NEWS RELEASE

New Research Published in Nature Links Clinical Activity with HIF-2a Biology in Advanced Kidney Cancer Patients Treated with Casdatifan

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- This is the first study to comprehensively interconnect clinical outcomes from patients receiving a HIF-2a inhibitor with peripheral biomarker changes and associated tumor biology
- HIF-2a inhibition with casdatifan resulted in deep and sustained suppression of the hormone erythropoietin in blood (serum EPO), which correlated with higher response rates and longer progression-free survival (PFS)
- A pooled analysis from four monotherapy cohorts (n=121) of the ARC-20 study showed that advanced kidney cancer patients treated with casdatifan lived beyond a year without cancer progression (median PFS of 12.2 months) despite multiple prior treatments with other standard regimens

HAYWARD, Calif.--(BUSINESS WIRE)-- Arcus Biosciences, Inc. (NYSE: RCUS), a clinical-stage, global biopharmaceutical company focused on developing differentiated molecules and combination therapies for people with cancer and inflammatory and autoimmune diseases, today announced a publication in Nature describing new research from the ARC-20 study. The publication evaluated casdatifan, an investigational, small-molecule HIF-2a inhibitor, as a monotherapy in patients with metastatic clear cell renal cell carcinoma (ccRCC). It is the first study to comprehensively describe the relationship between HIF-2a inhibitor-associated changes in circulating serum EPO, tumor biology and corresponding clinical activity. The study showed that in ccRCC patients with HIF-2a-driven tumors, deeper suppression of HIF-2a-associated production of serum EPO correlated with clinical benefit, including higher response rates and longer PFS.

“This is the first study to comprehensively assess the relationship between HIF-2a inhibitor-associated suppression

of serum EPO production with tumor biology and clinical outcomes," said Toni K. Choueiri, M.D., director of the Lank Center for Genitourinary (GU) Oncology at Dana-Farber Cancer Institute, the Jerome and Nancy Kohlberg chair and professor of medicine at Harvard Medical School, and lead investigator of ARC-20. "These findings were elucidated in parallel with demonstrating the meaningful clinical benefit of casdatifan, an investigational, HIF-2a inhibitor in development for the treatment of kidney cancer. Patients treated with casdatifan had a median progression-free survival of over one year despite half of patients having progressed on three or more prior treatments with other standard therapies."

The data showed that casdatifan monotherapy resulted in deep and sustained suppression of serum EPO, further validating EPO as a biomarker of HIF-2a inhibition. Deep suppression of serum EPO was correlated with higher response rates and longer PFS. High HIF-2a activity, as determined by expression of key genes in the HIF-2a pathway and baseline tumor EPO levels (evaluated by RNA levels and tissue imaging), correlated with improved clinical outcomes during casdatifan treatment. Taken together, these measures consistently supported the same conclusion and provide strong evidence linking the biology of HIF-2a-driven tumors to patient outcomes with casdatifan.

"The comprehensive translational work published in Nature validates EPO as a biomarker for HIF-2a suppression and correlates dramatic and sustained EPO suppression to durable response with monotherapy casdatifan," said Richard Markus, M.D., Ph.D., chief medical officer at Arcus Biosciences. "We believe this new research provides unambiguous evidence that casdatifan is a best-in-class HIF-2a inhibitor, and we are rapidly advancing a comprehensive development strategy so that every ccRCC patient has the opportunity to benefit from casdatifan across each line of therapy."

Arcus's holistic development strategy is intended to provide physicians and patients with: 1) a casdatifan-based TKI-sparing first-line treatment; 2) a casdatifan-based TKI-inclusive first-line regimen; 3) a second-line HIF-2a inhibitor treatment that builds on the second-line standard-of-care TKI, cabozantinib; and 4) a late-line therapy that has been clinically validated to also provide benefit in patients previously treated with a HIF-2a inhibitor-based therapy.

