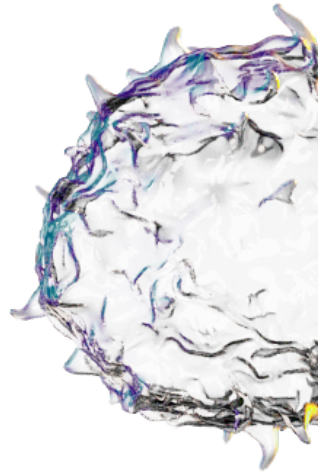
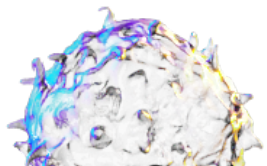
ARC-20 Data: Cas+Cabo

Phase 1b Study of Casdatifan + Cabozantinib in ccRCC

Data presented at ASCO 2025, June 1, 2025, based on data cutoff of March 14, 2025.





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Forward-looking Statements/Safe Harbor

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: being funded through the initial pivotal readouts for dom, quemli and cas, including PEAK-1; expected efficacy or safety of our investigational products, including the durability of patient responses to casdatifan; potential of our investigational products and portfolio, including our investigational products potential to be best or first in class; anticipated benefits of our collaborations with Gilead, Taiho and AstraZeneca; achievement and expected timing of clinical and developmental milestones, including the initiation of PEAK-1 and the timing of new data; initiation of new clinical trials and the design of current clinical trials, including planned cohorts and treatment regimen; the expectation that data from current studies such as ARC-20 are indicative of what will be shown in later studies such as PEAK-1; dosing for any of our investigation products and planned tablet formulation; the potential market and patient population for any of our investigational products; possible first to market advantage for any of our investigational products; adoption of any of our investigational products once improved, including any such product becoming a standard of care; and benefits of our collaboration, including the benefits we expect from our collaboration with AstraZeneca.

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Cas: casdatifan; dom: domvanalimab; quemli: quemliclustat

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Agenda

TOPIC	PRESENTER(S)
Casdatifan Value Proposition	**Dr. Terry Rosen** CEO, Arcus Biosciences
ARC-20 Cas + Cabo Cohort Data	**Dr. Richard Markus** CMO, Arcus Biosciences
Casdatifan Development Plan	**Dr. Richard Markus** CMO, Arcus Biosciences
Opportunity for Casdatifan	**Jennifer Jarrett** COO, Arcus Biosciences
Closing Remarks	**Dr. Terry Rosen** CEO, Arcus Biosciences
Q&A	**All**

Cabo: cabozantinib; cas: casdatifan

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Initial Data from the Cas + Cabo Cohort Were Presented in an Oral Presentation at ASCO 2025

2025 ASCO ANNUAL MEETING

Combination Casdatifan Plus Cabozantinib in Previously Treated Patients With Clear Cell Renal Cell Carcinoma: Results From the Expansion Cohort of the Phase 1 ARC-20 Study

Toni K Choueiri, MD, FASCO[1]; Moshe Ornstein, MD, MA[2]; Pedro Barata, MD, FACP[3]; Marc Matrana, MD, FACP[4]; Jamie Merchan, MD[5]; Craig Gedye, MBChB, FRACP, PhD[6]; Clara Hwang, MD[7]; Rohit Kumar, MD[8]; Jae Lyun Lee, MD, PhD[9]; Yinghui Guan, MS, PhD[10]; Mohammad Ghasemi, PhD[10]; Syed Quadri, MD[10]; Chris Negro, MS[10]; Jianfen Chen, MS[10]; Paul Foster, PhD[10]; Deepti Warad, MBBS[10]; Bradley A McGregor, MD[1]; Sun Young Rha, MD, PhD[11]; Alexandra Drakaki, MD, PhD[12]

[1]Dana-Farber Cancer Institute, Boston, MA, USA; [2]Cleveland Clinic, Cleveland, OH, USA; [3]University Hospitals Seidman Cancer Center, Cleveland, OH, USA; [4]Oschsner Health, New Orleans, LA, USA; [5]Department of Medical Oncology, University of Miami Leonard M. Miller School of Medicine, University of Miami, Miami, FL, USA; [6]ICON Cancer Centre Adelaide, Kurralta Park, SA, Australia; [7]Henry Ford Cancer-Detroit, Detroit, MI, USA; [8]James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA; [9]Asan Medical Center University of Ulsan College of Medicine, Seoul, South Korea; [10]Arcus Biosciences, Inc., Hayward, CA, USA; [11]Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, South Korea; [12]Division of Hematology/Oncology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA

2025 ASCO ANNUAL MEETING #ASCO25

PRESENTED BY: Toni K Choueiri, MD, FASCO

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ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

ASCO: American Society of Clinical Oncology; Cabo: cabozantinib; cas: casdatifan

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Arcus is Capitalized to Advance its Broad Portfolio of Late-Stage Programs Through Phase 3 Readouts

CASDATIFAN: POTENTIAL BEST-IN-CLASS HIF-2α INHIBITOR

Validated mechanism and compelling market opportunity

ARC-20
cas + cabo oral at ASCO

PEAK-1
Phase 3 initiation expected in 2Q25

DOMVANALIMAB: THREE PHASE 3 STUDIES

STAR-221
1L Gastric
Approaching Ph 3 Data

STAR-121
1L NSCLC (all comers)
Ongoing

PACIFIC-8
Stage 3 NSCLC
Ongoing

$1 BILLION IN CASH*

Funded through initial pivotal readouts for dom, quemli and cas, which include PEAK-1**

WORLD-CLASS DRUG DISCOVERY

Small molecules focused on oncology and I&I

1H25: first half of 2025; 1L: first-line; 2Q25: second quarter of 2025; ASCO: American Society of Clinical Oncology; cabo: cabozantinib; cas: casdatifan; dom: domvanalimab; I&I: immunology & inflammation; NSCLC: non-small cell lung cancer; Ph: phase; quemli: quemliclustat; R&D: research & development

* cash, cash equivalents and marketable securities as of March 31, 2025

** runway estimate based on cash, cash equivalents, marketable securities, and available facilities

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Casdatifan Value Proposition

Dr. Terry Rosen
CEO, Arcus Biosciences

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Initial Cas + Cabo Data Substantially De-Risk PEAK-1

ROBUST EFFICACY

- The 46% ORR 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 today
- 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

Belz: belzutifan; cabo: cabozantinib; cas: casdatifan; DCO: data cutoff date; IO: immunotherapy; ORR: overall response rate; SD: stable disease; TEAE: treatment-emergent adverse event

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

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Two Datasets Now Demonstrate Casdatifan's Potential to be the Best-in-Class HIF-2α Inhibitor for ccRCC

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

100mg Cas + 60mg cabo in IO-experienced ccRCC[a] (n=24)

ASCO GU SYMPOSIUM 2025

Cas mono in 2L+ ccRCC[b]
(n=89 across 3 cohorts)

	cas + cabo (ARC-20) 5m follow-up	belz + cabo (LS-003)[1] 24m follow-up	cas (ARC-20) 5-15m follow-up	belz (LS-005)[2] 26m follow-up
HIGH cORR:	**46%**	31%	**25-33%**	21%
LOW RATE OF PRIMARY PROGRESSION:	**4%**	6%	**<20%**	34%
MEDIAN PFS:	**TBD**	13.7m	**9.7-12m+**	5.6m

Despite limited follow-up, key efficacy measures exceed those for the Phase 2 LITESPARK-003 study (belzutifan + cabozantinib)

All three cohorts demonstrated improvement on every efficacy endpoint evaluated relative to the Phase 3 LITESPARK-005 study

