UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 25, 2024

2seventy bio, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-40791**	**86-3658454**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
60 Binney Street, Cambridge, MA		**02142**
(Address of principal executive offices)		**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617) 675-7270

Not Applicable

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	TSVT	The NASDAQ Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On September 25, 2024, 2seventy bio, Inc. (the "Company") issued a press release announcing the discontinuation of enrollment in its ongoing Phase 3 KarMMa-9 study evaluating *Abecma*® with lenalidomide maintenance versus lenalidomide maintenance alone in patients with newly diagnosed multiple myeloma who have suboptimal response to autologous stem cell transplant. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The Company from time to time presents and distributes to investors slide presentations to provide updates and summaries of its business. A copy of its current presentation is being furnished as Exhibit 99.2.

The information in this Current Report on Form 8-K, including Exhibit 99.1 and 99.2, pursuant to Item 7.01 is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section. It may only be incorporated by reference in another filing under the Exchange Act or the Securities Act of 1933, as amended, if such subsequent filing specifically references the information furnished pursuant to Item 7.01 of this Current Report on Form 8-K.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued by 2seventy bio, Inc. on September 25, 2024 furnished herewith.
99.2	Slide presentation of 2seventy bio, Inc. furnished herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document and incorporated as Exhibit 101).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: September 25, 2024

2seventy bio, Inc.

By: /s/ Victoria Eatwell
Victoria Eatwell
Chief Financial Officer
(Principal Financial and Accounting Officer)

2seventy bio Provides Update on KarMMa-9 Study and Previews Anticipated Strong Third Quarter Revenue Performance

2seventy and Bristol Myers Squibb discontinue enrollment in Phase 3 KarMMa-9 study

Decision results in over $80 million in anticipated cost savings for 2seventy over the next several years and accelerates path to breakeven in 2025

Expanded 3L+ label drives re-acceleration in Abecma *U.S. revenues with third quarter revenue expected to grow approximately 30% from second quarter revenue of $54 million*

CAMBRIDGE, Mass.— (BUSINESS WIRE)—September 25, 2024—2seventy bio, Inc. (Nasdaq: TSVT) today announced that the Company, in partnership with study sponsor Bristol Myers Squibb (BMS), will discontinue enrollment in its ongoing Phase 3 KarMMa-9 study evaluating *Abecma®* (idecabtagene vicleucel; ide-cel) with lenalidomide maintenance versus lenalidomide maintenance alone in patients with newly diagnosed multiple myeloma (NDMM) who have suboptimal response to autologous stem cell transplant.

"With a greatly improved NDMM treatment landscape and following our rigorous review of the business case for the KarMMa-9 study, we have decided to discontinue enrollment in this Phase 3 study," said Chip Baird, chief executive officer, 2seventy bio. "*Abecma* continues to show encouraging signs of growth with an expanded label in the third line and a differentiated safety profile. Consistent with our focus on capital allocation and creating value for all stakeholders, we anticipate this decision will conserve over $80 million in near-term expenditures and accelerate our path to breakeven in 2025. We will continue to look for ways to optimize our business for growth while remaining true to our mission of delivering more time for patients."

2seventy and its partner, BMS, remain committed to and strongly believe in the value that *Abecma* brings to patients and the important role it plays in the multiple myeloma treatment paradigm. *Abecma* has a differentiated safety profile and a competitive efficacy profile, particularly when combined with effective bridging therapies. The partners plan to continue expanding the reach of *Abecma* to as many multiple myeloma patients as possible.

Anna Truppel-Hartmann, chief medical officer, 2seventy bio, added, "Since we initiated the Phase 3 KarMMa-9 study in NDMM based on the positive data generated in a similar patient population in the KarMMa-2 cohort 2c study, the NDMM treatment landscape has improved considerably with the increasing use of quadruplet therapy induction, incorporation of more aggressive consolidation therapies, and the ongoing optimization of maintenance therapy regimens. As a result, there are considerably fewer eligible patients than when the study was first designed. We celebrate this progress in treatment options for patients and will continue to focus on serving patients with a high unmet need who will benefit most from *Abecma*. We would like to extend our deepest gratitude to the patients, their families, and the investigators and study staff who participated in this trial."

