable	10 (30)	8 (26)	7 (22)	9 (29)	34 (27)	79 (21)
Intermediate	21 (64)	17 (55)	20 (63)	19 (61)	77 (61)	249 (67)
Poor	2 (6)	5 (16)	3 (9)	3 (10)	13 (10)	46 (12)
Prior lines of therapy, n (%)						
1	**2 (6)**	**5 (16)**	**5 (17)**	**7 (23)**	**21 (17)**	**46 (12)**
2	**14 (42)**	**9 (29)**	**7 (24)**	**6 (19)**	**39 (30)**	**157 (42)**
3	**8 (24)**	**8 (26)**	**10 (34)**	**7 (23)**	**33 (26)**	**171 (46)**
4 or more	**9 (27)**	**9 (29)**	**7(24)**	**11 (36)**	**35 (28)**	**0 (0)**

DCO date: August 15, 2025
1. The safety-evaluable population included all dose expansion enrolled patients who received any amount of study treatment.
2. One patient in the 50mg QD group had an unknown IMDC risk score and one patient in the 100mg QD group had a missing IMDC risk score.
3. IA1 for LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023; *2 or 3 prior VEGF-R TKI regimens; DCO date: August 30, 2024.; Baseline was defined as the last non-missing assessment prior to the first dosing of treatment.
Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.
2L: second-line; BID: twice daily; ccRCC: clear cell renal cell carcinoma; DCO: data cutoff; ECOG PS: Eastern Cooperative Oncology Group Performance Status; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium; QD: once daily; VEGFR-TKI: vascular endothelial growth factor receptor tyrosine kinase inhibitor

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Confirmed ORR for the "Pooled" Cohort (n=121) is >30%

Efficacy-Evaluable Population[1]	Dose Expansion: 2L+ ccRCC					Belzutifan[2]
	50mg BID (n = 31)	50mg QD (n = 28)	100mg QD (n=31)	150mg QD (n = 31)	All Pooled (n = 121)	120mg QD (n = 374)
Median Follow-Up, mos (range)	22.8 (14.4, 26.0)	19.7 (15.9, 21.3)	12.4 (6.3, 13.5)	14.4 (12.5, 15.5)	15.2 (6.3, 26.0)	18.4 (9.4–31.7)
Median Time to Response, mos	**2.7**	**4.1**	**2.6**	**2.7**	**2.8**	**3.8**
Confirmed ORR (95% CI)	**26% (12, 45)**	**36% (19, 56)**	**35% (19, 55)**	**29% (14, 48)**	**31% (23, 40)**	**22% (18, 27)**
Complete Response, % (n)	0% (0)	4% (1)	0% (0)	0% (0)	1% (1)	3% (10)
Partial Response, % (n)	26% (8)	32% (9)	35% (11)	29% (9)	31% (37)	19% (72)
Stable Disease, % (n)	55% (17)	50% (14)	48% (15)	45% (14)	50% (60)	39% (147)
Progressive Disease, % (n)	19% (6)	14% (4)	16% (5)[3]	26% (8)	19% (23)[3]	34% (126)
ORR, including responses pending confirmation (95% CI)*	26% (12, 45)	36% (19, 56)	42% (25, 61)	29% (14, 48)	33% (25, 42)	NA

*Includes two unconfirmed responses, both pending confirmation, in the 100mg cohort. One was recorded prior to the DCO, and one was recorded after the DCO. If both confirm, the cORR for the 100mg cohort would increase from 35% to 42% and the cORR for the pooled analysis would increase from 31% to 33%.

DCO date: August 15, 2025

1. Efficacy-evaluable population for this expansion cohort is defined as all eligible participants who received any study treatment and have at least one post-baseline efficacy assessment, or who discontinued study treatment due to progressive disease or death, regardless of whether they had a scan.
2. IA1 for LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023; *2 or 3 prior VEGF-R TKI regimens; DCO date: August 30, 2024; Baseline was defined as the last non-missing assessment prior to the first dosing of treatment.
3. Includes three patients with radiological progressive disease and two patients who had clinical progression before the first scan, which have been included by do not meet criteria for progressive disease per RECIST.

Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

2L: second-line; BID: twice daily; ccRCC: clear cell renal cell carcinoma; CI: confidence interval; cORR: confirmed overall response rate; DCO: data cutoff; NA: not applicable; ORR: overall response rate; QD: once daily; RECIST: Response Evaluation Criteria in Solid Tumors; VEGFR-TKI: vascular endothelial growth factor receptor tyrosine kinase inhibitor

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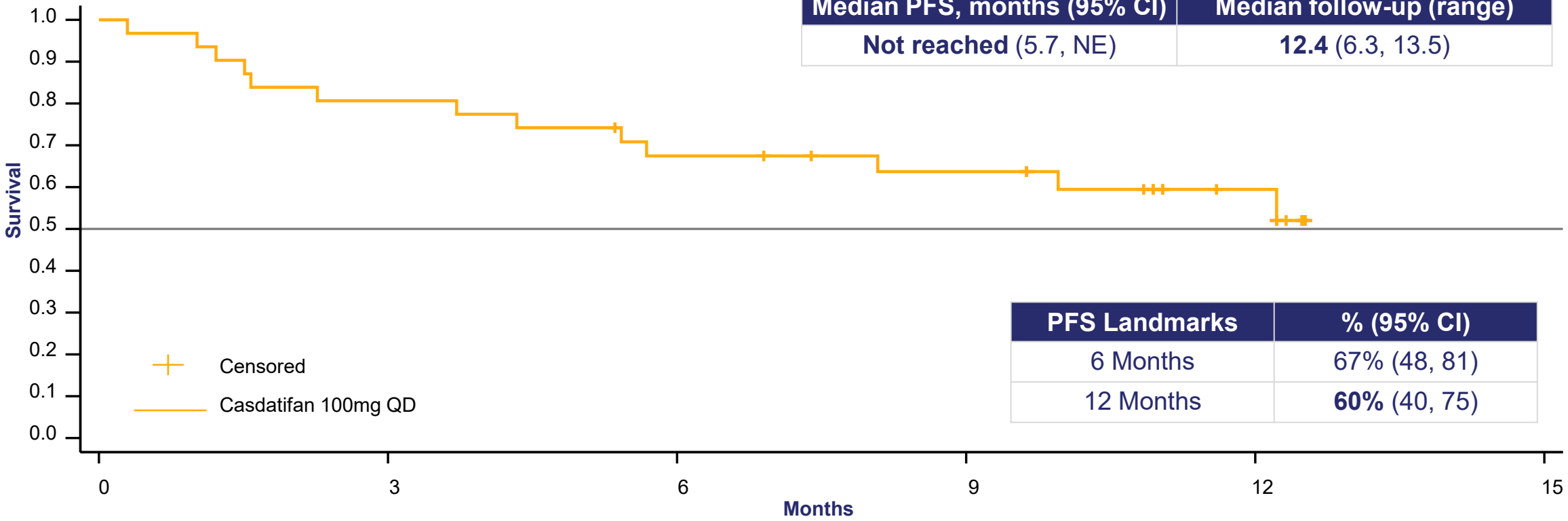
Median PFS for the 100mg QD Cohort Has Still Not Been Reached with >12 Months Follow-Up

Median PFS, months (95% CI)	Median follow-up (range)
Not reached (5.7, NE)	**12.4** (6.3, 13.5)



PFS Landmarks	% (95% CI)
6 Months	67% (48, 81)
12 Months	**60%** (40, 75)

Number at Risk

31	25	20	17	8	0

60% Landmark 12-Month PFS compares very favorably to the 34% for belzutifan in LITESPARK-005*

DCO date: August 15, 2025

*Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

CI: confidence interval; DCO: data cutoff; NE: not estimable; PFS: progression-free survival; QD: once daily