Data above 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; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear-cell renal cell carcinoma; cORR: confirmed overall response rate; IO: immunotherapy; m: month; PFS: progression-free survival; TBD: to be determined

a. Data cutoff date: March 14, 2025 b. Data cutoff date: January 3, 2025 1. Choueiri et al. 2023, Lancet Oncology 2. Albiges L. et al. Abstract LBA88, ESMO 2023

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Casdatifan has an Optimal Pharmacological Profile Relative to That of the Competitor Belzutifan

GREATER INHIBITION OF HIF-2α / PD EFFECT

- Belzutifan achieves its maximal PD effect (approx. 63% EPO suppression) at 120mg, its approved dose; dose reductions to 80mg or 40mg could result in a loss of efficacy
- **Casdatifan achieves this same effect on EPO at only 20mg, one-fifth the "going forward" dose** of 100mg
- Casdatifan's effect on EPO is highly durable over multiple months, while belzutifan appears to lose its PD effect within 3 months

LINEAR, DOSE PROPORTIONAL PK

- Belzutifan does not achieve meaningfully higher drug exposure at doses above 120mg and, therefore, cannot achieve a more robust PD effect
- **Casdatifan has linear, dose-proportional pharmacokinetics**

OPTIMAL HALF-LIFE AND FORMULATION

- **Belzutifan's half-life is only ~14h, versus ~24h for casdatifan**
- Belzutifan is dosed as three pills once-daily (40mg x 3) vs a planned 100mg tablet once-daily for casdatifan

EPO: erythropoietin; h: hours; PD: pharmacodynamic; PK: pharmacokinetic

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The HIF-2α Market is a 2-Horse Race and Cas is Poised to Become the HIF-2α Treatment of Choice in ccRCC

EFFICACY & SAFETY DATA BASED ON ARC-20 (CAS) AND LITESPARK-005 (BELZ), EACH FROM MONOTHERAPY COHORTS IN "LATE-LINE" PATIENTS	casdatifan 	belzutifan[1] 
Primary progressive disease	**<20%**	34%
cORR ("post anti-PD-1/TKI")	**25-33%**	21%
mPFS ("post anti-PD-1/TKI")	**9.7-12m+**	5.6m
Grade 3 Hypoxia	**High single digits**	Low teens
TKI combo partner in post-IO setting	**+ cabo**	+ lenva (data in 2027) + zanza (data in ??)
1L strategy	**+ anti-PD-1/CTLA-4 *(volru; TKI-free)***	+ pembro (anti-PD-1) + lenva (TKI)
Pill burden	**1 (+1 for cabo)**	3 (+2 for lenva)

1L: first-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear-cell renal cell carcinoma; cORR: confirmed overall response rate; IO: immunotherapy; lenva: lenvatinib; mPFS: median progression free survival; m: months; pembro: pembrolizumab; volru: volrustomig; zanza: zanzalintinib

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

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eVOLVE-RCC02 is Targeting the 1L Setting with the First HIF-2α-Containing TKI-Free Regimen

AstraZeneca

- Clinical collaboration between Arcus and AZ where both parties retain all economics / rights to their respective molecules
- Evaluating casdatifan in combination with AZ's volrustomig (anti-CTLA-4/anti-PD-1 bispecific)
- AZ to sponsor the study and study costs to be shared
- **Enables Arcus to target the 1L setting in a cost- and resource-efficient manner**

eVOLVE RCC02

cas + volrustomig
(anti-CTLA-4/anti-PD-1 bispecific)

- **Utilizing a seamless Phase 1b/3 design**
- Potential first-in-class, TKI-sparing combination
- Volru has demonstrated exciting preliminary data in 1L ccRCC

1L: first-line; AZ: AstraZeneca; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; volru: volrustomig

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Casdatifan Has the Potential to Change the Treatment Paradigm in ccRCC and Displace TKIs in Early Lines

	CURRENT SOC	POTENTIAL PARADIGM SHIFT
1L Favorable Risk	**Watch and Wait** **anti-PD-1 + TKI** **TKI mono**	**HIF-2α mono** cas
1L all-comers	**anti-PD-1 + anti-CTLA-4**	**HIF-2α + anti-PD-1/CTLA-4** cas +volrustomig
	anti-PD-1 + TKI	**HIF-2α + anti-PD-1** cas + zim
2L (Post-IO)	**TKI mono**	**HIF-2α + TKI** cas + cabo **HIF-2α mono** cas
3L+ (Post-IO & TKI)	**mTOR** **HIF-2α** (belz)	**TKI mono** **mTOR** **HIF-2α** (belz)

1L: first-line; 2L: second-line; 3L: third-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; zim: zimberelimab

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ARC-20 Cas + Cabo Cohort

Dr. Richard Markus
CMO, Arcus Biosciences

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Data Presented at ASCO Were From the Cas + Cabo Cohort of the ARC-20 Expansion Cohorts

- To date, over 200 patients have received casdatifan across all cohorts of ARC-20

DOSE ESCALATION

Patients with advanced solid tumors
Casdatifan monotherapy



DOSE EXPANSION

N = ~30 per cohort, except cas + cabo (n=45)

2L+ ccRCC
Casdatifan mono 50mg BID capsule

2L+ ccRCC
Casdatifan mono 50mg QD capsule

2L+ ccRCC
Casdatifan mono 100mg QD tablet

Post-IO ccRCC
Casdatifan 100mg QD +
Cabozantinib 60mg QD

2L+ ccRCC
Casdatifan mono 150mg QD

Favorable-risk 1L ccRCC
Casdatifan mono 100mg QD

1L ccRCC
Casdatifan 100mg QD +
Zimberelimab 360mg Q3W

Post-IO ccRCC
Casdatifan mono 100mg QD

At the March 14 data cutoff:

- **42 patients were evaluable for safety** (had received at least one dose of cas and had at least one month follow-up)
- **24 patients were evaluable for efficacy** (had reached at least 12 weeks follow-up)

1L: first-line; 2L: second-line; ASCO GU: American Society of Clinical Oncology Genitourinary Cancers; BID: twice daily; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; ORR: overall response rate; PFS: progression-free survival; Q3W: every three weeks; QD: once daily

Data presented at ASCO GU, February 2025
Data presented at ASCO, June 1, 2025

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Patient Characteristics in the Casdatifan Plus Cabozantinib Expansion Cohort

CHARACTERISTIC	SAFETY POPULATION[a] (N = 42)
Age, years, median (range)	63 (43–81)
Sex, female/male, n (%)	9 (21%) / 33 (79%)
ECOG PS 0/1, n (%)	29 (69%) / 13 (31%)
IMDC risk score, n (%)	
Favorable	9 (21%)
Intermediate	29 (69%)
Poor	4 (10%)
Number of prior regimens, n (%)	
1	35 (83%)
2+	7 (17%)
Prior treatment, n (%)	
VEGFR-TKI plus IO	17 (40%)
IO only	25 (60%)

Patients were enrolled at 15 sites across 3 countries

ECOG PS: Eastern Cooperative Oncology Group Performance Status; IMDC: International Metastatic Renal Cell Carcinoma Database Consortium; IO: immunotherapy;

Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff: 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.