Commercial Progress and Guidance

2seventy is pleased to report continued positive momentum in *Abecma*'s expected return to growth in the earlier line setting following the FDA's approval in April 2024. The Company expects third quarter

Abecma U.S. revenue growth of approximately 30% from second quarter revenue of $54 million. Demand, as measured by new patients undergoing apheresis in the third quarter, is also expected to reflect double-digit growth when compared to the second quarter of 2024. The Company remains committed to driving the continued success of *Abecma* in 2024 and beyond.

2seventy bio and BMS share equally in all profits and losses related to development, manufacturing, and commercialization of Abecma in the U.S.

***ABECMA* U.S. INDICATION**

ABECMA 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 two or more prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

U.S. Important Safety Information

BOXED WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGIC TOXICITIES, HLH/MAS, PROLONGED CYTOPENIA and SECONDARY HEMATOLOGICAL MALIGNANCIES

- 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.
- T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA
- ABECMA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS.

Warnings and Precautions:

Early Death: In KarMMa-3, a randomized (2:1), controlled trial, a higher proportion of patients experienced death within 9 months after randomization in the ABECMA arm (45/254; 18%) compared to the standard regimens arm (15/132; 11%). Early deaths occurred in 8% (20/254) and 0% prior to ABECMA infusion and standard regimen administration, respectively, and 10% (25/254) and 11% (15/132) after ABECMA infusion and standard regimen administration, respectively. Out of the 20 deaths that occurred prior to ABECMA infusion, 15 occurred from disease progression, 3 occurred from adverse events and 2 occurred from unknown causes. Out of the 25 deaths that occurred after ABECMA infusion, 10 occurred from disease progression, 11 occurred from adverse events, and 4 occurred from unknown causes.

Cytokine Release Syndrome (CRS): CRS, including fatal or life-threatening reactions, occurred following treatment with ABECMA. Among patients receiving ABECMA for relapsed refractory multiple myeloma in the KarMMa and KarMMa-3 studies (N=349), CRS occurred in 89% (310/349), including ≥ Grade 3 CRS (Lee grading system) in 7% (23/349) of patients and Grade 5 CRS in 0.9% (3/349) of patients. The median time-to-onset of CRS, any grade, was 1 day (range: 1 to 27 days), and the median duration of CRS was 5 days (range: 1 to 63 days). In the pooled studies, the rate of ≥Grade 3 CRS was 10% (7/71) for patients treated in dose range of 460 to 510 x 10^6 CAR-positive T cells and 5.4% (13/241) for patients treated in dose range of 300 to 460 x 10^6 CAR-positive T cells.

The most common manifestations of CRS (greater than or equal to 10%) included pyrexia (87%), hypotension (30%), tachycardia (26%), chills (19%), hypoxia (16%). Grade 3 or higher events that may be associated with CRS include hypotension, hypoxia, hyperbilirubinemia, hypofibrinogenemia, ARDS, atrial fibrillation, hepatocellular injury, metabolic acidosis, pulmonary edema, coagulopathy, renal failure, 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.

Of the 349 patients who received ABECMA in clinical trials, 226 (65%) patients received tocilizumab; 39% (135/349) received a single dose, while 26% (91/349) received more than 1 dose of tocilizumab. Overall, 24% (82/349) of patients received at least 1 dose of corticosteroids for treatment of CRS. Almost all patients who received corticosteroids for CRS also received tocilizumab. For patients treated in dose range of 460 to 510 x 10^6 CAR-positive T cells, 76% (54/71) of patients received tocilizumab and 35% (25/71) received at least 1 dose of corticosteroids for treatment of CRS. For patients treated in dose range of 300 to 460 x 10^6 CAR-positive T cells, 63% (152/241) of patients received tocilizumab and 20% (49/241) received at least 1 dose of corticosteroid for treatment of CRS.

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. Ensure that a minimum of 2 doses of tocilizumab are available prior to infusion of ABECMA. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time.