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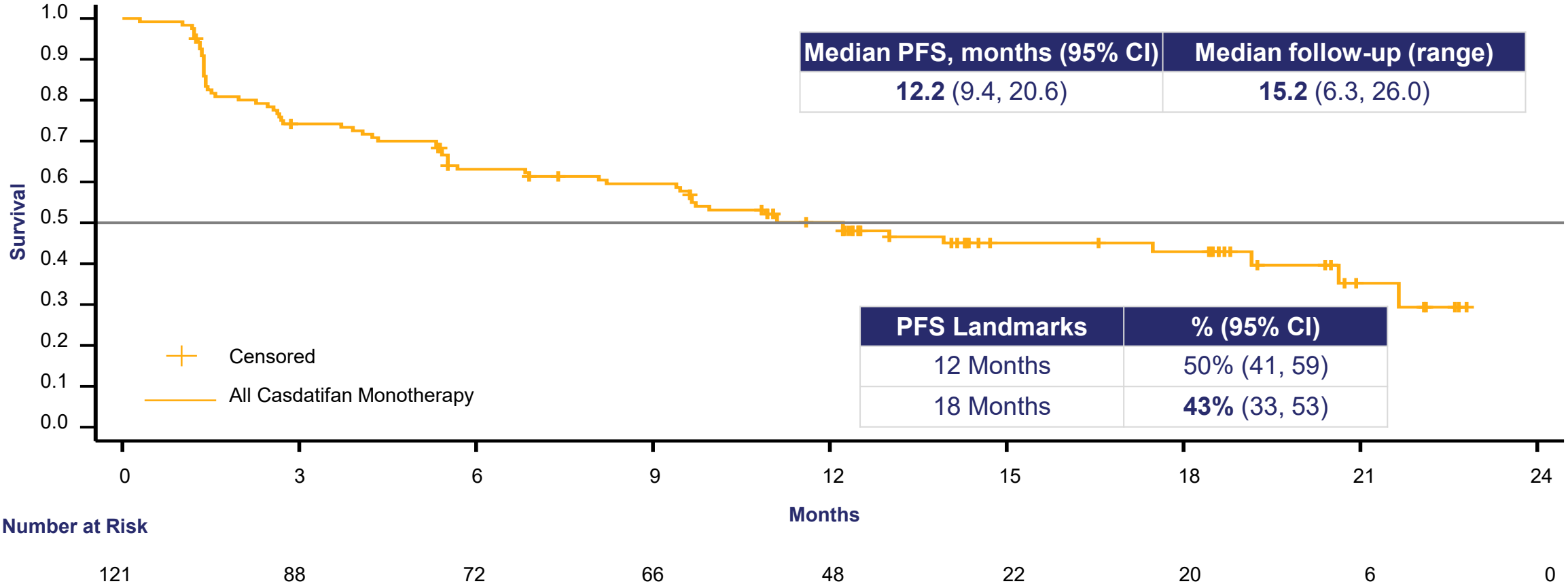
Median PFS for the Four Monotherapy Cohorts Pooled (n=121) is 2x+ the mPFS for Belz Monotherapy in LS-005



Median PFS, months (95% CI)	Median follow-up (range)
12.2 (9.4, 20.6)	**15.2** (6.3, 26.0)

PFS Landmarks	% (95% CI)
12 Months	50% (41, 59)
18 Months	**43%** (33, 53)

Number at Risk

0	3	6	9	12	15	18	21	24
121	88	72	66	48	22	20	6	0

12.2 months mPFS compares to 5.6 mos PFS for belzutifan in LITESPARK-005*

DCO date: August 15, 2025

*Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

Belz: belzutifan; CI: confidence interval; DCO: data cutoff; mPFS: median progression-free survival; PFS: progression-free survival

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With a 12+ Month PFS, Casdatifan Exceeds All PFS Benchmarks for Monotherapy

Earlier-line patient populations

TRIAL	TRIAL RECRUITMENT COMPLETION YEAR	PATIENT POPULATION	TRIAL DESIGN	cORR	mPFS
ARC-20 (Phase 1b/2)	**2025**	**PDx/TKI Experienced ccRCC (mostly 3L+)**	**Cas (Pooled)** **Cas (100mg QD)**	**31%** **35%**	**12.2m** **Not reached**
TIVO-3 (Phase 3)[1]	2017	3L-4L TKI Experienced ccRCC	Tivozanib vs. sorafenib	**18%** vs. 8%	**5.6m** vs. 3.9m
LITESPARK-005 (Phase 3)[2]	2022	PDx/TKI Experienced ccRCC (mostly 3L-4L)	Belz vs. everolimus	**22%** vs. 4%	**5.6m** vs 5.6m
RECORD-1 (Phase 3)[3]	2007	ccRCC with prior sunitinib and/or sorafenib (mostly 3L+)	Everolimus + BSC vs placebo + BSC	**2%** vs. 0%	**4.9m** vs. 1.9m
METEOR (Phase 3)[4]	2014	2L+ TKI Experienced ccRCC (mostly 2L)	Cabo vs everolimus	**17%** vs. 3%	**7.4m** vs. 3.9m
Lenva + ev (Phase 2)[5]	2013	2L TKI Experienced ccRCC	Lenva + everolimus vs. Lenva vs. everolimus	43% vs. **27%** vs 6%	14.6m vs. **7.4m** vs. 5.5m
AXIS (Phase 3)[6]	2010	2L ccRCC	Axitinib vs sorafenib	**19%** vs. 9.9%	**6.7m** vs. 4.7m
CONTACT-03 (Phase 3)[7]	2021	PDx Experienced ccRCC (did not require prior TKI)	Atezo + cabo vs. cabo	41% vs. **41%**	10.6m vs. **10.8m**
CANTATA[8]	2019	PDx Experienced ccRCC (did not require prior TKI)	Tela + cabo vs. cabo	31% vs **28%**	9.2m vs. **9.3m**

DCO date for casdatifan: August 15, 2025

1. Rini et al 2020 (TIVO-3); 2. Choueiri et al 2024 (LS-005); 3. Motzer et al 2010 (RECORD-1); 4. Choueiri et al 2016 (METEOR); 5. Motzer et al 2015 (lenva +everolimus); 6. Rini et al 2011 (AXIS); 7. Pal et al 2023 (CONTACT-03); 8. Tannir et al 2022 (CANTATA)

Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

2L: second-line; 3L: third-line; 4L: fourth-line; atezo: atezolizumab; belz: belzutifan; BSC: Biopharmaceutics Classification System; cabo: cabozantinib; cas: casdatifan; cORR: confirmed overall response rate; ccRCC: clear cell renal cell carcinoma; DCO: data cutoff; lenva: lenvatinib; m: months; mPFS: median progression-free survival; PFS: progression-free survival; tela: teleglenastat; TKI: tyrosine kinase inhibitor

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Casdatifan Was Well Tolerated in All Cohorts, With a Comparable Safety Profile to That of Belzutifan

Safety-Evaluable Population[1]	50mg BID (n=33)	50mg QD (n=31)	100mg QD (n=32)	150mg QD (n=31)	Pooled (n=127)	Belzutifan (LITESPARK-005)[1]
Anemia, n (%)						**Anemia:**
All grades	29 (88)	29 (94)	29 (91)	30 (97)	117 (92)	All grade: 83%
Grade ≥3 related to casdatifan	16 (49)	12 (39)	8 (25)	16 (52)	52 (41)	Grade 3+: 33%
Related to casdatifan leading to interruptions	11 (33)	10 (32)	9 (28)	15 (48)	45 (35)	
Leading to dose reductions	4 (12)	5 (16)	3 (9)	6 (19)	18 (14)	
Leading to discontin.	**0**	**0**	**0**	**0**	**0**	
Hypoxia, n (%)						**Hypoxia:**
All grades	6 (18)	5 (16)	5 (16)	7 (23)	23 (18)	All Grade: 15%
Grade ≥3 related to casdatifan	3 (9)	3 (10)	3 (9)	5 (16)	14 (11)	Grade 3+: 11%
Related to casdatifan leading to interruptions	5 (15)	4 (13)	3 (9)	6 (19)	18 (14)	
Leading to dose reductions	3 (9)	2 (6)	1 (3)	3 (10)	9 (7)	
Leading to discontin.	**0**	**1 (3)**	**1 (3)**	**1 (3)**	**3 (2)**	

DCO date: August 15, 2025

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

Data are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, sample size, inclusion and exclusion criteria and many other factors.