This research focused on various cohorts of the ARC-20 platform study that evaluated casdatifan monotherapy in patients with metastatic ccRCC. Four monotherapy cohorts (n=121) were included, across doses of 50mg twice daily (BID), 50mg once daily (QD), 100mg QD (tablet) and 150mg QD. Most of the patients had progressed on at least two prior lines of therapy, including both an anti-PD-1 and a VEGFR TKI. The patient population was heavily pretreated; in the pooled analysis, more than half (55%) of patients received at least three prior lines of therapy, and more than one quarter (29%) had received at least four prior lines of therapy. Most patients (71%) had an International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) risk factor of intermediate or poor.

At the time of the data cutoff (DCO, August 15, 2025), casdatifan produced durable antitumor activity. In the 100mg

QD tablet cohort, the confirmed objective response rate (cORR) was 35% and median PFS (mPFS) had not yet been reached, with 60% of patients remaining progression-free at 12 months. In the pooled analysis of all four monotherapy cohorts (n=121), cORR was 31% and mPFS was 12.2 months, with continued reductions in tumor size observed beyond 12 months of treatment.

In a later analysis with a January 30, 2026 DCO, conducted after these results were submitted for publication, mPFS was 15.1 months in the 100mg QD cohort, the same dose and formulation being used in the ongoing PEAK-1 Phase 3 study.

	100mg QD Tablet (Phase 3 dose) (n=31)	Pooled Analysis (50mg BID, 50mg QD, 100mg QD, 150mg QD) (n=121)
Efficacy		
Median Follow-Up	12.4 months	15.5 months
Median PFS [95% CI]	Not estimable [5.7,NE]	12.2 months [9.4,20.6]
12-month PFS [95% CI]	60% [40,75]	50% [41,59]
6-month PFS [95% CI]	67% [48,81]	63% [54,71]
Confirmed ORR [95% CI]	35% (11) [19,55]	31% (38) [23,40]
Confirmed BOR CR PR SD PD	 0 35% (11) 48% (15) 10% (3)	 <1% (1) 31% (37) 50% (60) 17% (21)
Median Time to Response	2.6 months	2.8 months
Disease Control Rate [95% CI]	84% (26) [66,95]	81% (98) [73,88]

BOR: best overall response; CI: confidence interval; CR: complete response; cORR: confirmed objective response rate; NE: not estimable; PD: progressive disease; PFS: progression-free survival; PR: partial response; SD: stable disease

At the time of the August 2025 DCO, no unexpected safety signals were observed, and casdatifan had an acceptable and manageable safety profile across all doses. The most common class-effect events were anemia and hypoxia; across all four cohorts, no patients discontinued treatment due to anemia, and three patients (2%) discontinued due to hypoxia.

	100mg QD Tablet (Phase 3 Dose) (n=32)	Pooled Analysis (50mg BID, 50mg QD, 100mg QD, 150mg QD) (n=127)
Safety		
Any Serious TEAEs	31% (10)	31% (39)
Grade ≥3 TEAEs related to casdatifan		
Anemia	25% (8)	41% (52)
Hypoxia	9% (3)	11% (14)
TEAEs resulting in discontinuation	9% (3)	9% (11)
Anemia	0	0% (0)
Hypoxia	3% (1)	2% (3)

TEAE: treatment-emergent adverse event

About Casdatifan (AB521)

Casdatifan is a small-molecule inhibitor of hypoxia-inducible factor 2-alpha (HIF-2a), a master switch that turns on hundreds of genes in response to low oxygen levels. In a majority of people with the most common form of kidney cancer (clear cell renal cell carcinoma), genetic anomalies result in the dysregulation of this master switch and transformation of normal kidney cells into cancerous ones.

Casdatifan was designed to provide deep and durable inhibition of the HIF-2a pathway. Early clinical studies have shown high response rates and a low primary progression rate relative to clinical benchmarks, warranting further investigation in late-stage studies. Casdatifan, which is administered in pill form once daily, has a safety profile that allows it to be investigated in combination with other treatments.