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Confirmed ORR of 46% in Patients Eligible for a Minimum of 12 Weeks Follow-Up

- To date, all responses have confirmed and all responders remain on treatment

	EFFICACY-EVALUABLE POPULATION (n = 24)[a]
Follow-up, months, median (range)	5.3 (2.8–9.1)
Confirmed ORR[b], % (n)	**46% (11)**
(95% CI)	**(26%, 67%)**
Best Overall Response, n (%)	
CR	1 (4%)
PR[b]	10 (42%)
SD	12 (50%)
PD	1 (4%)

AE: adverse event; CR: complete response; ORR: overall response rate; PD: progressive disease; PR: partial response; SD: stable disease

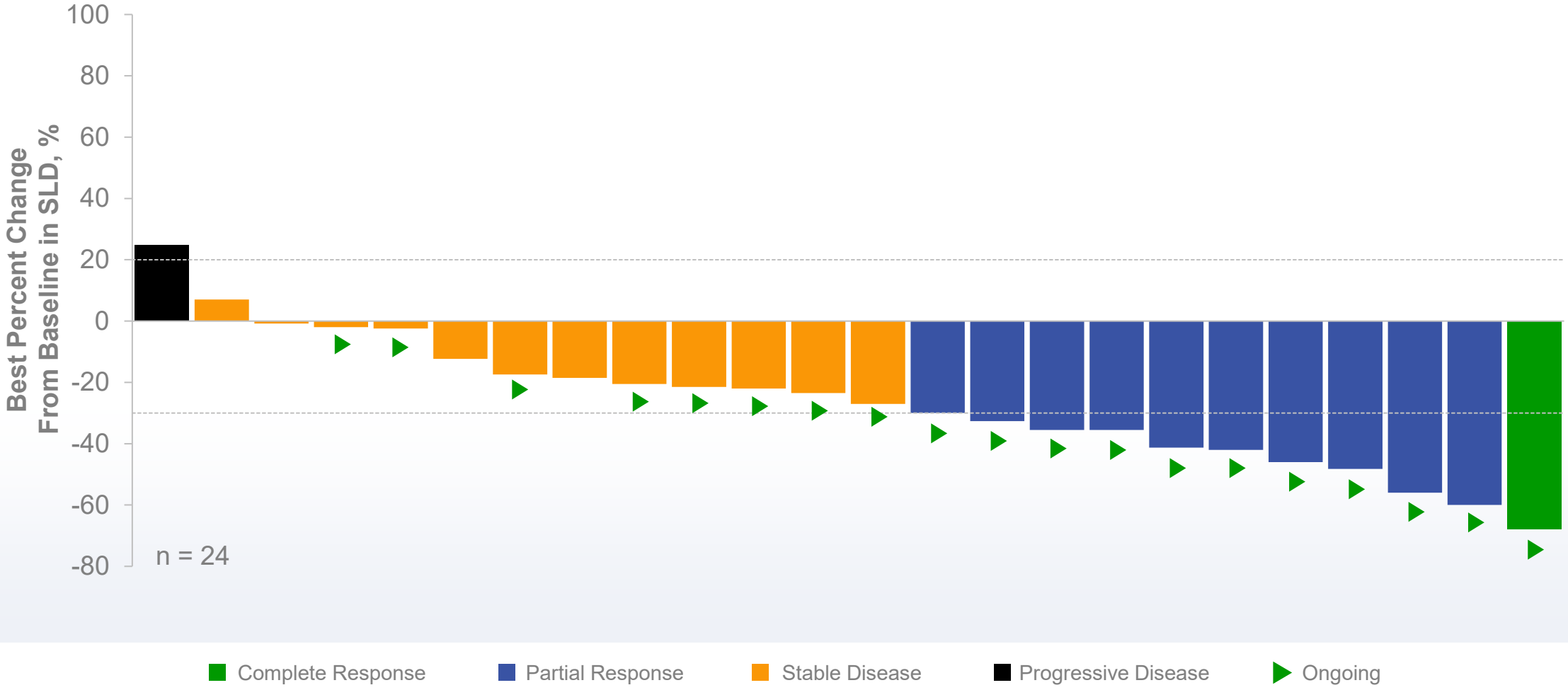
Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff date: March 14, 2025.

[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.

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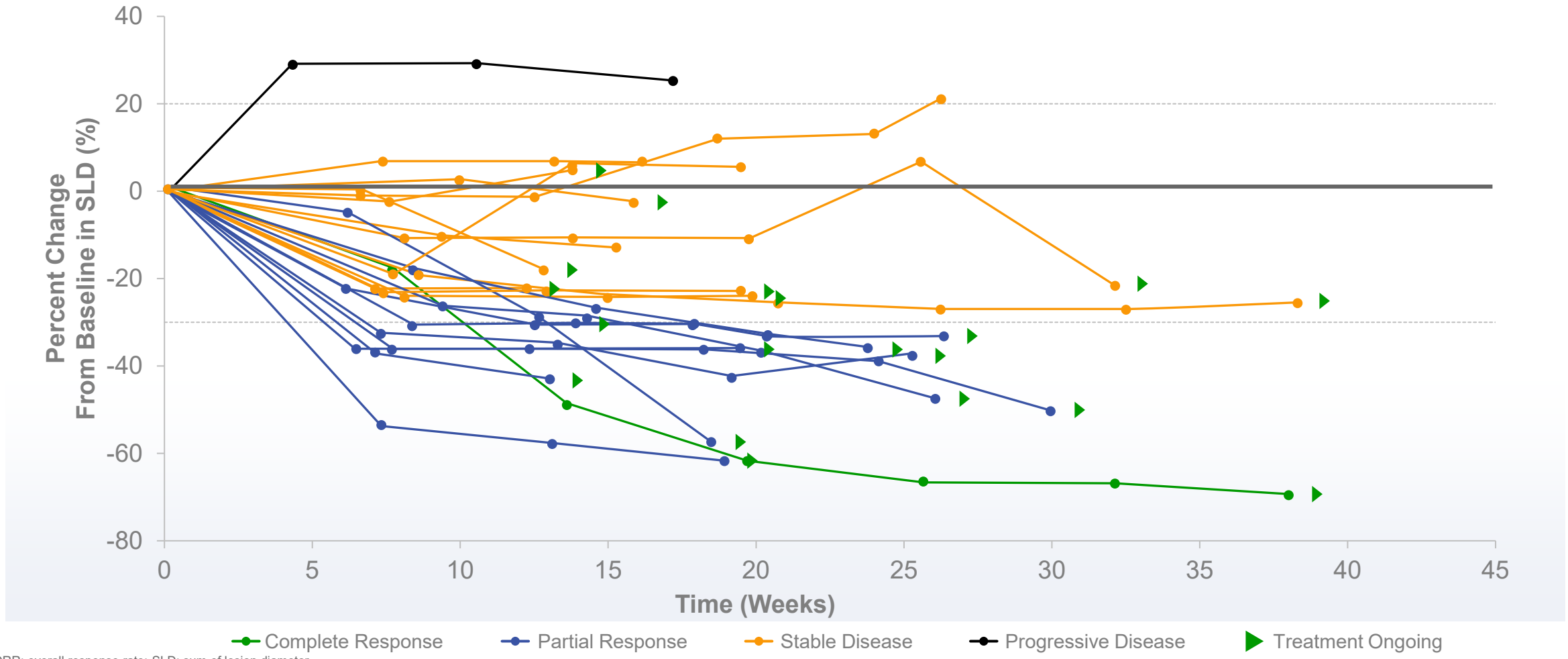
Almost All Patients Achieved Tumor Reduction[a,b]



SLD: sum of lesion diameter; ORR: overall response rate
Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff 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.

