2seventy bio Announces Additional Data from KarMMa Studies of Abecma (idecabtagene vicleucel) at ASCO 2023 and EHA 2023

May 11, 2023 4:37 PM EDT

Subgroup analysis of outcomes for patients with high-risk relapsed and refractory multiple myeloma (RRMM) from the pivotal Phase 3 KarMMa-3 trial accepted for oral presentation at EHA

Analysis from KarMMa-3 study of health-related quality of life in patients who received Abecma *will be presented at ASCO*

Breadth of data underscores 2seventy bio's commitment to meeting the individual needs of patients with RRMM or newly diagnosed multiple myeloma

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 11, 2023-- 2seventy bio, Inc. (Nasdaq: TSVT) today announced the presentation of four abstracts at the American Society of Clinical Oncology (ASCO) Annual Meeting taking place from June 2-6, 2023 in Chicago, Illinois and six abstracts at the European Hematology Association (EHA) Congress, taking place in Frankfurt, Germany from June 8-11, 2023.

The presentations will highlight clinical and correlative data from the KarMMa-2 and KarMMa-3 clinical trials evaluating *Abecma* (idecabtagene vicleucel) in patients with relapsed and/or refractory multiple myeloma (RRMM) or newly diagnosed multiple myeloma.

"These data highlight the growing body of evidence that further support the value of Abecma across various subgroups of patients with triple-class-exposed relapsed and/or refractory multiple myeloma, who, despite recent advancements, still need more effective treatment options sooner," said Steve Bernstein, M.D., chief medical officer, 2seventy bio. "We are pleased to share new findings of Abecma from KarMMa-3, including an analysis of health-related quality of life in patients with RRMM, a subgroup analysis of outcomes for patients with high-risk disease, and a biomarker correlative analysis of response to Abecma. We remain committed to bringing this innovative CAR T cell therapy to patients earlier in their treatment course."

Key abstracts include:

- Subgroup analysis of outcomes with *Abecma* in high-risk patient groups from the Phase 3 KarMMa-3 clinical study in patients with triple-class exposed RRMM.
- Additional analysis of outcomes by number of prior lines of therapy from the KarMMa-3 clinical trial showcasing the use of *Abecma* in patients who received two to four prior lines of therapy.
- Patient-reported outcomes from the pivotal Phase 3 KarMMa-3 trial in patients with triple-class exposed RRMM treated with *Abecma* versus standard regimens.

The full list of accepted data abstracts include:

ASCO 2023 Presentation Details

Poster Presentation [#8031]: Baseline and early post-infusion biomarkers associated with optimal response to idecabtagene vicleucel (ide-cel) in the KarMMa-3 study of triple-class–exposed (TCE) relapsed and refractory multiple myeloma (RRMM)
Presenting Author: Julia Piasecki, Bristol Myers Squibb
Date/Time: Monday, June 5, 2023, 8:00 – 11:00 a.m. CDT

Poster Presentation [#8032]: Health related quality of life (HRQoL) in patients with triple-class-exposed relapsed/refractory multiple myeloma (TCE RRMM) treated with idecabtagene vicleucel (ide-cel) versus standard regimens: patient-reported outcomes (PROs) from KarMMa-3 phase 3 randomized controlled trial (RCT)
Presenting Author: Michel Delforge, M.D., Ph.D., University of Leuven, Leuven, Belgium
Date/Time: Monday, June 5, 2023, 8:00 – 11:00 a.m. CDT

Poster Presentation [#8035]: Tumor-intrinsic features associated with progression-free survival (PFS) in patients (pts) with relapsed and refractory multiple myeloma (RRMM) treated with idecabtagene vicleucel (ide-cel)
Presenting Author: Nicholas Stong, Ph.D., Bristol Myers Squibb
Date/Time: Monday, June 5, 2023, 8:00 – 11:00 a.m. CDT

Poster Presentation [e-pub only]: Baseline characteristics identifying patients (pts) with multiple myeloma (MM) treated with idecabtagene vicleucel (ide-cel; bb2121) who are at risk for severe/refractory inflammatory adverse events (iAEs)
Presenting Author: Afshin Mashadi-Hossein, Bristol Myers Squibb
Date/Time: N/A

EHA 2023 Presentation Details

Oral Presentation [#S195]: Idecabtagene vicleucel (ide-cel) vs standard regimens in patients with triple-class–exposed (TCE) relapsed and refractory multiple myeloma (RRMM): a KarMMa-3 analysis in high-risk subgroups
Presenting Author: Krina Patel, M.D., MD Anderson Cancer Center, University of Texas, Houston, Texas
Date/Time: Saturday, June 10, 2023, 4:30 – 5:45 p.m. CEST