The casdatifan development strategy is designed to generate evidence needed to establish casdatifan as a backbone therapy so that every ccRCC patient has the opportunity to benefit from casdatifan across each line of therapy. In addition to partner-operationalized studies, including combinations with casdatifan and anti-PD-X/VEGF bispecifics, Arcus is investigating casdatifan across multiple cohorts in the ARC-20 platform study, alone and in combination with other potential new treatment options, including in:

- the first-line setting with cohorts evaluating casdatifan plus zimberelimab, an anti-PD-1 (ongoing); casdatifan plus zimberelimab and ipilimumab, an anti-CTLA-4 (ongoing); and casdatifan plus an anti-PD-1/VEGF bispecific (planned)
- the second-line setting with a cohort evaluating casdatifan plus cabozantinib, a TKI, in immunotherapy-experienced patients (ongoing)
- a cohort evaluating casdatifan plus a TKI, in HIF-2a inhibitor-experienced patients (planned)

Arcus is also enrolling PEAK-1, the global Phase 3 study evaluating casdatifan plus cabozantinib versus cabozantinib in IO-experienced patients with metastatic ccRCC. Arcus expects to complete enrollment in PEAK-1 and to initiate a Phase 3 study in the first-line metastatic ccRCC setting by year-end 2026.

Casdatifan is an investigational molecule. Approval from any regulatory authority for its use has not been received, and its safety and efficacy have not been established. Taiho has development and commercial rights in Japan and other countries in Asia, excluding China. Arcus Biosciences holds full rights to casdatifan everywhere else globally.

About Kidney Cancer

According to the American Cancer Society, kidney cancer is among the top 10 most commonly diagnosed forms of cancer among both men and women in the U.S., and an estimated 80,450 Americans will be diagnosed with kidney cancer in 2026. ccRCC is the most common type of kidney cancer in adults. If detected in its early stages, the five-year survival rate for kidney cancer is high; for patients with advanced or late-stage metastatic kidney cancer, however, the five-year survival rate is only 19%. For metastatic kidney cancer, targeted drug therapies are one of the main treatment options.

About Arcus Biosciences

Arcus Biosciences is a clinical-stage, global biopharmaceutical company focused on developing differentiated molecules for the treatment of cancer and inflammatory and autoimmune diseases. In partnership with industry collaborators, patients and physicians around the world, Arcus is expediting the development of its late-stage portfolio of first- and/or best-in-class medicines against well-characterized biological targets and pathways and studying novel, biology-driven combinations that have the potential to help people with cancer live longer. Founded in 2015, the company has advanced multiple investigational medicines into registrational clinical trials including casdatifan, a HIF-2a inhibitor for clear cell renal cell carcinoma, and quemliclustat, a small-molecule CD73 inhibitor for pancreatic cancer. For more information about Arcus Biosciences' clinical and preclinical programs, please visit **www.arcusbio.com**.

Arcus Forward-Looking Statements

This press release contains forward-looking statements. All statements regarding events or results to occur in the future contained herein are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to, Arcus's development strategy and plans for casdatifan across each line of therapy. All forward-looking statements involve known and unknown risks and uncertainties and other important factors that may cause Arcus's actual results, performance or achievements to differ materially from those expressed or implied

by the forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, risks associated with: interim data not being a guarantee of future data and may not be replicated in other studies evaluating casdatifan, including the Phase 3 PEAK-1 study; the unexpected emergence of adverse events or other undesirable side effects with casdatifan; risks associated with manufacturing or supplying product for clinical trials evaluating casdatifan; changes in the competitive landscape for Arcus's programs; and the inherent uncertainty associated with pharmaceutical product development and clinical trials. Risks and uncertainties facing Arcus are described more fully in the "Risk Factors" section of Arcus's most recent periodic report filed with the U.S. Securities and Exchange Commission (SEC) and in other filings that Arcus makes with the SEC from time to time, which are available at **www.sec.gov**. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this press release. Arcus disclaims any obligation or undertaking to update, supplement or revise any forward-looking statements contained in this press release, except to the extent required by law.

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