Neurologic Toxicities: Neurologic toxicities, including immune-effector cell-associated neurotoxicity (ICANS), which may be severe or life- threatening, occurred concurrently with CRS, after CRS resolution, or in the absence of CRS following treatment with ABECMA.

In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, CAR T cell-associated neurotoxicity occurred in 40% (139/349), including Grade 3 in 4% (14/349) and Grade 4 in 0.6% (2/349) of patients. The median time to onset of neurotoxicity was 2 days (range: 1 to 148 days). The median duration of CAR T cell-associated neurotoxicity was 8 days (range: 1 to 720 days) in all patients including those with ongoing neurologic events at the time of death or data cut off. CAR T cell-associated neurotoxicity resolved in 123 of 139 (88%) patients and median time to resolution was 5 days (range: 1 to 245 days). One-hundred and thirty four out of 349 (38%) patients with neurotoxicity

had CRS. The onset of neurotoxicity during CRS was observed in 93 patients, before the onset of CRS in 12 patients, and after the CRS event in 29 patients. The rate of Grade 3 or 4 CAR T cell-associated neurotoxicity was 5.6% (4/71) and 3.7% (9/241) for patients treated in dose range of 460 to 510 x 10^6 CAR-positive T cells and 300 to 460 x 10^6 CAR-positive T cells, respectively. The most frequent (greater than or equal to 5%) manifestations of CAR T cell-associated neurotoxicity include encephalopathy (21%), headache (15%), dizziness (8%), delirium (6%), and tremor (6%).

At the safety update for KarMMa-3 study, one patient developed fatal neurotoxicity 43 days after ABECMA. In KarMMa, 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.

Cerebral edema has been associated with ABECMA in a patient in another study in multiple myeloma. Grade 3 myelitis and Grade 3 parkinsonism have occurred 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 or symptoms of neurologic toxicities and monitor patients for signs or symptoms of neurologic toxicities for at least 4 weeks after ABECMA infusion and treat promptly. Rule out other causes of neurologic symptoms. Neurologic toxicity should be managed with supportive care and/or corticosteroids as needed. Counsel patients to seek immediate medical attention should signs or symptoms occur at any time.

Hemophagocytic Lymphohistiocytosis (HLH)/Macrophage Activation Syndrome (MAS): In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, HLH/MAS occurred in 2.9% (10/349) of patients. All events of HLH/MAS had onset within 10 days of receiving ABECMA, with a median onset of 6.5 days (range: 4 to 10 days) and occurred in the setting of ongoing or worsening CRS. Five patients with HLH/MAS had overlapping neurotoxicity. The manifestations of HLH/MAS include hypotension, hypoxia, multiple organ dysfunction, renal dysfunction and cytopenia.

In KarMMa-3, one patient had Grade 5, two patients had Grade 4 and two patients had Grade 3 HLH/MAS. The patient with Grade 5 HLH/MAS also had Grade 5 candida sepsis and Grade 5 CRS. In another patient who died due to stroke, the Grade 4 HLH/MAS had resolved prior to death. Two cases of Grade 3 and one case of Grade 4 HLH/MAS had resolved.

In KarMMa, one patient treated in the 300 x 10^6 CAR-positive T cells 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.

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 contact Bristol-Myers Squibb at 1-866-340-7332.

