



NEWS RELEASE

Arcus Biosciences Presents Promising Initial Data from Phase 1 Portion of ARC-8 Study for AB680 in Metastatic Pancreatic Cancer

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- 41% objective response rate (ORR) observed to-date across first four cohorts in the Phase 1 dose-escalation portion of ARC-8, comparing favorably to the current standard-of-care

- Initiated Phase 1b expansion portion of study

HAYWARD, Calif.--(BUSINESS WIRE)-- Arcus Biosciences, Inc. (NYSE:RCUS), an oncology-focused biopharmaceutical company working to create best-in-class cancer therapies, today presented preliminary data from the dose-escalation portion of its ARC-8 Phase 1/1b study, evaluating the safety and tolerability of AB680, the first small-molecule CD73 inhibitor to enter the clinic, in metastatic pancreatic cancer at the ASCO 2021 Virtual Gastrointestinal Cancers Symposium (ASCO GI).

The ongoing, open-label, multicenter trial is a Phase 1/1b study evaluating the safety profile and clinical activity of AB680 in combination with nab-paclitaxel plus gemcitabine (NP/Gem) and zimberelimab, an anti-PD-1 antibody, as a first-line treatment in patients with metastatic pancreatic ductal adenocarcinoma (PDAC).

- Preliminary Safety Results (as of the safety DCO of Nov. 11th 2020)
 - 19 patients had received AB680 plus NP/Gem plus zimberelimab at doses of AB680 ranging from 25 to 100 mg, administered once every two weeks.
 - Across all four dose-escalation cohorts, no significant additive toxicity from AB680 plus NP/Gem plus zimberelimab has been observed beyond that expected from NP/Gem plus anti-PD-1 combined.

- One dose-limiting toxicity (Grade 2 autoimmune hepatitis) occurred in the 50mg AB680 cohort; the event resolved completely with steroid treatment, and the patient resumed study treatment, including immunotherapy, without subsequent autoimmune events.
 - The most common treatment emergent adverse events (AE) were fatigue (68%), anemia (53%), alopecia (42%), diarrhea (42%) and neutrophil count decrease (42%). These AE results are very similar to what would be expected with NP/Gem alone.
- Since the safety DCO, no additional dose-limiting toxicities have been reported.
- Preliminary Efficacy Results (as of the efficacy DCO of Dec. 9th 2020)
 - 17 out of 19 patients enrolled in the Phase 1 dose-escalation portion of the study were evaluable for response, and 16 of the evaluable patients remained on active treatment at the time of the efficacy DCO.
 - 88% (15/17) of patients experienced at least some shrinkage of their lesions.
 - 41% ORR (7/17) was observed for the AB680 combination across all dose-escalation cohorts, including one patient who converted to a complete response for both target and non-target lesions since the efficacy DCO.
 - Of the partial responses (PRs), 3 are confirmed responses and of the 4 unconfirmed responders, 3 responded at the first tumor assessment and the fourth responded at the second tumor assessment, and all remain on study.
 - For patients that had been on drug for more than 16 weeks, an 85% disease control rate (11/13) was achieved with the AB680 combination.
 - Treatment benefit appears durable; of the evaluable patients from the first three dose-escalation cohorts, 10 of 12 (83%) continue on treatment with a median time on treatment of 180 days.
 - The last drug to be approved in the first-line metastatic pancreatic cancer setting is Abraxane® (nab-paclitaxel). As stated in the FDA approved label for Abraxane® (nab-paclitaxel) for use in combination with gemcitabine in first-line metastatic pancreatic cancer:
 - The ORR from the registrational Phase 3 study was 23%.^{1,2}
 - A 48% DCR (>16 weeks) was achieved in the registrational Phase 3 study.

“Based on the results to date, 100mg of AB680 every two weeks has been selected as the dose for the Phase 1b expansion portion of the trial. Given the lack of toxicity observed from the addition of AB680 to chemotherapy and anti-PD-1 therapy to date, we are also evaluating a 125mg every two weeks cohort,” said Bill Grossman, MD, PhD, Chief Medical Officer of Arcus. “We believe that AB680 has the potential to represent the first meaningful advancement for the treatment of pancreatic cancer since Abraxane was approved in 2013. Assuming AB680 continues to show encouraging clinical activity in the ongoing expansion portion of the trial, we expect to open a randomized control arm in ARC-8 shortly.”

"I am encouraged by the emerging safety and efficacy data from this AB680-based novel therapeutic regimen in my patients," said Johanna Bendell, MD, Chief Development Officer and Director, Drug Development Unit Nashville, Sarah Cannon Research Institute at Tennessee Oncology. "The initial response rate is promising, and thus far there has not been significant additive toxicity from AB680 to chemotherapy. There is a need for advances in the treatment of metastatic pancreatic cancer, and this unique molecule has the potential to improve outcomes for patients with this difficult-to-treat disease. I look forward to continuing to work closely with the Arcus team to further evaluate the role of AB680."

Even with recent advancements in cancer therapies, such as anti-PD-1 antibodies, additional clinical benefit over NP/Gem alone has not been demonstrated in pancreatic cancer. Overall, PDAC has a 5-year survival rate of less than 10%,^{1,3} and high expression of CD73 has been shown to be associated with poor prognosis.⁴ One hypothesis is that the presence of high adenosine levels in the tumor impairs the ability of the highly immunogenic standard-of-care chemotherapeutic regimen to generate a full T cell response. Therefore, blockade of adenosine generation by inhibiting CD73 may restore this immune response, which may be further enhanced by the addition of anti-PD-1 therapy.