BID: twice daily; DCO: data cutoff; QD: once daily

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Development Strategy for Casdatifan in IO-Experienced and 1L ccRCC

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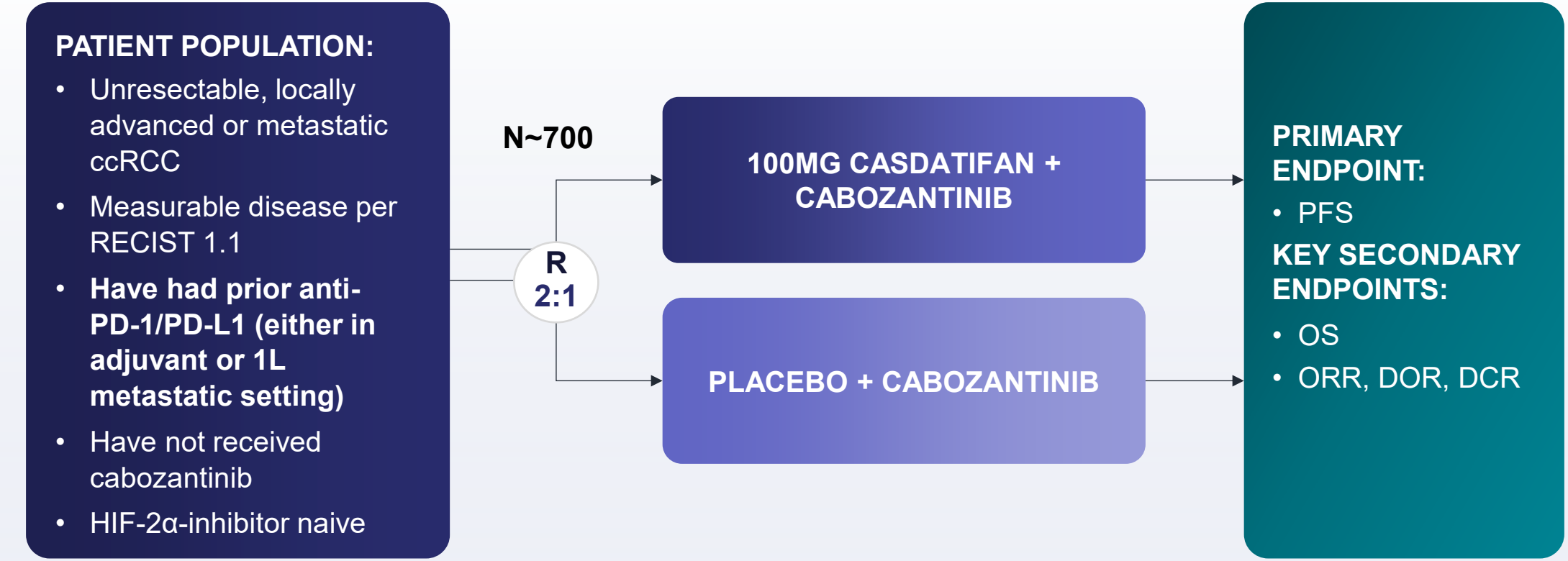
First Phase 3 Study for Cas Has a Simple Design that Utilizes the Preferred SOC in Post-IO ccRCC



✓ **PEAK-1 Initiated**

1L: first-line; cabo: cabozantinib: cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DCR: disease control rate; DOR: duration of response; HIF: hypoxia-induced factor; IO: immuno-oncology; mg: milligram; ORR: objective response rate; OS: overall survival; PD-1/PD-L1: programmed death protein 1/programmed death ligand 1; PFS: progression free survival; RCC: renal cell carcinoma; RECIST: Response Evaluation Criteria in Solid Tumors

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Cas + Cabo Data Presented at ASCO Substantially De-Risk PEAK-1

ROBUST EFFICACY

- The 46% cORR for cas + cabo **exceeds benchmarks for either agent alone[1] and the Phase 2 LITESPARK-003 benchmark for belz + cabo[2]**

RESPONSES ALREADY APPEAR DURABLE

- **All responses to date have confirmed** and all 11 responders remain on treatment as of July 28, 2025
- Majority of patients with best response of SD also remain on treatment, indicating that even SD patients are experiencing meaningful benefit

NO SIGNS OF OVERLAPPING TOXICITY

- **AE profile for cas + cabo is consistent with that expected for either agent alone**
- No cas-related TEAEs > grade 3

HIGH DOSE INTENSITY OF BOTH DRUGS

- **88-95% dose intensity achieved for both cas and cabo** enabling optimization of efficacy for the combination
- As of the DCO, only 5% of safety evaluable patients discontinued a drug due to an AE and no patients have discontinued both drugs

DCO date: March 14, 2025.

1. For cabo monotherapy - Phase 3, CONTACT-03 , Pal et al 2023; Phase 3 METEOR, Choueiri et al 2015; cas monotherapy: Arcus ENA 2024 presentation
2. Choueiri et al. 2023, Lancet Oncology

AE: adverse event; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; cORR: confirmed overall response rate; DCO: data cutoff; IO: immunotherapy; SD: stable disease; TEAE: treatment-emergent adverse event

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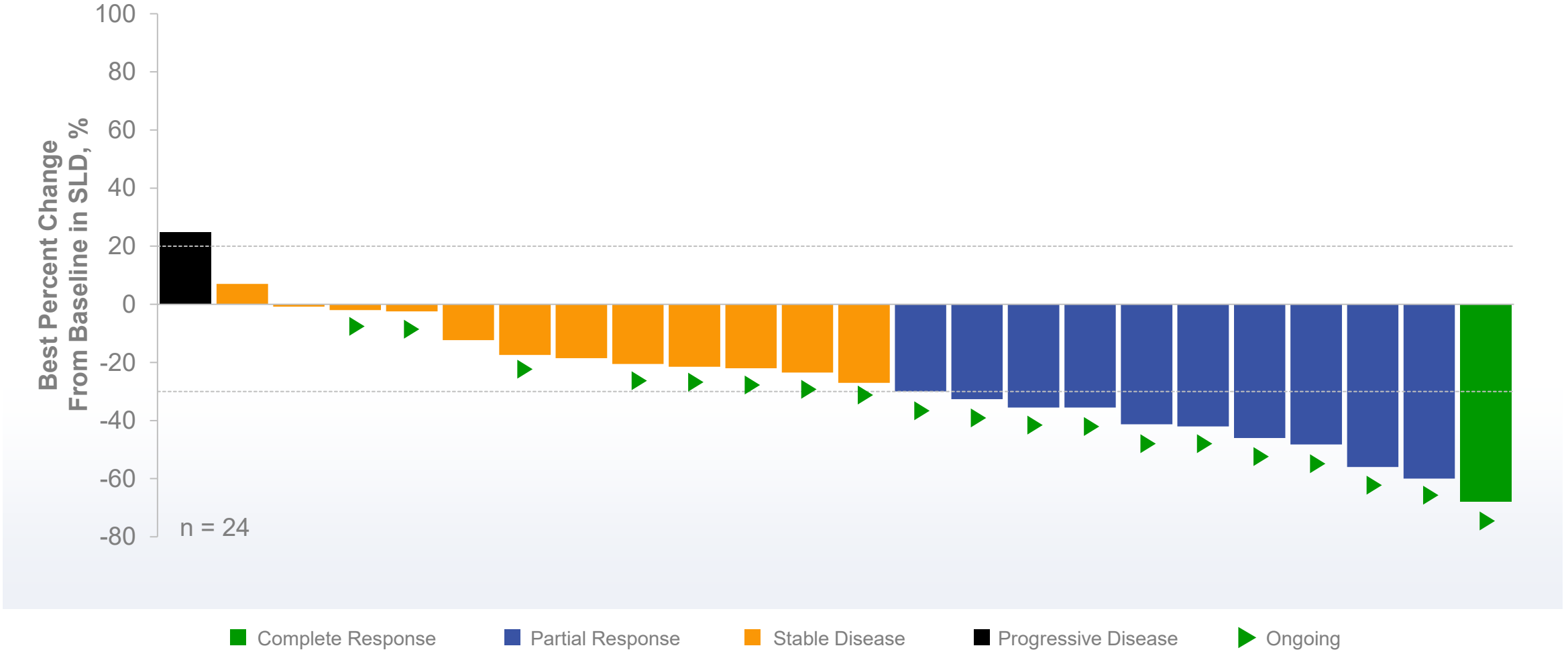
2025 ASCO ANNUAL MEETING #ASCO25
May 30 – June 3, 2025
McCormick Place | Chicago, IL & Online
am.asco.org