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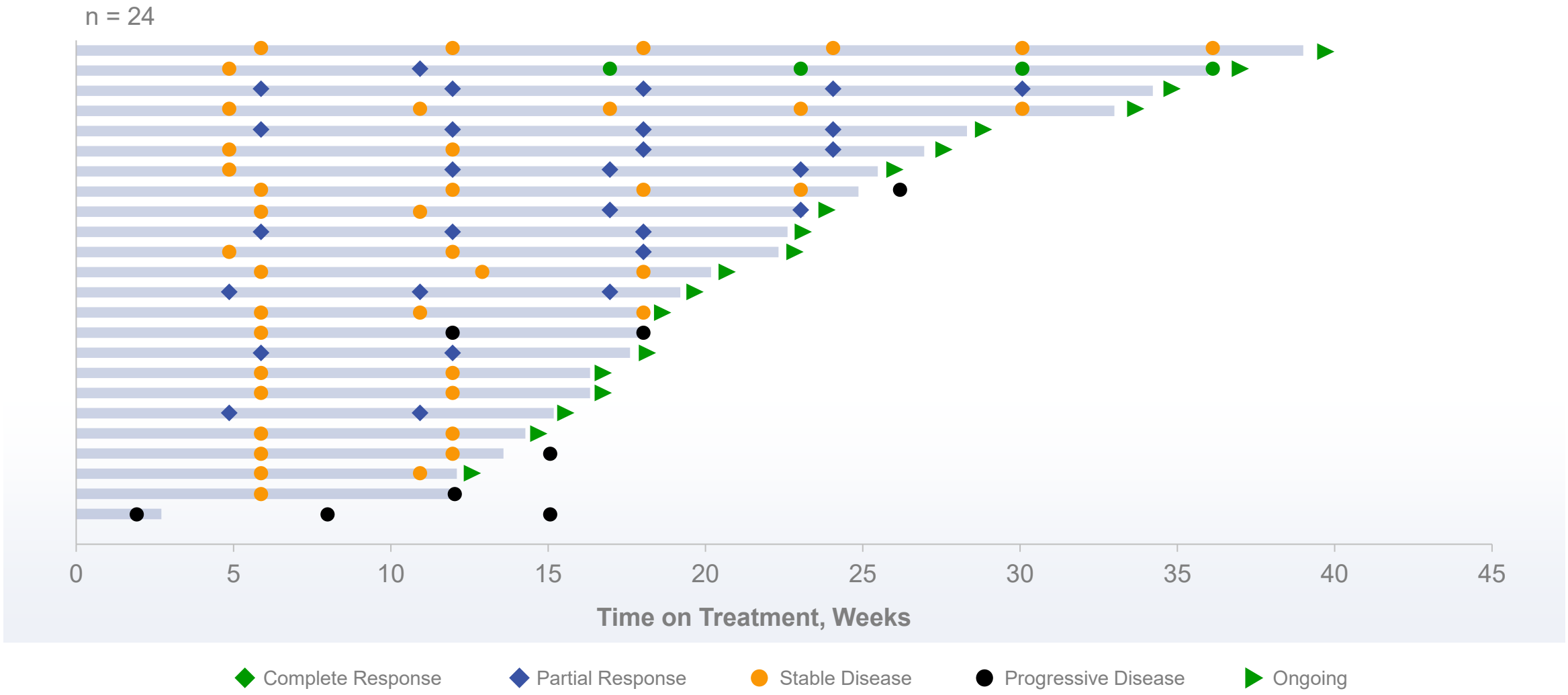
Tumor Reduction Has Deepened Over Time and Responses Already Appear Very Durable



ORR: overall response rate; SLD: sum of lesion diameter
Data cutoff 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.

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Most Patients Remain on Treatment[a,b]



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[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.

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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

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

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TRAEs (Any Grade): Safety Profile was Consistent with Expectations for Cas and Cabo

	SAFETY POPULATION,[a] n (%) (N = 42)		
	AE RELATED TO:		
	casdatifan	cabozantinib	Any study drug
Follow-up, months, median (range)		3.7 (1.1–9.1)	
Patients with any treatment-related AE[b], n (%)	41 (98%)	39 (93%)	41 (98%)
Anemia	29 (69%)	18 (43%)	29 (69%)
Fatigue	20 (48%)	23 (55%)	23 (55%)
Alanine aminotransferase increased	8 (19%)	16 (38%)	16 (38%)
Diarrhea	6 (14%)	15 (36%)	15 (36%)
Aspartate aminotransferase increased	6 (14%)	14 (33%)	14 (33%)
Platelet count decreased	5 (12%)	12 (29%)	12 (29%)
Nausea	5 (12%)	10 (24%)	10 (24%)
Dizziness	7 (17%)	6 (14%)	8 (19%)

- Most cases of anemia and fatigue did not require a dose change and resolved

Cabo: cabozantinib, cas: casdatifan; TRAE: treatment related adverse event

Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff: 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 (any grade) related to casdatifan, cabozantinib, or any study drug reported in ≥ 15% of patients in any treatment arm.

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Very Few Grade 3 or Higher Treatment Related AEs

	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%)

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

AE: adverse event

Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff: 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.

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AEs Were Manageable with Dose Reductions, Leading to Very Few Discontinuations

	SAFETY POPULATION,[a] n (%) (N = 42)		
	LEADING TO REDUCTION IN:		
	casdatifan	cabozantinib	any study drug
Patients with any AE leading to dose reduction[b]	10 (24%)	16 (38%)	22 (52%)
Fatigue	1 (2%)	5 (12%)	6 (14%)
Anemia	4 (10%)	1 (2%)	4 (10%)
Hypoxia	4 (10%)	0	4(10%)
Palmar-plantar erythrodysesthesia	0	2 (5%)	2 (5%)
Stomatitis	0	2 (5%)	2 (5%)

- Only 2 patients (of 42 safety evaluable) discontinued a treatment due to a TEAE (hypoxia and drug hypersensitivity), and no patients discontinued both treatments due to a TEAE

TEAE: treatment-emergent adverse event

Presented at ASCO 2025 by Toni K Choueiri, MD, FASCO. Data cutoff: 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 (any grade) leading to dose reduction in casdatifan, cabozantinib, or any study drug reported in ≥ 3% of patients in any treatment arm.

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Key Takeaways from the Cas + Cabo Cohort

- **ORR for cas + cabo already exceeds that of belzutifan + cabo in LITESPARK-003**
- **Vast majority of patients experience some tumor reduction and clinical benefit**
- **While follow-up is limited, responses already appear very durable**
- **Safety profile of the combination appears very manageable, and consistent with the individual agents**
  - Dose intensity of cas in the combination is very high and similar to monotherapy
- **Very low rate of discontinuations and "short" dose interruptions ensure that drug is "on board" almost continuously**

Cabo: cabozantinib; cas: casdatifan; ORR: overall response rate

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8 Cohorts of ARC-20 Study Enable A Steady Cadence of Data Over the Next ~18 Months

TIMING	ARC-20 COHORTS	EVENT
Early 2025	• 50mg BID • 50mg QD • 100mg QD	✓ Updated data from 50mg BID, 50mg QD (ORR, PFS) ✓ Initial data from 100mg QD tablet (ORR) mono cohort
June 2025	• cas + cabo (post-IO)	✓ Safety and initial efficacy data for the cas + cabo cohort oral presentation at ASCO
Fall 2025	• 50mg BID • 50mg QD • 100mg QD • 150mg QD	• More mature safety and efficacy data for monotherapy cohorts (ORR, PFS)
2026	• cas + cabo • cas mono (1L favorable risk) • cas +zim (1L) • cas mono (post-IO)	• More mature data on cas + cabo combination • Data from new ARC-20 cohorts in earlier line settings