Poster Presentation [#P801]: Baseline and early post-infusion biomarkers associated with optimal response to idecabtagene vicleucel (ide-cel) in KarMMa-3 study of triple class exposed relapsed and refractory multiple myeloma
Presenting Author: Marc S. Raab, M.D., Heidelberg University Hospital, Heidelberg, Germany
Date/Time: Friday, June 9, 2023, 6:00 - 7:00 p.m. CEST

Poster Presentation [#P809]: Baseline characteristics identifying patients with multiple myeloma treated with idecabtagene vicleucel (ide-cel; bb2121) who are at risk for severe/refractory inflammatory adverse events
Presenting Author: Yi Lin, M.D., Ph.D., Mayo Clinic, Rochester, Minn.
Date/Time: Friday, June 9, 2023, 6:00 - 7:00 p.m. CEST

Poster Presentation [#P866]: Idecabtagene vicleucel (ide-cel) vs standard regimens in patients with triple-class-exposed (TCE) relapsed and refractory multiple myeloma (RRMM): KarMMa-3 subgroup analysis by prior lines of therapy
Presenting Author: Salomon Manier, Centre Hospitalier Universitaire de Lille, Université de Lille, Lille, France
Date/Time: Friday, June 9, 2023, 6:00 - 7:00 p.m. CEST

Poster Presentation [#P871]: Idecabtagene vicleucel (ide-cel) in patients with an inadequate response to frontline autologous stem cell transplantation (ASCT): results from KarMMa-2 cohort 2c
Presenting Author: Melissa Alsina, M.D., Moffitt Cancer Center, Tampa, Fla.
Date/Time: Friday, June 9, 2023, 6:00 - 7:00 p.m. CEST

Poster Presentation [#P905]: Patient reported outcomes in triple class exposed, relapsed/refractory multiple myeloma (TCE RRMM) patients in KarMMa-3 trial (phase 3 RCT): idecabtagene vicleucel (ide-cel) versus standard regimens
Presenting Author: Michel Delforge, M.D., Ph.D., University of Leuven, Leuven, Belgium
Date/Time: Friday, June 9, 2023, 6:00 - 7:00 p.m. CEST

About KarMMa-3

KarMMa-3 (NCT03651128) is a pivotal, Phase 3, open-label, global, randomized, controlled trial evaluating *Abecma* compared to standard regimens in patients with relapsed and refractory multiple myeloma who have received two to four prior lines of treatment, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody, and were refractory to the last treatment regimen. Patients were randomized to receive *Abecma* or standard regimens that consisted of combinations that included daratumumab, pomalidomide, and dexamethasone (DPd), daratumumab, bortezomib, and dexamethasone (DVd), ixazomib, lenalidomide, and dexamethasone (IRd), carfilzomib and dexamethasone (Kd) or elotuzumab, pomalidomide and dexamethasone (EPd) chosen based on their most recent treatment regimen and investigator discretion. The primary endpoint evaluated in this study is progression-free survival, defined as time from randomization to the first documentation of progressive disease or death due to any cause, whichever occurs first. Key secondary endpoints include overall response rate and overall survival.

About *Abecma*

Abecma recognizes and binds to BCMA on the surface of multiple myeloma cells leading to CAR T cell proliferation, cytokine secretion, and subsequent cytolytic killing of BCMA-expressing cells. *Abecma* is being jointly developed and commercialized in the U.S. as part of a Co-Development, Co-Promotion, and Profit Share Agreement between Bristol Myers Squibb and 2seventy bio.

The companies' broad clinical development program for *Abecma* includes clinical studies (KarMMa-2, KarMMa-3, KarMMa-9) in earlier lines of treatment for patients with multiple myeloma. For more information visit clinicaltrials.gov.

Indication

ABECMA (idecabtagene vicleucel) is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

Important Safety Information

BOX WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, AND PROLONGED CYTOPENIA

- Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients following treatment with ABECMA. Do not administer ABECMA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.
- Neurologic Toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS. Monitor for neurologic events after treatment with ABECMA. Provide supportive care and/or corticosteroids as needed.
- Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS) including fatal and life-threatening reactions, occurred in patients following treatment with ABECMA. HLH/MAS can occur with CRS or neurologic toxicities.
- Prolonged Cytopenia with bleeding and infection, including fatal outcomes following stem cell transplantation for hematopoietic recovery, occurred following treatment with ABECMA.
- ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS.

WARNINGS AND PRECAUTIONS:

Cytokine Release Syndrome (CRS): CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA in 85% (108/127) of patients. Grade 3 or higher CRS occurred in 9% (12/127) of patients, with Grade 5 CRS reported in one (0.8%) patient. The median time to onset of CRS, any grade, was 1 day (range: 1 - 23 days) and the median duration of CRS was 7 days (range: 1 - 63 days). The most common manifestations included pyrexia, hypotension, tachycardia, chills, hypoxia, fatigue, and headache. Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, acute respiratory distress syndrome (ARDS), atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, multiple organ dysfunction syndrome, and HLH/MAS.