Almost All Patients in Cas + Cabo Cohort Achieved Tumor Reduction[a,b]



Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. DCO date: March 14, 2025.
[a]All eligible patients who received any study treatment and achieved a minimum of 12 weeks follow-up or discontinued due to progression or death.
[b]Inclusive of one patient who had confirmed PR after March 14, 2025.
Cabo: cabozantinib; cas: casdatifan; DCO: data cutoff; SLD: sum of lesion diameter

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May 30 – June 3, 2025
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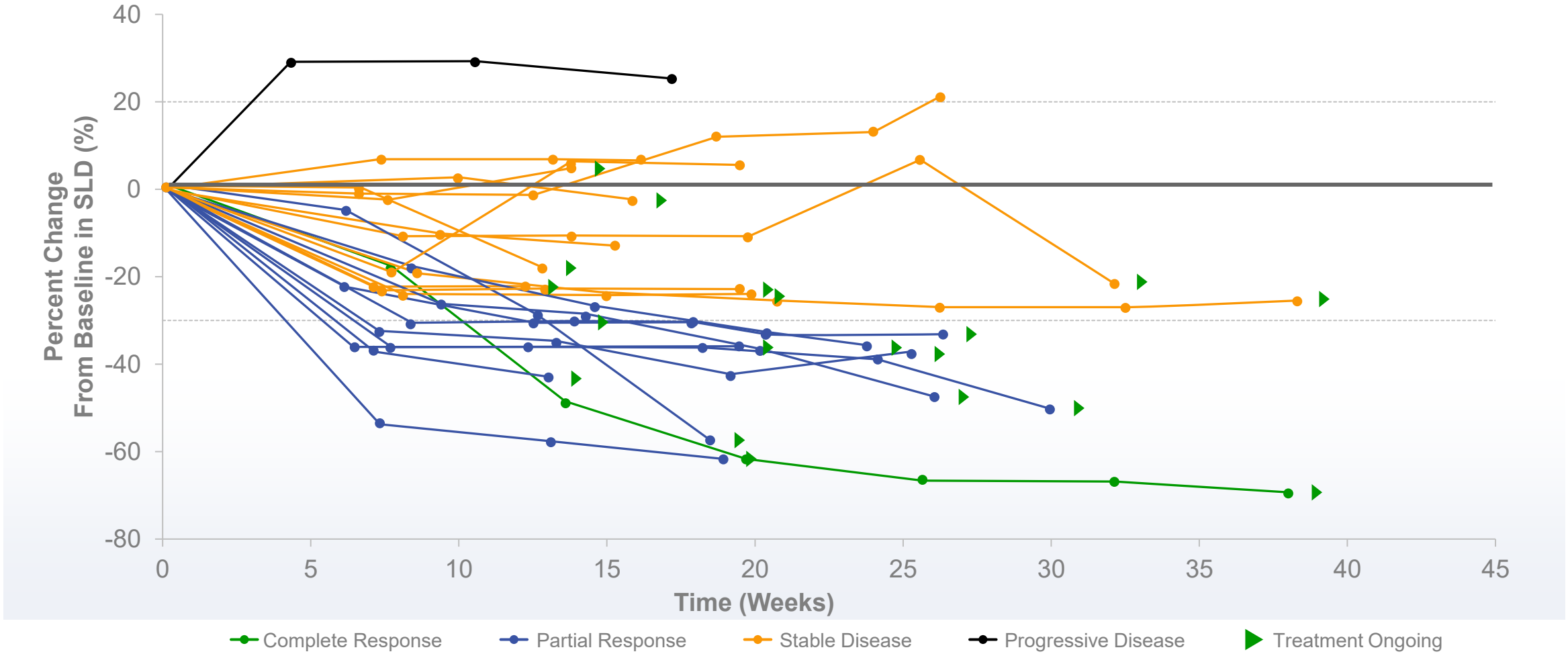
Tumor Reduction Has Deepened Over Time and Responses Already Appear Very Durable for Cas + Cabo



DCO date: March 14, 2025.
All eligible patients who received any study treatment and achieved a minimum of 12 weeks follow-up or discontinued due to progression or death.
Cabo: cabozantinib; cas: casdatifan; DCO: data cutoff; SLD: sum of lesion diameter

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Casdatifan Dose Intensity was Consistently 95%+, Driving Efficacy and Durability

	CAS 100MG QD + CABO 60MG QD* N=27	CAS 100MG QD* N=29	CAS 50MG QD* N=31	CAS 50MG BID* N=33
Median duration of follow-up, months	3.7	5.1	12.3	15.5
Median Tx duration, months	3.0	4.1	10.6	7.1
Cas relative dose intensity, median	**94.9%**	**98.6%**	**100.0%**	**98.6%**
Cabo relative dose intensity, median	**88.0%**	NA	NA	NA

*DCO date: January 3, 2025
BID: twice daily; cabo: cabozantinib; cas: casdatifan; DCO: data cutoff; NA: not applicable; QD: once daily; tx: therapy

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Very Few Grade 3 or Higher Treatment Related AEs in Cas + Cabo Cohort

- No casdatifan-related grade 4 or 5 AEs were observed

	SAFETY POPULATION,[a] n (%) (N = 42)		
	GRADE 3 OR HIGHER AE RELATED TO:		
	casdatifan	cabozantinib	any study drug
Patients with any treatment-related ≥ grade 3 AE[b]	13 (31%)	16 (38%)	20 (48%)
Anemia	10 (24%)	6 (14%)	10 (24%)
Hyponatremia	0	3 (7%)	3 (7%)
Hypoxia	3 (7%)	0	3 (7%)
Hypertension	0	2 (5%)	2 (5%)
Neutrophil count decreased	1 (2%)	2 (5%)	2 (5%)

Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. DCO date: March 14, 2025.