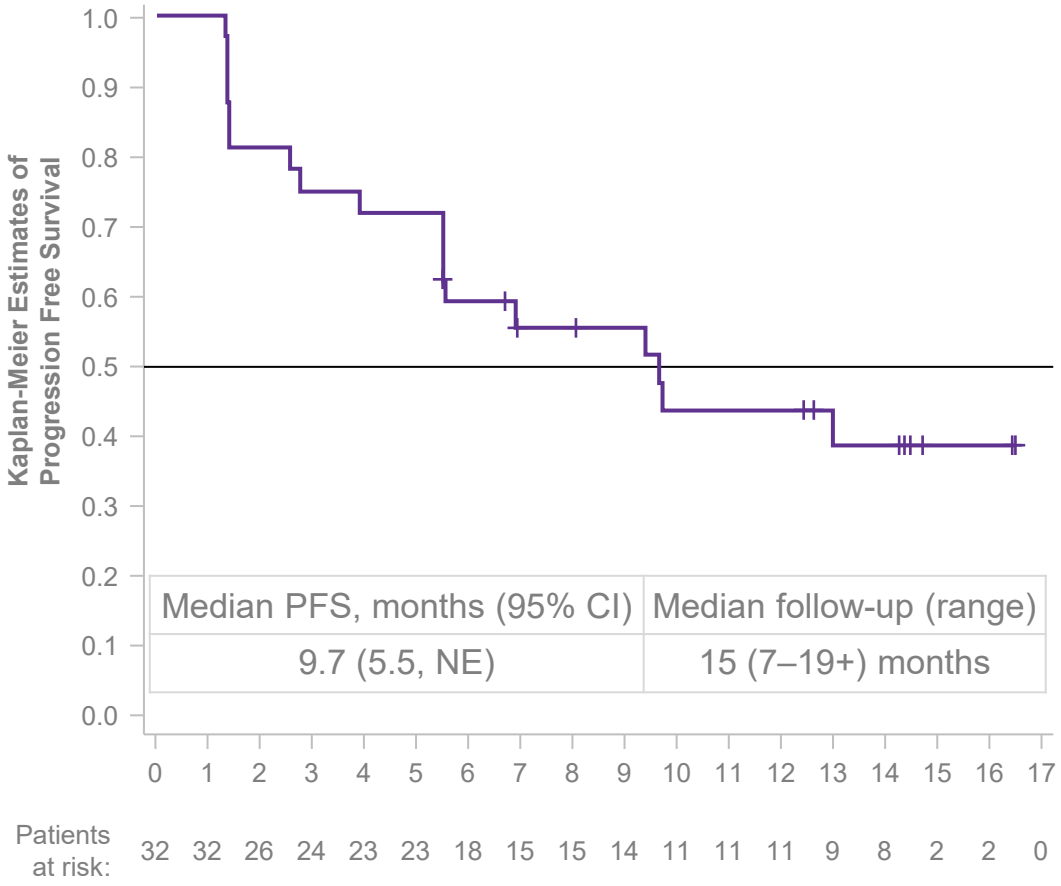
1L: first-line; ASCO: American Society of Clinical Oncology; BID: twice daily; cabo: cabozantinib; cas: casdatifan; IO: immunotherapy; mono: monotherapy; ORR: overall response rate; PFS: progression-free survival; QD: once daily; zim: zimberelimab

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PFS Kaplan-Meier Curves Shown at ASCO GU Bode Well for Updated PFS for Cas Mono Cohorts Later this Year

50mg BID Cohort (n=32)

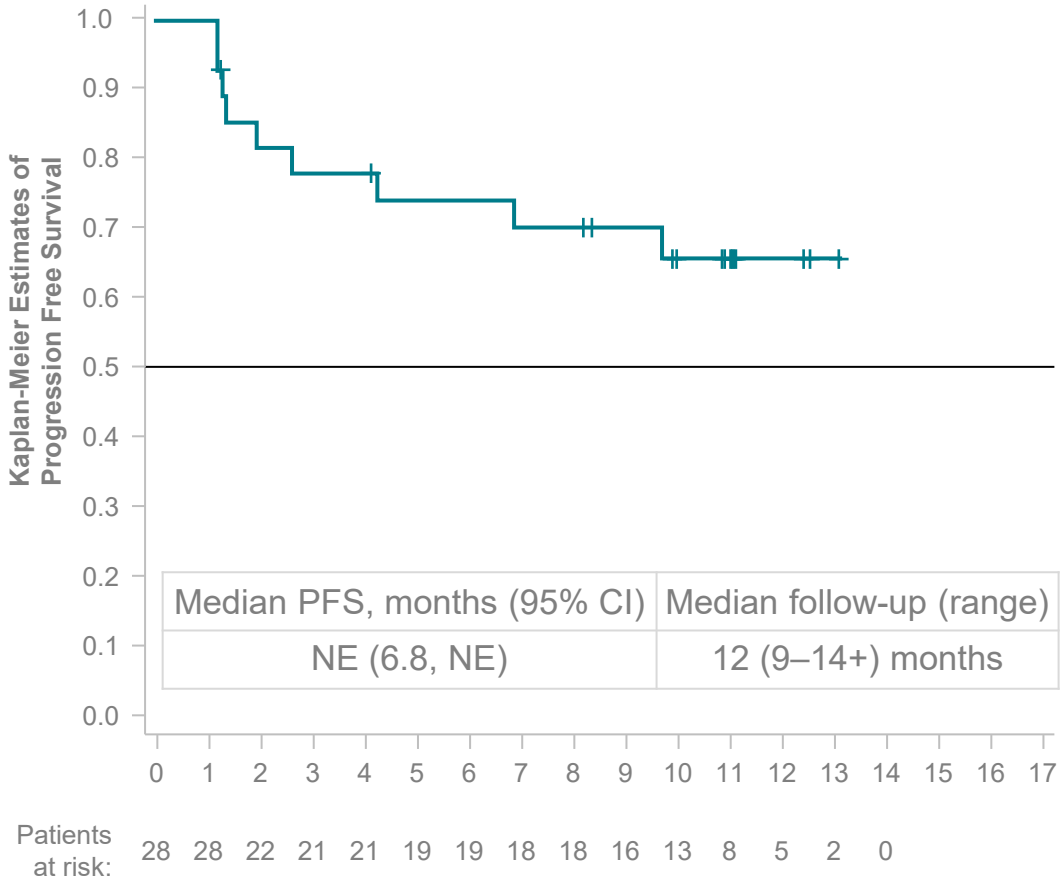
Median follow-up of 15 months



Median PFS, months (95% CI)	Median follow-up (range)
9.7 (5.5, NE)	15 (7–19+) months

50mg QD Cohort (n=28)

Median follow-up of 12 months



Median PFS, months (95% CI)	Median follow-up (range)
NE (6.8, NE)	12 (9–14+) months

+ Censored

- mPFS for belzutifan in Phase 3 LITESPARK-003 was 5.6 months with 18 months median follow-up

ASCO GU: American Society of Clinical Oncology Genitourinary Cancers Symposium; BID: twice daily; CI: confidence interval; DCO: data cutoff; mPFS: median progression-free survival; NE: not estimable; QD: once daily

1. IA1 for LITESPARK-005. Source: Albiges L. et al. Abstract LBA88, ESMO 2023;
PFS was measured according to RECIST v1.0 and estimated using Kaplan-Meier methodology.
Data cutoff date: January 3, 2025