Identify CRS based on clinical presentation. Evaluate for and treat other causes of fever, hypoxia, and hypotension. CRS has been reported to be associated with findings of HLH/MAS, and the physiology of the syndromes may overlap. In patients with progressive symptoms of CRS or refractory CRS despite treatment, evaluate for evidence of HLH/MAS.

Fifty four percent (68/127) of patients received tocilizumab (single dose: 35%; more than 1 dose: 18%). Overall, 15% (19/127) of patients received at least 1 dose of corticosteroids for treatment of CRS. All patients that received corticosteroids for CRS received tocilizumab. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs or symptoms of CRS and monitor patients for signs or symptoms of CRS for at least 4 weeks after ABECMA infusion. At the first sign of CRS, institute treatment with supportive care, tocilizumab and/or corticosteroids as indicated.

Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Neurologic Toxicities: Neurologic toxicities, which may be severe or life-threatening, occurred following treatment with ABECMA, including concurrently with CRS, after CRS resolution, or in the absence of CRS. CAR T cell-associated neurotoxicity occurred in 28% (36/127) of patients receiving ABECMA, including Grade 3 in 4% (5/127) of patients. One patient had ongoing Grade 2 neurotoxicity at the time of death. Two patients had ongoing Grade 1 tremor at the time of data cutoff. The median time to onset of neurotoxicity was 2 days (range: 1 - 42 days). CAR T cell-associated neurotoxicity resolved in 92% (33/36) of patients with a median duration of neurotoxicity was 5 days (range: 1 - 61 days). The median duration of neurotoxicity was 6 days (range: 1 - 578) in all patients including those with ongoing neurotoxicity at the time of death or data cut off. Thirty-four patients with neurotoxicity had CRS. Neurotoxicity had onset in 3 patients before, 29 patients during, and 2 patients after CRS. The rate of Grade 3 neurotoxicity was 8% in the 450 x 10^6 CAR+ T cell dose cohort and 1.4% in the 300 x 10^6 CAR+ T cell dose cohort. The most frequently reported (greater than or equal to 5%) manifestations of CAR T cell-associated neurotoxicity include encephalopathy (20%), tremor (9%), aphasia (7%), and delirium (6%). Grade 4 neurotoxicity and cerebral edema in 1 patient has been reported with ABECMA in another study in multiple myeloma. Grade 3 myelitis and Grade 3 parkinsonism have been reported after treatment with ABECMA in another study in multiple myeloma.

Monitor patients at least daily for 7 days following ABECMA infusion at the REMS-certified healthcare facility for signs and symptoms of neurologic toxicities. Rule out other causes of neurologic symptoms. Monitor patients for signs or symptoms of neurologic toxicities for at least 4 weeks after infusion and treat promptly. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed.

Counsel patients to seek immediate medical attention should signs or symptoms of neurologic toxicity occur at any time.

Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS): HLH/MAS occurred in 4% (5/127) of patients receiving ABECMA. One patient developed fatal multi-organ HLH/MAS with CRS and another patient developed fatal bronchopulmonary aspergillosis with contributory HLH/MAS. Three cases of Grade 2 HLH/MAS resolved. All events of HLH/MAS had onset within 10 days of receiving ABECMA with a median onset of 7 days (range: 4 - 9 days) and occurred in the setting of ongoing or worsening CRS. Two patients with HLH/MAS had overlapping neurotoxicity. The manifestations of HLH/MAS include hypotension, hypoxia, multiple organ dysfunction, renal dysfunction, and cytopenia. HLH/MAS is a potentially life-threatening condition with a high mortality rate if not recognized early and treated. Treatment of HLH/MAS should be administered per institutional guidelines.

ABECMA REMS: Due to the risk of CRS and neurologic toxicities, ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS. Further information is available at www.AbecmaREMS.com or 1-888-423-5436.

Hypersensitivity Reactions: Allergic reactions may occur with the infusion of ABECMA. Serious hypersensitivity reactions, including anaphylaxis, may be due to dimethyl sulfoxide (DMSO) in ABECMA.

Infections: ABECMA should not be administered to patients with active infections or inflammatory disorders. Severe, life-threatening, or fatal infections occurred in patients after ABECMA infusion. Infections (all grades) occurred in 70% of patients. Grade 3 or 4 infections occurred in 23% of patients. Overall, 4 patients had Grade 5 infections (3%); 2 patients (1.6%) had Grade 5 events of pneumonia, 1 patient (0.8%) had Grade 5 bronchopulmonary aspergillosis, and 1 patient (0.8%) had cytomegalovirus (CMV) pneumonia associated with Pneumocystis jirovecii. Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, preemptive, and/or therapeutic antimicrobials according to standard institutional guidelines.