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.
In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, infections (all grades) occurred in 61% of patients. Grade 3 or 4 infections occurred in 21% of patients. Grade 3 or 4 infections with an unspecified pathogen occurred in 12%, viral infections in 7%, bacterial infections in 4.3%, and fungal infections in 1.4% of patients. Overall, 15 patients had Grade 5 infections (4.3%); 8 patients (2.3%) with infections of pathogen unspecified, 3 patients (0.9%) with fungal infections, 3 patients (0.9%) with viral infections, and 1 patient (0.3%) with bacterial infection.
Monitor patients for signs and symptoms of infection before and after ABECMA infusion and treat appropriately. Administer prophylactic, pre-emptive, and/or therapeutic antimicrobials according to standard institutional guidelines.
Febrile neutropenia was observed in 38% (133/349) 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. Consider antiviral therapy to prevent viral reactivation per local institutional guidelines/clinical practice.
Prolonged Cytopenias: In patients receiving ABECMA in the KarMMa and KarMMa-3 studies, 40% of patients (139/349) experienced prolonged Grade 3 or 4 neutropenia and 42% (145/349) experienced prolonged Grade 3 or 4 thrombocytopenia that had not resolved by Month 1 following ABECMA infusion. In 89% (123/139) 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 76% (110/145) of patients who recovered from Grade 3 or 4 thrombocytopenia, the median time to recovery was 1.9 months. Five patients underwent stem cell therapy for hematopoietic reconstitution due to prolonged cytopenia. The rate of Grade 3 or 4 thrombocytopenia was 62% (44/71) and 56% (135/241) for patients treated in dose range of 460 to 510 x 10^6 CAR-positive T cells and 300 to 460 x 10^6 CAR-positive T cells, respectively.
Monitor blood counts prior to and after ABECMA infusion. Manage cytopenia with myeloid growth factor and blood product transfusion support according to local institutional guidelines.
Hypogammaglobulinemia: In all patients receiving ABECMA in the KarMMa and KarMMa-3 studies, hypogammaglobulinemia was reported as an adverse event in 13% (46/349) of patients; laboratory IgG levels fell below 500 mg/dL after infusion in 37% (130/349) of patients treated with ABECMA.

Hypogammaglobulinemia either as an adverse reaction or laboratory IgG level below 500 mg/dL after infusion occurred in 45% (158/349) of patients treated with ABECMA. Forty-one percent of patients received intravenous immunoglobulin (IVIG) post-ABECMA for serum IgG <400 mg/dL.
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.
Use of Live Vaccines: 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. In KarMMa-3, myeloid neoplasms (four cases of myelodysplastic syndrome and one case of acute myeloid leukemia) occurred in 2.2% (5/222) of patients following treatment with ABECMA compared to none in the standard regimens arm at the time of the safety update. The median time to onset of myeloid neoplasm from ide-cel infusion was 338 days (Range: 277 to 794 days). Three of these five patients have died following the development of myeloid neoplasm. One out of the five cases of myeloid neoplasm occurred after initiation of subsequent antimyeloma therapy.
T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including ABECMA. Mature T cell malignancies, including CAR-positive tumors, may present as soon as weeks following infusion, and may include fatal outcomes.
Monitor life-long for secondary malignancies. In the event that a secondary malignancy occurs, contact Bristol-Myers Squibb at 1-888-805-4555 for reporting and to obtain instructions on collection of patient samples for testing of secondary malignancy.
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 pyrexia, CRS, hypogammaglobulinemia, infections – pathogen unspecified, musculoskeletal pain, fatigue, febrile neutropenia, hypotension, tachycardia, diarrhea, nausea, headache, chills, upper respiratory tract infection, encephalopathy, edema, dyspnea and viral infections.
Please see full Prescribing Information, including **Boxed WARNINGS** and Medication Guide.

About Bristol Myers Squibb and 2seventy bio
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. Bristol Myers

Squibb assumes sole responsibility for *Abecma* drug product manufacturing and commercialization outside of the U.S. The companies' broad clinical development program for *Abecma* includes ongoing and planned clinical studies (KarMMa-2, KarMMa-3) in earlier lines of treatment for patients with multiple myeloma. For more information visit clinicaltrials.gov.

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. 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 the first FDA-approved CAR T cell therapy for multiple myeloma to as many patients as possible. Importantly, we remain focused on accomplishing our mission 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.

Follow 2seventy bio on social media: X (Twitter) and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

