Bristol Myers Squibb and 2seventy bio Announce Top-Line Results from KarMMa-3 Trial Showing Abecma (idecabtagene vicleucel) Significantly Improves Progression- Free Survival Versus Standard Regimens in Relapsed and Refractory Multiple Myeloma

August 10, 2022 10:49 AM EDT

Abecma is the first BCMA-directed CAR T cell therapy to demonstrate superiority versus standard regimens in relapsed and refractory multiple myeloma

(PRINCETON, N.J., & CAMBRIDGE, Mass., AUGUST 10, 2022) -- Bristol Myers Squibb (NYSE: BMY) and 2seventy bio, Inc. (Nasdaq: TSVT) today announced positive topline results from KarMMa-3, a Phase 3, global, randomized, multicenter, open-label study evaluating *Abecma* (idecabtagene vicleucel) compared to standard combination regimens in adults with multiple myeloma that is relapsed and refractory after two to four prior lines of therapy and refractory to the last regimen. KarMMa-3 is the first randomized clinical trial to evaluate a CAR T cell therapy in multiple myeloma. Results of a pre-specified interim analysis conducted through an independent review committee showed that KarMMa-3 met its primary endpoint of demonstrating a statistically significant improvement in progression-free survival. Treatment with *Abecma* also showed an improvement in the key secondary endpoint of overall response rate compared to standard regimens. Follow-up for overall survival, a key secondary endpoint, remains ongoing.

Safety results in the trial were consistent with the well-established and predictable safety profile of *Abecma* previously demonstrated in the pivotal KarMMa trial. No new safety signals were reported in this study.

"Results from the KarMMa-3 study clearly demonstrate the clinical benefit of using a CAR T cell therapy earlier in the multiple myeloma treatment paradigm," said Anne Kerber, senior vice president, head of Cell Therapy Development, Bristol Myers Squibb. "These data reinforce our commitment to unlocking the full potential of cell therapy as we strive to build on the company's heritage of innovation in blood cancers and transform patients' lives through science."

"We are extremely pleased to have met the KarMMa-3 primary endpoint at an interim analysis. These results help to advance our efforts to make *Abecma* available for earlier lines of treatment for patients and we look forward to discussing these results with regulatory authorities," said Steve Bernstein, M.D., chief medical officer, 2seventy bio. "Today's results are another important proof point for the transformative potential of autologous cell therapy and underscore the importance of continuing to study *Abecma* in earlier treatment settings for multiple myeloma."

Bristol Myers Squibb and 2seventy bio will complete a full evaluation of the KarMMa-3 data and work with investigators to present detailed results at an upcoming medical meeting, as well as discuss these results with health authorities. The companies thank the patients and investigators who are participating in the KarMMa-3 clinical trial.

Abecma was approved by the U.S. Food and Drug Administration (FDA) in March 2021 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. Please see the Important Safety Information section below, including **Boxed WARNINGS** for *Abecma* regarding cytokine release syndrome, neurologic toxicities, Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome and Prolonged Cytopenia. *Abecma* is also approved in the European Union, Switzerland, Japan, Canada and the United Kingdom for adult patients with relapsed or refractory multiple myeloma who have received at least three prior therapies.

About KarMMa-3

KarMMa-3 (NCT03651128) is a pivotal, Phase 3, global, randomized, multicenter trial evaluating *Abecma* compared to standard regimens in patients with multiple myeloma that is relapsed and refractory multiple myeloma after two to four prior lines of treatment and refractory to the last treatment regimen. Patients were randomized to receive *Abecma* or standard regimens that consisted of combinations that included daratumumab, pomalidomide, dexamethasone, bortezomib, ixazomib, lenalidomide, carfilzomib or elotuzumab. 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 is the first-in-class B-cell maturation antigen (BCMA)-directed chimeric antigen receptor (CAR) T cell immunotherapy approved in the U.S. 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. *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-7) in earlier lines of treatment for patients with multiple myeloma. For more information visit clinicaltrials.gov.

Important Safety Information

BOXED 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.