[a]Safety population included patients who received any amount of study drug and had at least 1 month of safety follow-up at the data cutoff date.
[b]Treatment-emergent adverse events (grade 3 or higher) related to casdatifan, cabozantinib, or any study drug reported in ≥ 3% of patients in any treatment arm.
AE: adverse event; cabo: cabozantinib; cas: casdatifan; DCO: data cutoff

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Emerging Data Will Support Casdatifan's Early-Line Registrational Strategy

eVOLVE RCC02

1L ccRCC
casdatifan + volrustomig (anti-PD-1/CTLA-4 bispecific)

Potential anti-PD-1 / CTLA-4 + HIF-2α combination

Go / No Go Decision on Phase 3 Expected in 2H:26

ARC-20

Favorable-risk 1L ccRCC
casdatifan mono

Potential for cas mono in favorable risk patients where no SOC exists

1L ccRCC
casdatifan + zimberelimab (anti-PD-1)

Potential for cas + anti-PD-1 combinations in 1L ccRCC

Initial Data Expected to be Presented in 2H:26

Post-IO ccRCC
casdatifan mono

Potential for cas mono to displace TKI mono in IO-experienced patients

Goal is to start one Phase 3 trial in an early-line ccRCC setting in 2H 2026

1L: first-line; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; PD-1: programmed cell death protein 1; SOC: standard of care; TKI: tyrosine kinase inhibitor

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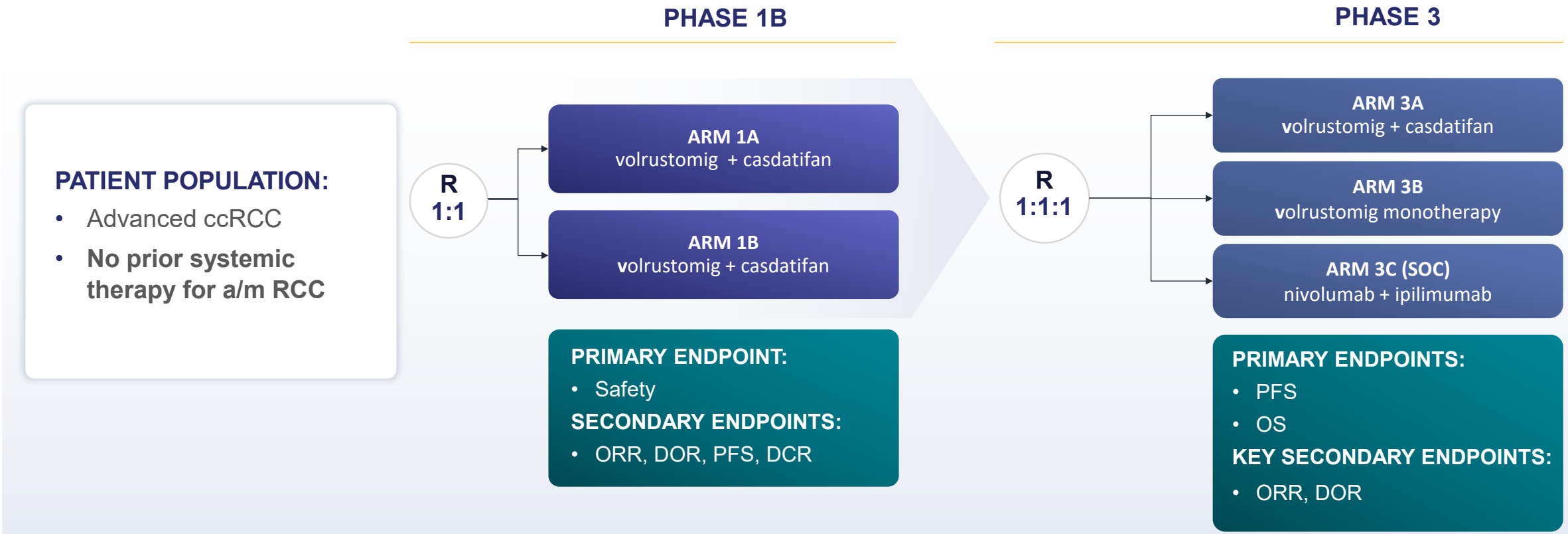
eVOLVE-RCC02: Seamless Phase 1b/3 Design to Evaluate Cas + Volru in 1L Advanced ccRCC



Sponsored by AstraZeneca

- Phase 1b enrollment paused; patients already enrolled will continue to be treated
- Longer-term follow-up data, along with any discussions with health authorities, will inform next steps

1L: first-line; a/m: advanced or metastatic; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DCR: disease control rate; DOR: duration of response; ORR: objective response rate; OS: overall survival; P: poor risk; PFS: progression free survival; RCC: renal cell carcinoma; SOC: standard of care; volru: volrustomig

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Quemliclustat in Pancreatic Cancer

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Quemliclustat: A Small Molecule CD73 Inhibitor with Several Key Attributes

QUEMLICLUSTAT

- Highly potent small molecule
- Target coverage achieved at doses as low as 25mg Q2W
- 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 of CD73, the main source of intra-tumor adenosine
- Immunogenic chemotherapy (e.g., gemcitabine/nab-paclitaxel) releases ATP and contributes to adenosine production
- Tumors such as pancreatic cancer become sensitive to immune attack if adenosine production (i.e., CD73 activity) is blocked by quemli while administering SOC chemotherapy

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

Quemliclustat is an investigational molecule and its safety and efficacy have not been established.
1. Arcus Biosciences data on file; based on preclinical studies
ATP: adenosine triphosphate; IV: intravenous; quemli: quemliclustat; Q2W: every 2 weeks

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Highlights from the Randomized Phase 1 Study in 1L PDAC

Wainberg ZA, et al. ASCO GI Jan. 19, 2024, DCO date of June 19, 2023

- **Median overall survival (mOS) was 15.7 months** (n=122) 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]
- **The quemli-based regimen was well-tolerated**, with no new safety signals or significant added toxicity compared to chemotherapy alone[1]

- **Enrollment completed for Phase 3 PRISM-1 study**

1. Wainberg ZA, et al. ASCO GI, Jan. 19, 2024, DCO date 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

1L first-line; DCO: data cutoff; G/nP: gemcitabine/nab-paclitaxel; mOS: median overall survival; PDAC: pancreatic ductal adenocarcinoma; quemli: quemliclustat

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PRISM-1

Phase 3 Study of Quemli + Chemo in 1L Metastatic PDAC



1L: first-line; ECOG PS: Eastern Cooperative Oncology Group performance status; GnP: gemcitabine/nab-paclitaxel; PDAC: pancreatic ductal adenocarcinoma; OS: overall survival; PFS: progression-free survival; N: number; Q2W: every two weeks; quemli: quemliclustat; YE: year end

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Domvanalimab in Non-Small Cell Lung Cancer