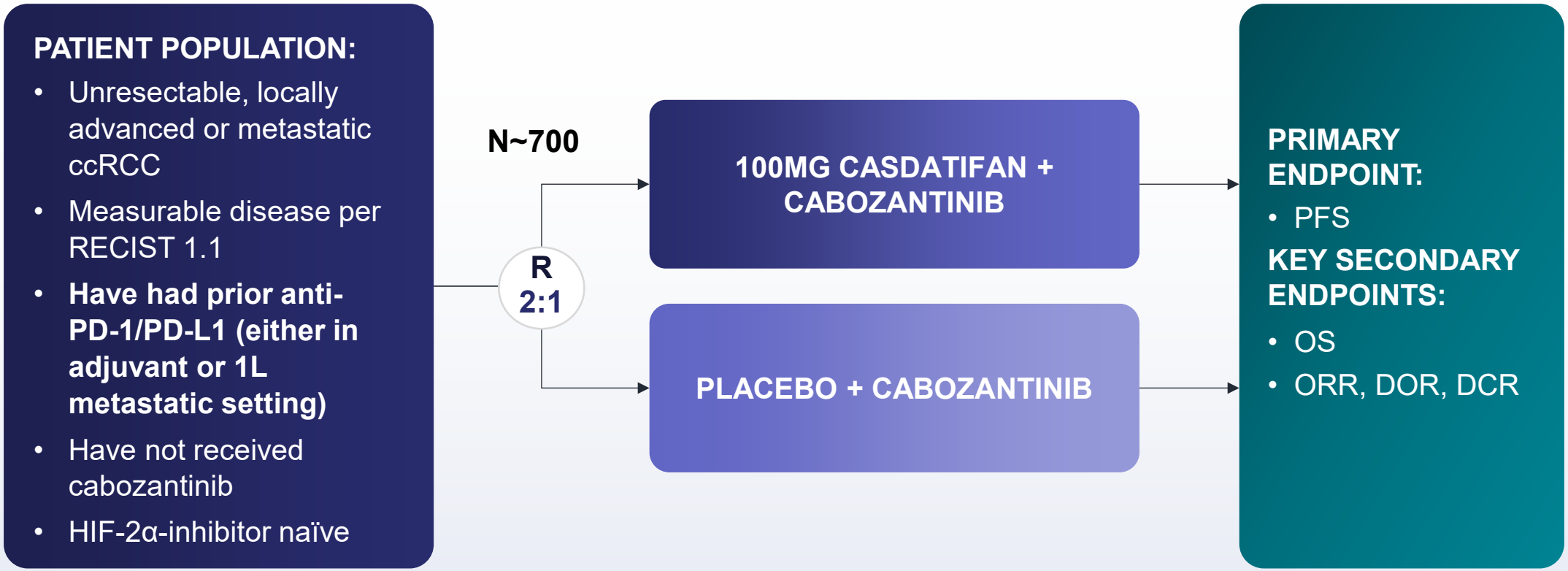
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Casdatifan Development Plan

Dr. Richard Markus
CMO, Arcus Biosciences

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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 is Expected to Initiate Imminently

1L: first-line; cabo: cabozantinib: cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DCR: disease control rate; DOR: duration of response; IO: immunotherapy; ORR: objective response rate; OS: overall survival; PFS: progression free survival; R: randomized; RCC: renal cell carcinoma; RECIST: Response Evaluation Criteria in Solid Tumors; SOC: standard of care

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New Cohorts Added to ARC-20 to Evaluate New Opportunities to Displace TKIs

EXPANSION COHORTS		
2L+ ccRCC casdatifan mono 50mg BID capsule	Data presented at ASCO GU 2025	Satisfies Project Optimus and confirmed 100mg QD tablet as the "going forward" dose and formulation
2L+ ccRCC casdatifan mono 50mg QD capsule		
2L+ ccRCC casdatifan mono 100mg QD tablet		
2L+ ccRCC casdatifan mono 150mg QD		
Post-IO ccRCC casdatifan 100mg QD + cabozantinib 60mg QD	Data presented at ASCO 2025	Generated data to support the Phase 3 PEAK-1 study
Favorable-risk 1L ccRCC casdatifan mono 100mg QD	**New cohorts added and currently enrolling; Designed to inform the potential of cas in early-line settings**	
1L ccRCC casdatifan 100mg QD + zimberelimab 360mg Q3W		
Post-IO ccRCC casdatifan mono 100mg QD		

1L: first-line; 2L: second-line; ASCO: American Society of Clinical Oncology Genitourinary Cancers; BID: twice daily; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; Q3W: every three weeks; QD: once daily

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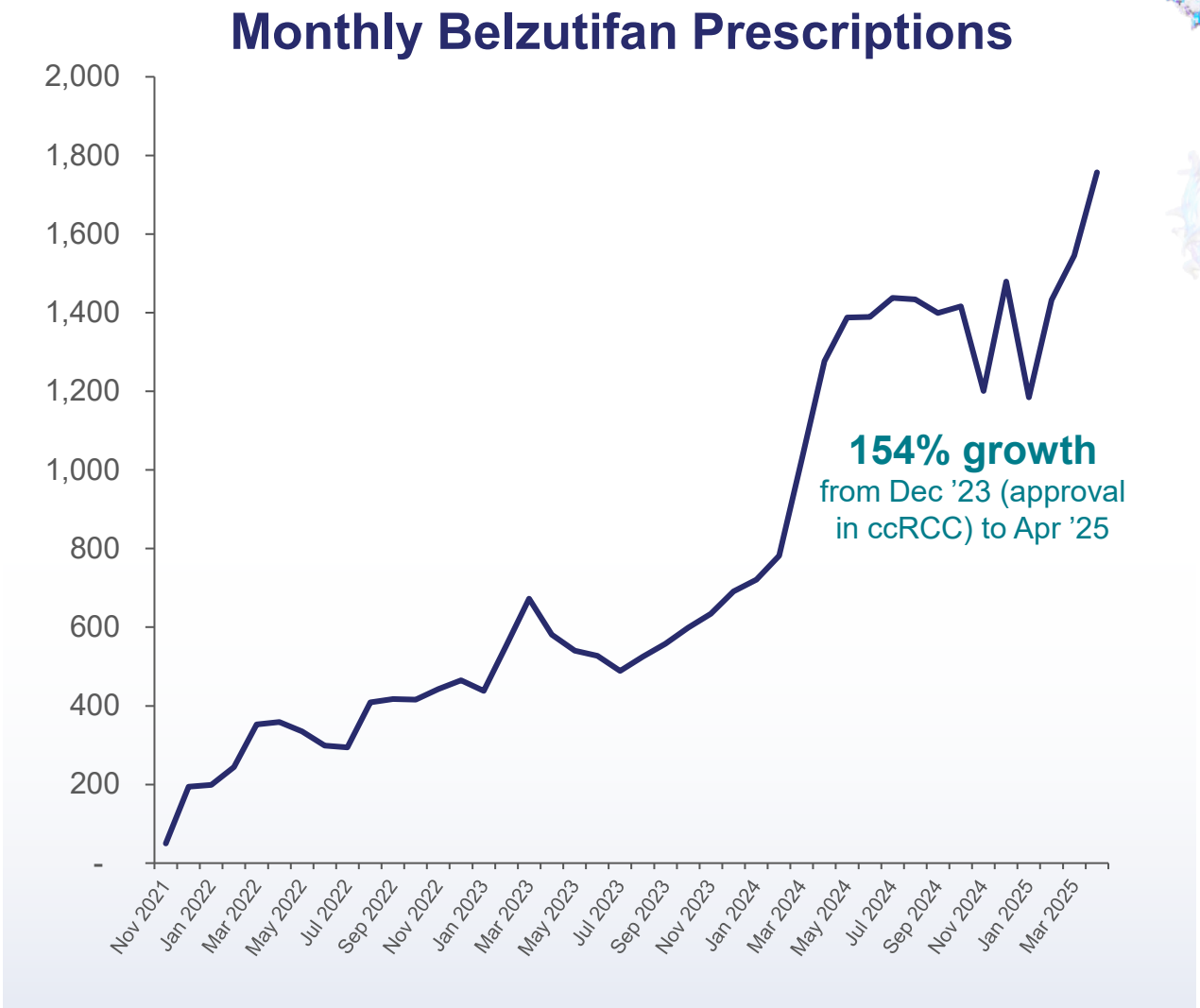
Opportunity for Casdatifan