Cytokine Release Syndrome (CRS): CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. CRS occurred in 85% (108/127) of patients receiving ABECMA. Grade 3 or higher CRS (Lee grading system) 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) in all patients including the patient who died. The most common manifestations of CRS included pyrexia (98%), hypotension (41%), tachycardia (35%), chills (31%), hypoxia (20%), fatigue (12%), and headache (10%). 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. HLH/MAS is a potentially life-threatening condition. 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; 35% (45/127) received a single dose while 18% (23/127) received more than 1 dose of tocilizumab. Overall, across the dose levels, 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.

Overall rate of CRS was 79% and rate of Grade 2 CRS was 23% in patients treated in the 300 x 10^6 CAR+ T cell dose cohort. For patients treated in the 450 x 10^6 CAR+ T cell dose cohort, the overall rate of CRS was 96% and rate of Grade 2 CRS was 40%. Rate of Grade 3 or higher CRS was similar across the dose range. The median duration of CRS for the 450 x 10^6 CAR+ T cell dose cohort was 7 days (range: 1-63 days) and for the 300 x 10^6 CAR+ T cell dose cohort was 6 days (range: 2-28 days). In the 450 x 10^6 CAR+ T cell dose cohort, 68% (36/53) of patients received tocilizumab and 23% (12/53) received at least 1 dose of corticosteroids for treatment of CRS. In the 300 x 10^6 CAR+ T cell dose cohort, 44% (31/70) of patients received tocilizumab and 10% (7/70) received corticosteroids. All patients that received corticosteroids for CRS also 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 and symptoms of CRS. Monitor patients for signs or symptoms of CRS for at least 4 weeks after 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 treated in the 300 x 10^6 CAR+ T cell dose cohort developed fatal multi-organ HLH/MAS with CRS. In another patient with fatal bronchopulmonary aspergillosis, HLH/MAS was contributory to the fatal outcome. Three cases of Grade 2 HLH/MAS resolved. The rate of HLH/MAS was 8% in the 450 x 10^6 CAR+ T cell dose cohort and 1% in the 300 x 10^6 CAR+ T cell dose cohort. 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 standards.

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: Patients may exhibit prolonged cytopenias following lymphodepleting chemotherapy and ABECMA infusion. In the KarMMa 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. Rate of prolonged neutropenia was 49% in the 450 x 10^6 CAR+ T cell dose cohort and 34% in the 300 x 10^6 CAR+ T cell dose cohort. 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. Median time to cytopenia recovery was similar across the 300 and 450 x 10^6 dose cohort.

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 according to institutional guidelines.

Hypogammaglobulinemia: Plasma cell aplasia and hypogammaglobulinemia can occur in patients receiving treatment with ABECMA. 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 per local institutional guidelines, including infection precautions and antibiotic or antiviral prophylaxis.

The safety of immunization with live viral vaccines during or following 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.

Bristol Myers Squibb: Creating a Better Future for People with Cancer

Bristol Myers Squibb is inspired by a single vision—transforming patients' lives through science. The goal of the company's cancer research is to deliver medicines that offer each patient a better, healthier life and to make cure a possibility. Building on a legacy across a broad range of cancers that have changed survival expectations for many, Bristol Myers Squibb researchers are exploring new frontiers in personalized medicine, and through innovative digital platforms, are turning data into insights that sharpen their focus. Deep scientific expertise, cutting-edge capabilities and discovery platforms enable the company to look at cancer from every angle. Cancer can have a relentless grasp on many parts of a patient's life, and Bristol Myers Squibb is committed to taking actions to address all aspects of care, from diagnosis to survivorship. Because as a leader in cancer care, Bristol Myers Squibb is working to empower all people with cancer to have a better future.

Learn more about the science behind cell therapy and ongoing research at Bristol Myers Squibb here.

About Bristol Myers Squibb

Bristol Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube, Facebook and Instagram.

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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Bristol Myers Squibb Cautionary Statement 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 pharmaceutical products. 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 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 risks, assumptions, uncertainties and other factors include, among others, that future study results may not be consistent with the results to date, that Abecma® (idecabtagene vicleucel), may not receive regulatory approval for the additional indication described in this release in the currently anticipated timeline or at all, that any marketing approvals, if granted, may have significant limitations on their use, and, if approved, whether such product candidate for such additional indication described in this release will be commercially 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 Bristol Myers Squibb's business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2021, 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, Bristol Myers Squibb 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.

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 ide-cel. 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 risks, assumptions, uncertainties and other factors include, among others, the possibility that Abecma 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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