Febrile neutropenia was observed in 16% (20/127) of patients after ABECMA infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids, and other supportive care as medically indicated.

Viral Reactivation: Cytomegalovirus (CMV) infection resulting in pneumonia and death has occurred following ABECMA administration. Monitor and treat for CMV reactivation in accordance with clinical guidelines. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients treated with drugs directed against plasma cells. Perform screening for CMV, HBV, hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines before collection of cells for manufacturing.

Prolonged Cytopenias: In the clinical study, 41% of patients (52/127) experienced prolonged Grade 3 or 4 neutropenia and 49% (62/127) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following ABECMA infusion. In 83% (43/52) of patients who recovered from Grade 3 or 4 neutropenia after Month 1, the median time to recovery from ABECMA infusion was 1.9 months. In 65% (40/62) of patients who recovered from Grade 3 or 4 thrombocytopenia, the median time to recovery was 2.1 months.

Three patients underwent stem cell therapy for hematopoietic reconstitution due to prolonged cytopenia. Two of the three patients died from complications of prolonged cytopenia. Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support.

Hypogammaglobulinemia: Hypogammaglobulinemia was reported as an adverse event in 21% (27/127) of patients; laboratory IgG levels fell below 500 mg/dl after infusion in 25% (32/127) of patients treated with ABECMA.

Monitor immunoglobulin levels after treatment with ABECMA and administer IVIG for IgG <400 mg/dl. Manage appropriately per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

The safety of immunization with live viral vaccines during or after ABECMA treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during ABECMA treatment, and until immune recovery following treatment with ABECMA.

Secondary Malignancies: Patients treated with ABECMA may develop secondary malignancies. Monitor life-long for secondary malignancies. If a secondary malignancy occurs, contact Bristol-Myers Squibb at 1-888-805-4555 to obtain instructions on patient samples to collect for testing of secondary malignancy of T cell origin.

Effects on Ability to Drive and Operate Machinery: Due to the potential for neurologic events, including altered mental status or seizures, patients receiving ABECMA are at risk for altered or decreased consciousness or coordination in the 8 weeks following ABECMA infusion. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.

Adverse Reactions: The most common nonlaboratory adverse reactions (incidence greater than or equal to 20%) include CRS, infections – pathogen unspecified, fatigue, musculoskeletal pain, hypogammaglobulinemia, diarrhea, upper respiratory tract infection, nausea, viral infections, encephalopathy, edema, pyrexia, cough, headache, and decreased appetite.

Please see full Prescribing Information, including **Boxed WARNINGS** and Medication Guide.

About 2seventy bio

Our name, 2seventy bio, reflects why we do what we do - TIME. Cancer rips time away, and our goal is to work at the maximum speed of translating human thought into action – 270 miles per hour – to give the people we serve more time. We are building the leading immuno-oncology cell therapy company, focused on discovering and developing new therapies that truly disrupt the cancer treatment landscape With a deep understanding of the human body's immune response to tumor cells and how to translate cell therapies into practice, we're applying this knowledge to deliver next generation cellular therapies that focus on a broad range of hematologic malignancies, including the first FDA-approved CAR T cell therapy for multiple myeloma, as well as solid tumors. Our research and development is focused on delivering therapies that are designed with the goal to "think" smarter and faster than the disease. Importantly, we remain focused on accomplishing these goals by staying genuine and authentic to our "why" and keeping our people and culture top of mind every day.

For more information, visit www.2seventybio.com.

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2seventy bio Cautionary Note Regarding Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 regarding, among other things, the research, development, and commercialization of Abecma. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on historical performance and current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. These statements include, but are not limited to: statements about our plans, timelines and expectations with respect to the development of ide-cel, including the results and expected timing of ongoing and planned clinical trials; statements about the efficacy and perceived therapeutic benefits of ide-cel and the potential indications and market opportunities and demand therefor. These risks, assumptions, uncertainties, and other factors include, among others, the possibility that ide-cel will not be successful in earlier lines of therapy, may not be commercially successful, that continued approval of such product candidate for such indication described in this release may be contingent upon verification and description of clinical benefit in confirmatory trials, and that the collaboration with Bristol Myers Squibb may not continue or be successful. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect 2seventy bio's business, particularly those identified in the risk factors discussion in 2seventy bio's Annual Report on Form 10-K, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, 2seventy bio undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

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Investors:
Jenn Snyder
617-448-0281
jenn.snyder@2seventybio.com

Media:
Morgan Adams
774.313.9852
morgan.adams@2seventybio.com

Source: 2seventy bio, Inc.