Jennifer Jarrett
COO, Arcus Biosciences

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Belzutifan Sales Have Grown Exponentially Despite its Usage Being Limited to Late-line ccRCC

- **Belzutifan has rapidly established itself as the SOC in the 3L+ ccRCC setting**
  - High rate of primary progression likely limits use in earlier line settings
- **LTM Sales of >$560M in the U.S.; Run rate sales based on April Rx's are now $720M+**
- **Cas has the potential to meaningfully exceed this based on an improved efficacy profile and superior combination strategy in earlier lines**

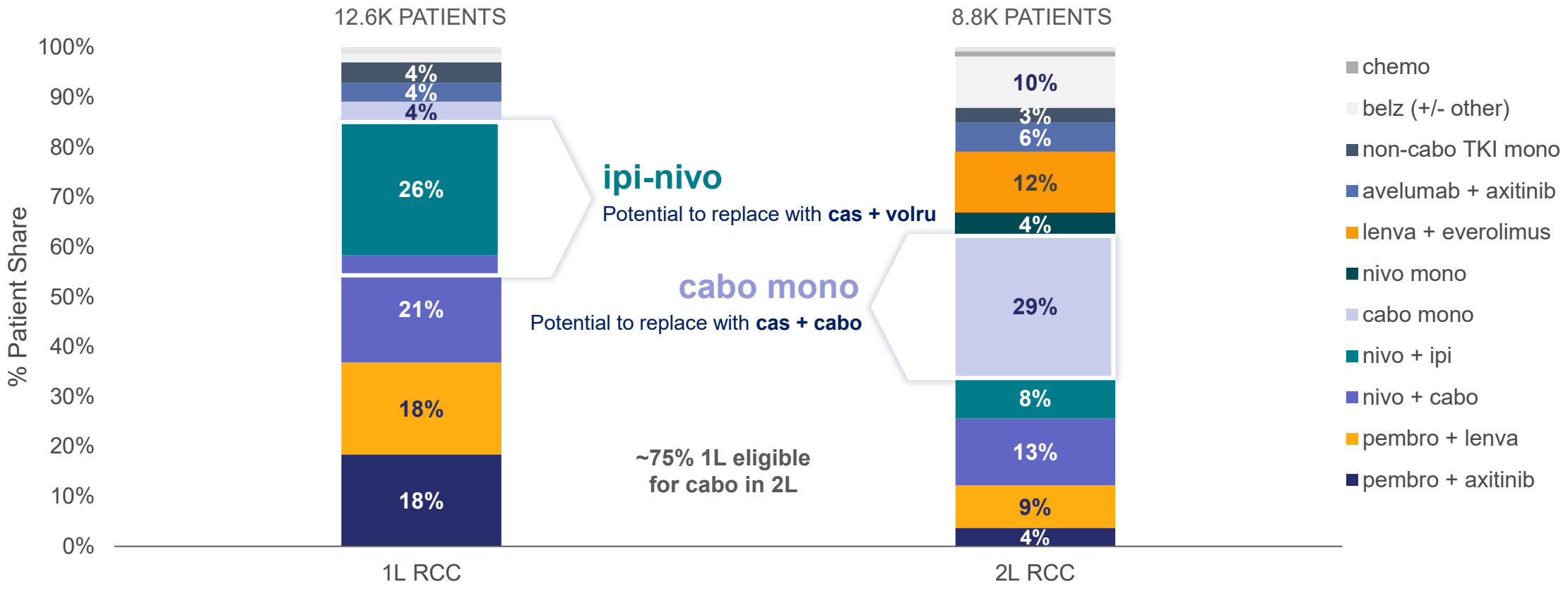


3L: third-line; Apr: April; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; Dec: December; LTM: last twelve months; Rx: prescriptions; SOC: standard of care
Source: IQVIA, Merck Q1 2025 Earnings

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Initial Cas Development Plan Targets the Largest Market Segments and Could Expand Share Within These Segments

2024 ccRCC | US Market Share



1L: first-line; 2L: second-line; belz: belzutifan; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; chemo: chemotherapy; ipi: ipilimumab; lenva: lenvatinib; mono: monotherapy; nivo: nivolumab; pembro: pembrolizumab; volru: volrustomig

Sources - Epi: DRG, GlobalData | Share: Arcus primary research, US May 2024 (n=49)

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Cas + Cabo Has the Potential to Establish a New SOC in IO-Experienced ccRCC

Cas 100mg
(1 x 100mg)



Cabo 20-60mg
(1 x Xmg)



Establishing Cas + Cabo as the HIF-2α + TKI Combination of Choice

- Cabo is the preferred TKI in IO-experienced ccRCC due to a perceived better safety profile and simpler titration
- **Cas is the only HIF-2α inhibitor being developed in Phase 3 with cabo**
- Cas + cabo has the potential to displace TKI monotherapy by prolonging PFS without significant additional toxicity
- 2-drug regimen enables continued treatment on at least one therapy and optimal management of TKI-related toxicities
- With LITESPARK-011 readout delayed, the gap between this study and PEAK-1 has significantly narrowed

Cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; PFS: progression-free survival; SOC: standard of care

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Avoiding Overlapping Toxicity is Key to Maintaining Patients on Therapy and Positions HIF-2α as the Ideal Backbone

Casdatifan





100mg coated tablet



25mg coated tablet

- Anemia
- Hypoxia
- Fatigue

TKIs



- Diarrhea
- Rash
- Hepatotoxicity
- Hypothyroidism
- Hypertension
- Fatigue
- PPE

anti-PD-1



- Diarrhea
- Rash
- Hepatotoxicity
- Hypothyroidism
- Pneumonitis

anti-PD-1/CTLA-4



- Diarrhea
- Rash
- Hepatotoxicity
- Hypothyroidism
- Fatigue
- Pneumonitis
- Pyrexia

PPE: palmar-plantar erythrodysesthesia

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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])
IO-naive metastatic	**Anti-PD-1 + CTLA4**	AstraZeneca eVOLVE RCC02 cas + volru	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

CAS FUTURE DEVELOPMENT

New cohorts added to ARC-20:

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

New tumor types

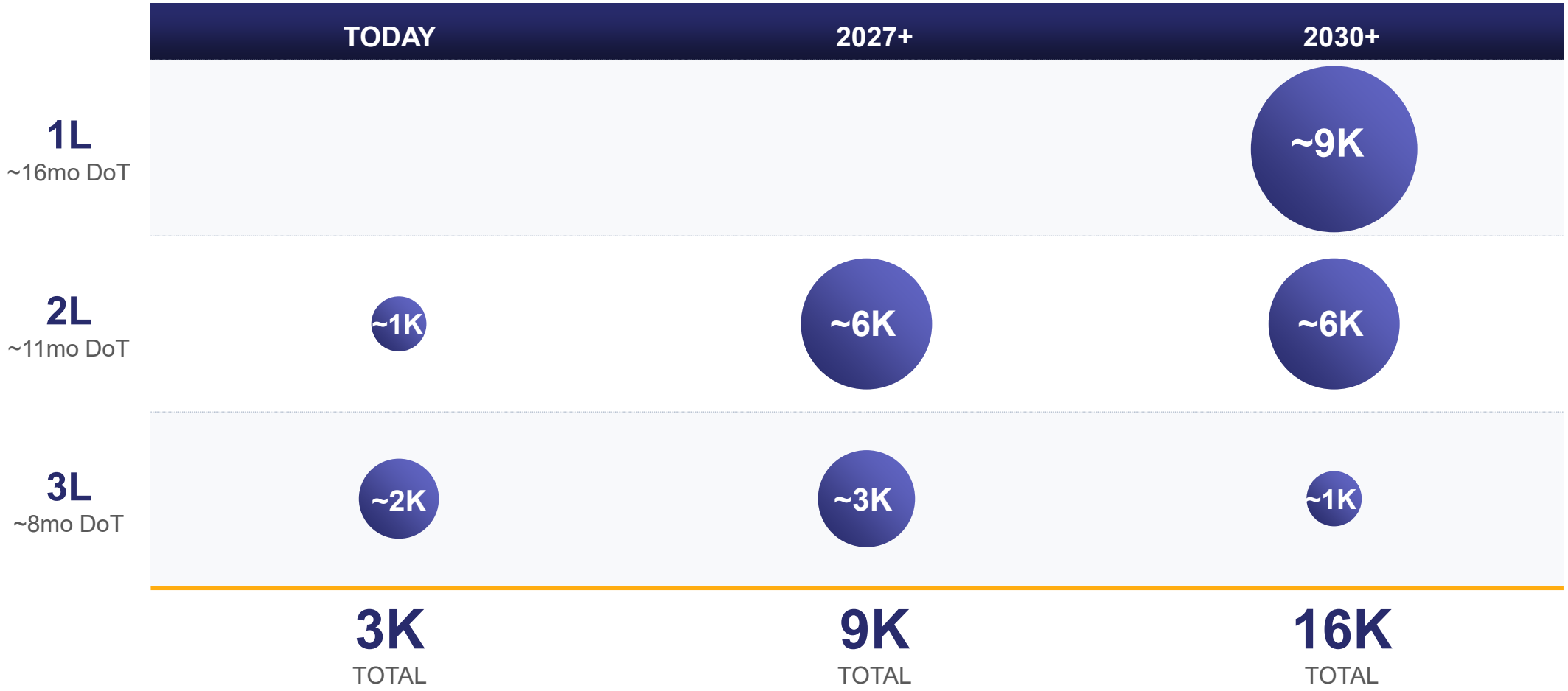
1L: first-line; 2L: second-line; B: billion; cabo: cabozantinib; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; mTOR: mechanistic target of rapamycin; SOC: standard of care; volru: volrustomig; zim: zimberelimab

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

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As Casdatifan Moves Up in the Treatment Paradigm, the U.S. Market Opportunity Will Grow Substantially

Potential ccRCC Patients on HIF-2α Inhibitors over Time (US, Annual)



1L: first-line; 2L: second-line; 3L: third-line; ccRCC: clear cell renal cell carcinoma; DoT: duration of therapy; mo: months

Source: Primary market research. DRG epi projections.

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Closing Remarks

Dr. Terry Rosen
CEO, Arcus Biosciences

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Rapid Advancement and Expansion of the Cas Program Is Our Priority over the Next Year

Cas is Poised to Be the HIF-2α Inhibitor of Choice for RCC

- HIF-2α inhibitors is expected to become another SOC in the $6B+ ccRCC market*, in addition to anti-PD-1's and TKIs
- HIF-2α market is currently a "2-horse" race between cas and belz
- Cas has a potential best-in-class profile, both as monotherapy and in combination with other agents
- We are pursuing a broad and differentiated development strategy to drive cas usage to earlier lines of therapy

Multiple Data Events Coming Over the Next ~18 Months

TIMING	SETTING	EVENT
Fall 2025	2L+ (Post-IO & TKI) ccRCC	• More mature data for cas mono from ARC-20
Throughout 2026	1L/2L ccRCC	• More mature cas + cabo data from ARC-20 • Data from three new cas cohorts added to ARC-20 (cas + zim in 1L, cas mono in 1L favorable risk, and cas mono in 1L/2L TKI-naive)

1L: first-line; 2L: second-line; belz: belzutifan; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; IO: immunotherapy; mono: monotherapy; mPFS: median progression-free survival; ORR: overall response rate; PD: progressive disease; SOC: standard of care; zim: zimberelimab

*https://www.precedenceresearch.com/kidney-cancer-drugs-market

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Three Phase 3 Programs Targeting Substantial Market Opportunities and Unmet Medical Need

Designed to improve upon the current standard of care

	PEAK INVESMENT YEAR	PHASE 3 TRIAL NAME	STATUS	INDICATION	PATIENTS (MAJOR MARKETS[1,2])	MARKET POTENTIAL (MAJOR MARKETS[2])
CAS HIF-2α small molecule inhibitor	2027+	PEAK-1	To Begin Shortly	Post-IO ccRCC	19K	**~$2B**
		eVOLVE RCC02	To Begin Shortly	IO-naive ccRCC	21K	**~$3B**
DOM (+ ZIM) Fc-silent anti-TIGIT mAb + anti-PD-1 mAb	2025	STAR-221	Data Expected 2026 (event-driven)	1L Gastric/GEJ/EAC – all comers	105K	**~$3B**
		STAR-121	Ongoing	1L NSCLC – all comers	307K	**~$10B**
		PACIFIC-8	Ongoing	Stage 3 NSCLC, PD-L1>1%	35K[3]	**~$2B**
QUEMLI CD73 small molecule inhibitor	2025	PRISM-1	Ongoing	1L PDAC	109K	**>$4B**

1L: first-line; 2L: second-line; 3L: third-line; casdatifan; ccRCC: clear cell renal cell carcinoma; dom: domvanalimab; EAC: esophageal adenocarcinoma; GEJ: gastroesophageal junction; IO: immunotherapy; mAb: monoclonal antibody; NSCLC: non-small cell lung cancer; PDAC: pancreatic ductal adenocarcinoma; quemli: quemliclustat; zim: zimberelimab

1. Drug Treatable Addressable Populations (Major Markets, 2024); Decision Resources Group, Arcus analysis
2. Major Markets (US, EU5, JP) - total projected 2034 PD-(L)1 + TIGIT opportunity, Q opportunity & Hif2α opportunity
3. cCRT responding patients

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Appendix

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

PATIENT POPULATION:

- Advanced ccRCC
- **No prior systemic therapy for a/m RCC**

PHASE 1B

R 1:1

- **ARM 1A** volrustomig + casdatifan
- **ARM 1B** volrustomig + casdatifan

PRIMARY ENDPOINT:

- Safety

SECONDARY ENDPOINTS:

- ORR, DOR, PFS, DCR

PHASE 3

R 1:1:1

- **ARM 3A** volrustomig + casdatifan
- **ARM 3B** volrustomig monotherapy
- **ARM 3C (SOC)** nivolumab + ipilimumab

PRIMARY ENDPOINTS:

- PFS
- OS

KEY SECONDARY ENDPOINTS:

- ORR, DOR

Sponsored by AstraZeneca | Expected to Initiate Soon

1L: first-line; a/m: advanced or metastatic; cas: casdatifan; ccRCC: clear cell renal cell carcinoma; DCR: disease control rate; DOR: duration of response; I: intermediate risk; IMDC: International Metastatic RCC Database Consortium: IO: immunotherapy; ORR: objective response rate; OS: overall survival; P: poor risk; PFS: progression free survival; RCC: renal cell carcinoma

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