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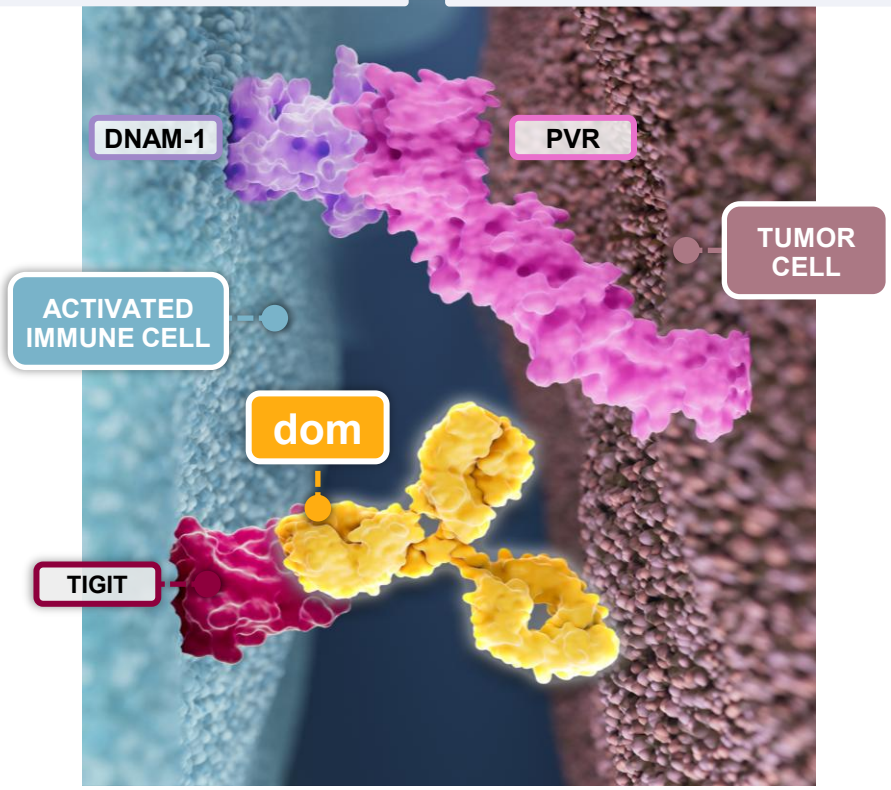
Dom is the Most Clinically Advanced Fc-Silent Anti-TIGIT Antibody in Development

TIGIT inhibition turns an immuno-suppressive "brake" into an accelerator of adaptive immunity

1 **Dom blocks TIGIT, an inhibitory "brake" on immune cells,** from binding to CD155 (PVR) on tumor cells

2 TIGIT blockade **enables PVR to bind CD226 (DNAM-1), an "accelerator" on immune cells,** driving tumor cell kill



First-to-Market Potential in Ph3 NSCLC

Fc-silent

Avoids depletion of TIGIT-bearing cells:

- Minimizes treatment interruptions by avoiding Treg depletion-related immune AEs
- Maximizes efficacy by avoiding potential depletion of cancer-fighting Teff cells

Individual Agents

Administered as individual agents (vs. co-formulation)

- Pursuing 30-minute co-administration infusion time for dom and zim

Optimized Development Strategy

Positioned to be first to market in 1L NSCLC (all-comers) and Stage 3 NSCLC

Note: co-administration of dom + zim was not part of STAR-121 Phase 3 study in 1L NSCLC
1L: first-line; AE: adverse event; DNAM-1: DNAX accessory molecule; dom: domvanalimab; NSCLC: non-small cell lung cancer; Ph: phase; Teff: effector T-cells; Treg: regulatory T-cells; zim: zimberelimab

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ARC-7 and ARC-10 Demonstrated Consistent Improvement for Dom + Zim in 1L PD-L1 High NSCLC

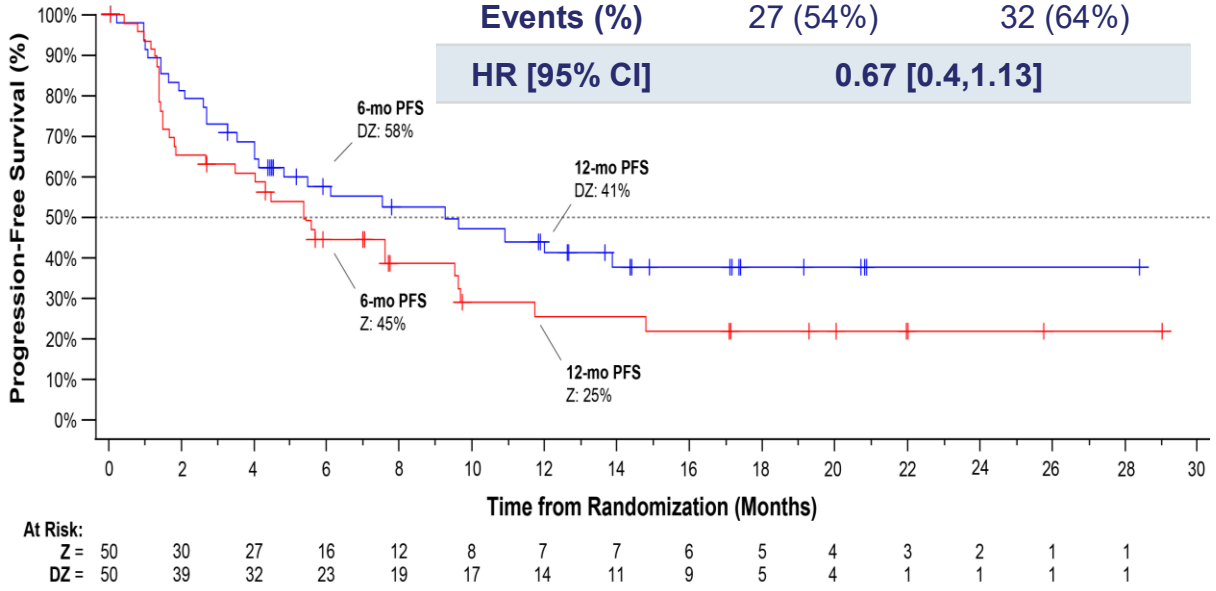
ARC-7 1L PD-L1 High NSCLC

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

Johnson, et al. ASCO, Jun. 2, 2023; DCO date of Feb. 7, 2023

2023 ASCO ANNUAL MEETING

	Dom + Zim	Zim
Median PFS [95% CI]	9.3 months [4.1,NE]	5.4 months [2.7,9.7]
Events (%)	27 (54%)	32 (64%)
HR [95% CI]	**0.67 [0.4,1.13]**	



Dom + Zim vs. Zim PFS HR = 0.67

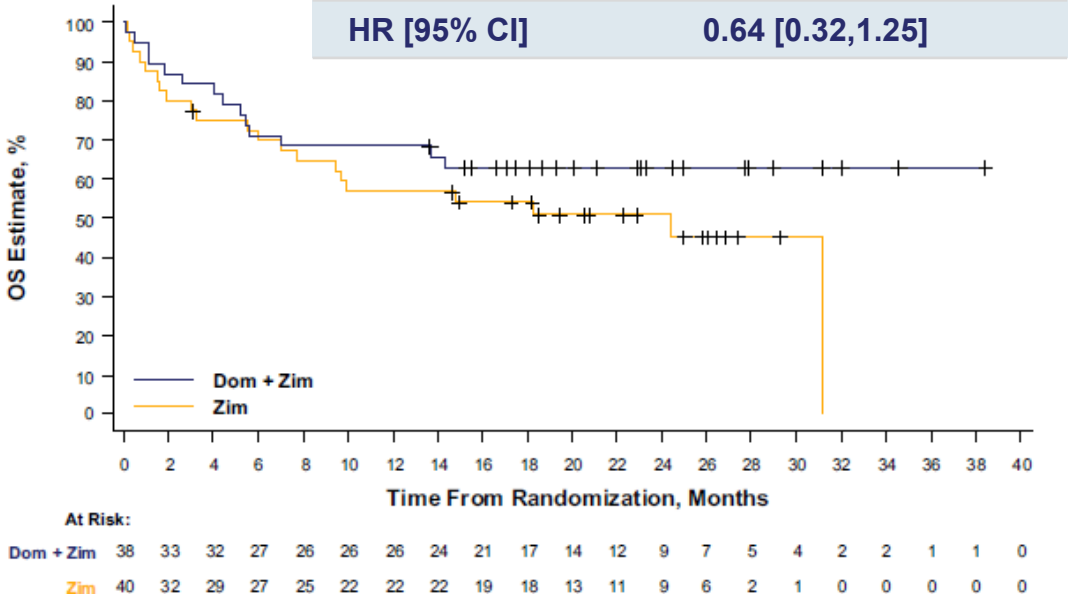
ARC-10 1L PD-L1 High NSCLC

dom + zim *vs.* zim *or* chemo (n=95)