Arcus expects to report more mature data from the Phase 1/1b portions of ARC-8, including data on progression-free survival, at medical conferences later this year.

Additional information about the data may be found in the poster presented at ASCO GI, which is located on the Arcus website at **Arcus Publications**.

Pancreatic Cancer

Pancreatic cancer is the fourth leading cause of cancer-related deaths in Europe and the United States¹ and the seventh leading cause of cancer-related deaths worldwide³.

Pancreatic ductal adenocarcinoma (PDAC) is the most prevalent neoplastic disease of the pancreas, with high metastatic potential, accounting for more than 90% of all pancreatic malignancies and is a highly devastating disease with poor prognosis and rising incidence.^{5,6}

Few treatment options exist for metastatic pancreatic cancer, and response rates to the standard of care therapy of gemcitabine/nab-paclitaxel remain very low. Based on the FDA approved label for nab-paclitaxel in combination with gemcitabine, the phase 3 registrational trial demonstrated objective and complete response rates in patients with metastatic pancreatic cancer that were 23% and <1%, respectively.^{1,2}

To date, addition of anti-PD-1 antibodies to gemcitabine/nab-paclitaxel in controlled clinical trials in this setting has

shown no added benefit when compared to that obtained with the chemotherapy alone.^{7,8}

About ARC-8 Study

ARC-8 is a Phase 1/1b study to evaluate safety and tolerability of AB680 + zimberelimab (AB122) + chemotherapy in patients with treatment-naïve metastatic pancreatic adenocarcinoma.

For additional information on this trial (NCT04104672), please visit www.clinicaltrials.gov.

About AB680

AB680 is an extremely potent and selective small-molecule CD73 inhibitor designed to provide differential benefits relative to monoclonal antibodies, such as greater inhibition of CD73 enzymatic activity (both soluble and cell-bound) and deeper tumor penetration. CD73 is the primary enzymatic producer of immunosuppressive adenosine in the tumor microenvironment, and high CD73 expression is associated with significantly poorer prognosis in several tumor types, including pancreatic cancer.⁴ By effectively eliminating CD73-derived adenosine, AB680 may improve the efficacy of treatment approaches expected to elicit anti-cancer immune responses (e.g., platinum-based chemotherapy with/without anti-PD-1 therapy). AB680 was the first small-molecule CD73 inhibitor to enter the clinic and demonstrated a favorable safety profile with a long half-life in a healthy volunteer study. AB680 is currently in a Phase 1/1b study for the treatment of first-line metastatic pancreatic cancer.

About Arcus Biosciences

Arcus Biosciences is an oncology-focused biopharmaceutical company leveraging its deep cross-disciplinary expertise to discover highly differentiated therapies and to develop a broad portfolio of novel combinations addressing significant unmet needs. Arcus currently has four molecules in clinical development: **Etrumadenant (AB928)**, the first dual A2a/A2b adenosine receptor antagonist to enter the clinic, is being evaluated in multiple Phase 2 and 1b studies across different indications, including prostate, colorectal, non-small cell lung, pancreatic and triple-negative breast cancers. **AB680**, the first small-molecule CD73 inhibitor to enter the clinic, is in Phase 1/1b development for first-line treatment of metastatic pancreatic cancer in combination with zimberelimab and gemcitabine/nab-paclitaxel. **Domvanalimab (AB154)**, an anti-TIGIT monoclonal antibody and new potential immuno-oncology backbone therapy, is in a three-arm randomized Phase 2 study for first-line treatment of PD-L1-high metastatic non-small cell lung cancer (NSCLC) evaluating zimberelimab monotherapy, domvanalimab with zimberelimab and domvanalimab plus AB928 with zimberelimab. In addition, domvanalimab is advancing into ARC-10, Arcus's "two in one trial" to support the potential approvals of both zimberelimab and zimberelimab + domvanalimab and a registrational study, in collaboration with AstraZeneca, evaluating the curative-intent stage III NSCLC setting. **AB308**, an anti-TIGIT antibody that is FcR enabled, is advancing into clinical development to

investigate additional indications, with a focus on hematological malignancies. **Zimberelimab (AB122)**, Arcus's anti-PD-1 monoclonal antibody, was in-licensed to enable the development of Arcus's combination regimens and is being evaluated in various combinations across the portfolio. For more information about Arcus Biosciences, please visit www.arcusbio.com.

Forward-Looking Statements

This press release contains forward-looking statements. All statements other than statements of historical facts contained herein, including, but not limited to, the potential benefit of AB680 combination therapy for patients with pancreatic cancer, Arcus's development plans for AB680 and the progress and anticipated milestones from the ARC-8 study, 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. All forward-looking statements involve known and unknown risks, uncertainties and other important factors that may cause Arcus's actual results, performance or achievements to differ significantly from those expressed or implied. Factors that could cause or contribute to such differences include, but are not limited to: the inherent uncertainty associated with pharmaceutical product development and clinical trials; risks associated with preliminary and interim data; the emergence of adverse events or other undesirable side effects; delays in our clinical trials due to difficulties or delays in the regulatory process, enrolling subjects or manufacturing or supplying product for such clinical trials; the inherent uncertainty associated with the COVID-19 pandemic, including the duration and/or severity of the outbreak and actions by government authorities to contain or slow the spread of the virus; and changes in the competitive landscape for our programs. Risks and uncertainties facing Arcus are described more fully in Arcus's quarterly report on Form 10-Q for the quarter ended September 30, 2020 filed on November 5, 2020 with the SEC. You are cautioned not to place undue reliance on the 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.

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