Johnson, et al. SITC 2024; DCO date of May 17, 2024

Society for Immunotherapy of Cancer sitc2024 NOV. 6-10 | HOUSTON

	Dom + Zim	Zim
Median OS [95% CI]	NR [13.7,NE]	24.4 months [7.8, NE]
HR [95% CI]	**0.64 [0.32,1.25]**	



Dom + Zim vs. Zim OS HR = 0.64

1L: first-line; chemo: chemotherapy; CI: confidence interval; DCO: data cutoff; dom: domvanalimab; etruma: etrumadenant; HR: hazard ratio; NE: not estimable; NR: not reached; NSCLC: non-small cell lung cancer; OS: overall survival; PFS: progression-free survival; SITC: Society for Immunotherapy of Cancer; zim: zimberelimab

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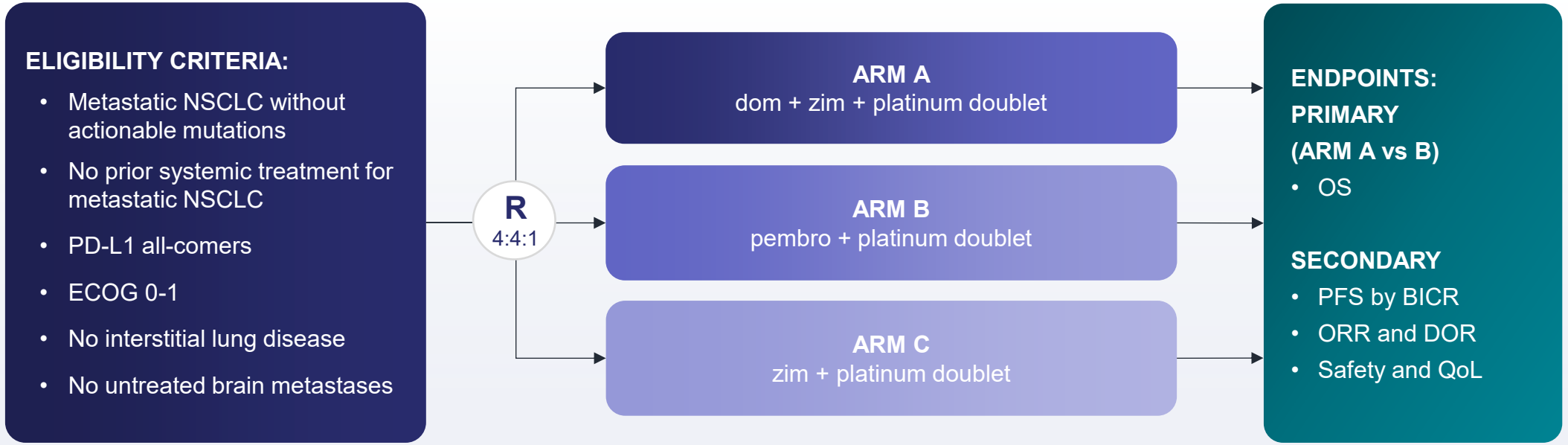
Phase 3 Study Evaluating Dom + Zim + Chemo vs. Pembro + Chemo in 1L NSCLC (All PD-L1 Subgroups)

Uses standard of care, pembrolizumab, in the comparator arm



Gilead Sciences is operationalizing STAR-121.

NCT #: NCT05502237

1L: first-line; BICR: blinded independent central review; chemo: chemotherapy; 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; PD-L1: programmed cell death ligand 1; PFS: progression-free survival; QoL: quality of life; R: randomized; sq: squamous; zim: zimberelimab

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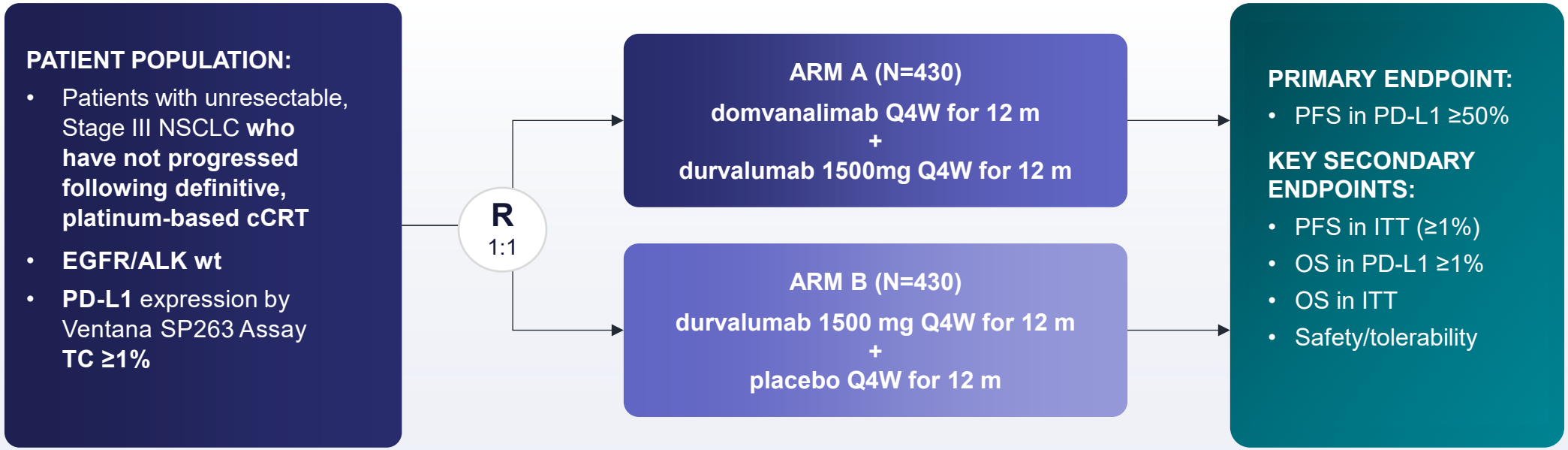
Phase 3 Study Evaluating Dom + Durva vs Placebo + Durva in Unresectable, Stage III NSCLC

Uses durvalumab, the standard-of-care in Stage III NSCLC, in both arms



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)

NCT #: NCT05211895

cCRT: concurrent chemoradiotherapy; dom: domvanalimab; durva: durvalumab; 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; R: randomized; sq: squamous; TC: tumor count; wt: wild type

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Our Emerging I&I Portfolio



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Our I&I Drug Discovery Strategy

IN-HOUSE EXPERTISE IN IMMUNOLOGY has been a core aspect of our discovery group since Arcus founding

MINIMIZE BIOLOGICAL RISK by leveraging validated mechanisms with applications to common diseases with large addressable populations

2-PRONG I&I STRATEGY:

- Small-molecule improvements of cytokine-targeted therapeutics with validated clinical benefit
- Target immune cell types that play key roles in human disease and have been historically “under-studied”
  - Multi-year interest in mast cell biology (e.g., KIT, MRGPRX2), neutrophil biology

I&I: inflammation and autoimmune; KIT: tyrosine kinase receptor for stem cell factor SCF; MRGPRX2: mas-related G protein-coupled receptor member X2

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Our I&I Drug Discovery Portfolio

TARGET	MODALITY	DISEASE AREA	STATUS
MRGPRX2	SM	CSU, AD	FIH Expected in 2026
TNF (TNFR1)	SM	RA, Psoriasis, IBD	FIH Expected Late 2026 / Early 2027
CCR6	SM	Psoriasis	Advanced Discovery
CD89	mAb	RA	Advanced Discovery
CD40L	SM	SLE; MS	Discovery

We expect to advance two small molecule candidates into the clinic over the next 12 months

AD: atopic dermatitis; CSU: chronic spontaneous urticaria; IBD: inflammatory bowel disease; I&I: inflammation and autoimmune; mAb: monoclonal antibody; MRGPRX2: mas-related G protein-coupled receptor member X2; MS: multiple sclerosis; RA: rheumatoid arthritis; SLE: systemic lupus erythematosus; SM: small-molecule

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MRGPRX2 Inhibition for the Treatment of Atopic Skin Diseases

Validated Biology with Multi-Billion $ Potential

- MRGPX2 is a mast cell-specific G protein-coupled receptor (GPCR) that triggers robust mast cell activation
- Approved biologics are highly successful and effective in treating mast-cell driven diseases
- Dupixent® is approved in AD and CSU, among other indications, and generates >$15B in LTM sales[1]

Opportunity for Improvement

- Anti-IgE (e.g., Xolair®) and anti-IL-4R (e.g., Dupixent®) are not sufficient to address clinical need in CSU and/or AD (non-IgE mast cell pathology)
- KIT mAbs (e.g., barzolvolimab/ Celldex) address mast cell biology but at the cost of some safety/convenience
- MRGPRX2 represents a novel (and potentially safer) way to address mast cell contribution in these conditions
- Need for improved potency/PK relative to early entrants into the clinic

Program Status

- Expect FIH in 2026
- Great opportunity to establish preliminary efficacy in Ph1b study (e.g., CIndU)

1. Sanofi earnings releases

AD: atopic dermatitis; CIndU: chronic inducible urticaria; CSU: chronic spontaneous urticaria; FIH: first-in-human; IgE: immunoglobin E; KIT: tyrosine kinase receptor for stem cell factor SCF; mAb: monocolonal antibody; MRGPRX2: mas-related G protein-coupled receptor member X2; PK: pharmacokinetics

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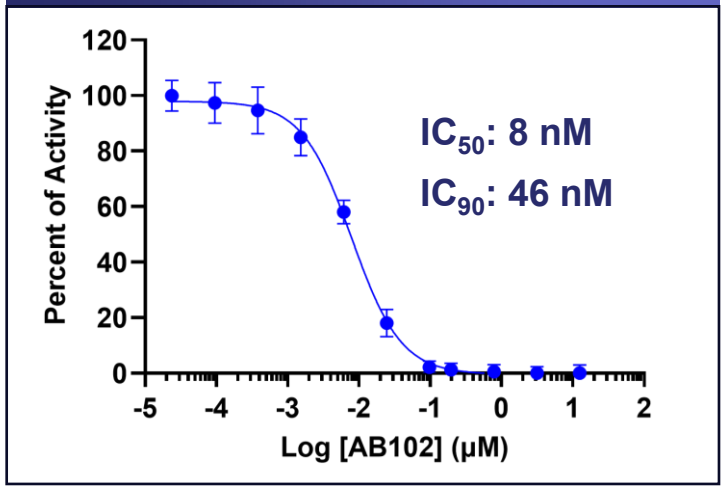
Key Criteria Expected to Enable an MRGPRX2 Antagonist to be Best-in-Class

Potency

- We perform stringent evaluation of potency under physiologically relevant conditions
- Molecules that can block 90%+ of the effects of MRGPRX2 activators at double-digit nM concentrations (see below for AB102)

MAST CELL (LAD2) DEGRANULATION (CD107A) IN 100% HUMAN SERUM



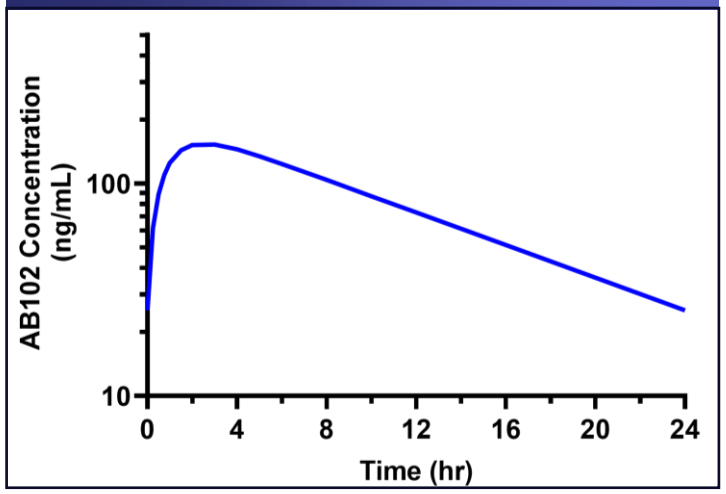
Selectivity / Safety

- Exploratory safety studies completed in 3 species
- Competitor molecules have reported safety signals that may not support continued development
- Ongoing GLP studies progressing on schedule with AB102
- Additional molecules continue to be profiled

Human PK

- Based on the predicted human PK for our leading molecule, it could achieve clinically relevant exposures at 1/30 the exposures shown by the leading competitor

MODELED STEADY-STATE HUMAN PK



GLP: Good Laboratory Practice; IC: inhibitory concentration; LAD2: leukocyte adhesion deficiency type II; MRGPRX2: mas-related G protein-coupled receptor member X2; ng/mL: nanograms per milliliter; nM: nanometer; PK: pharmacokinetics

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Small-molecule Inhibitors of TNF with Potentially Improved Efficacy/Safety Relative to anti-TNF Biologics

Validated Biology with Multi-Billion $ Potential

- Anti-TNF antibodies are among the most successful biologic drugs ever developed
- Humira® was the world's top-selling drug for nearly a decade, with peak sales over $20B[1,2]
- They are approved in several large autoimmune indications, including rheumatoid arthritis, psoriatic arthritis, Crohn's and ulcerative colitis, among others
- Administered as IV infusion or self-injection

Opportunity for Improvement

- Anti-TNF antibodies block TNF signaling at 2 receptors:
  - TNFR1 (pro-inflammatory)
  - TNFR2 (pro-Treg)
- As a result, TNF antibodies can drive a fraction of patients to develop "paradoxical inflammation" (e.g., psoriasis)
- Small-molecule disruptors of TNF selectively block only the activation with TNFR1, with potential for efficacy & better safety
- Opportunity for molecules with better potency / human PK, relative to early entrant into the clinic

Program Status

- Final stages of Development Candidate selection
- FIH in late 2026 / early 2027
- Clinical strategy to be disclosed at a later date
  - An orally delivered & safe small molecule could open up many opportunities for combination treatment

Sources: 1. AbbVie 2021 Annual Report 2. List of best-selling drugs 2020
FIH: first-in-human; IV: intravenous; PK: pharmacokinetics

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Conclusions

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Multiple Upcoming Potential Catalysts

TIMING	STUDY	PRODUCT	EVENT
Early 2026	ARC-20	Casdatifan	• Additional analysis of the cas monotherapy cohorts in late-line ccRCC, including updated PFS for the 100mg QD cohort
Mid-2026	ARC-20	Casdatifan	• ORR and PFS data from the cas + cabo cohort in IO-experienced ccRCC
2026	Phase 1	MRGPRX2	• Initiation of first-in-human study
2H 2026	ARC-20 eVOLVE RCC02	Casdatifan	• Data from one or more of the early-line cohorts of ARC-20 and go / no go decision on the Phase 3 portion of eVOLVE-RCC02
Late 2026	Phase 3	Casdatifan	• Target initiation of first Phase 3 study for cas in an early-line setting of ccRCC
Late 2026 / Early 2027	Phase 1	TNF	• Initiation of first-in-human study
2027	PRISM-1	Quemliclustat	• Phase 3 data in pancreatic cancer

1L: first-line; 2L: second-line; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; ORR: overall response rate; PFS: progression-free survival; QD: once daily

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COMBINING TO CURE®