This release contains "forward-looking statements" within the meaning of applicable laws and regulations. These statements include, but are not limited to: statements about the discontinuation of the ongoing Phase 3 KarMMa-9 study, including the potential cost savings; statements regarding expected ABECMA *(ide-cel) U.S. revenue and demand in the third quarter of 2024; statements regarding expected benefits from our strategic collaboration with BMS; statements about the efficacy and perceived therapeutic benefits of* ABECMA*; statements regarding our financial condition, expenses, results of operations, and expectations regarding our path to breakeven; and statements about our business plans and strategies. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, our limited independent operating history and the risk that our accounting and other management systems may not be prepared to meet the financial reporting and other requirements of operating as an independent public company; the risk that* Abecma *will not be as commercially successful as we may anticipate; the risk that our strategic realignment to focus on the development and commercialization of* Abecma *may not be as successful as anticipated, may fail to achieve the anticipated cost savings, and may cause disruptions in our business that could make it difficult to achieve our strategic objectives; and the risk that we are unable to manage our operating expenses or cash use for operations. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our annual Report on Form 10-K for the year ended December 31, 2023, as supplemented and/or modified by any other subsequent filings that we have made and will make with the Securities and Exchange Commission in the future. All information in this press release is as of the date of this release, and we undertakes no duty to update this information unless required by law.*

# # #

Investors and Media:
Vicki Eatwell, CFO
vicki.eatwell@2seventybio.com

Morgan (Adams) Shields
Morgan.adams@2seventybio.com

Unleash Time

2seventy bio company presentation

September 2024

2seventybio

Cautionary note regarding forward-looking statements

These slides and the accompanying oral presentation may contain "forward-looking statements". These statements include, but are not limited to: statements about our plans, strategies, timelines and expectations with respect to the development and commercialization of Abecma (ide-cel); statements about the discontinuation of the ongoing Phase 3 KarMMa-9 study, including the potential cost savings; the timing or likelihood of regulatory filings and acceptances and approvals thereof; expectations as to the market size for Abecma; the progress and results of our commercialization of *Abecma*, including our goal of increasing manufacturing capacity and improving the manufacturing process and the number of patients that are expected to be treated with *Abecma* in the commercial setting and potential late line global revenue for *Abecma*; anticipated revenues resulting from sales of *Abecma*; statements about the efficacy and perceived therapeutic benefits of *Abecma*; and expectations regarding our use of capital, expenses and other future financial results, including our net cash spend and cash runway. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, the risk that the market opportunities for our approved product or any future approved product are smaller than we believe they are; the risk that BMS, upon whom we rely for the successful development and commercialization of *Abecma* does not devote sufficient resources thereto, is unsuccessful in its efforts, or chooses to terminate its agreements with us; the risk that we and/or BMS or our third party vendors will be unable to increase manufacturing and supply capacity for *Abecma*; the risk that *Abecma* will not be as commercially successful as we may anticipate; and the risk that we are unable to manage our operating expenses or cash use for operations. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in the information statement contained in our most recent Form 10-K and most recent quarterly reports any other filings that we have made or will make with the Securities and Exchange Commission in the future. All information in this presentation is as of the date of the release, and 2seventy bio undertakes no duty to update this information unless required by law. This presentation has been prepared by 2seventy bio for the exclusive use of the party to whom 2seventy bio delivers this presentation. This presentation does not constitute an offer to sell or the solicitation of an offer to buy any securities of the Company. The information contained herein is for informational purposes and may not be relied upon in connection with the purchase or sale of any security. Neither 2seventy bio nor any of its affiliates or representatives makes any representation or warranty, expressed or implied, as to the accuracy or completeness of this presentation or any of the information contained herein, or any other written or oral communication transmitted or made available to the you or your affiliates or representatives. 2seventy bio and its affiliates and representatives expressly disclaim to the fullest extent permitted by law any and all liability based, in whole or in part, on the presentation or any information contained herein or any other written or oral communication transmitted or made available to you or your affiliates or representatives, including, without limitation, with respect to errors therein or omissions therefrom.

Unlocking *Abecma* Value in 2024

Abecma (idecabtagene vicleucel)

- First-in-class CAR T treatment for 3L+ r/r multiple myeloma
- $358M total US commercial revenue in 2023; $106M YTD through Q2 2024
- ~5 months into the launch of *Abecma* in earlier lines in partnership with BMS

***Abecma* opportunity to see sustainable growth**	FDA approval in April in 3L+ setting, supported by robust KarMMa-3 ph. 3 data	Continue to invest in additional studies to generate data and further optimize real world use of Abecma
Strong cash and path to profitability	~$202M cash balance as of June 30; runway beyond 2027	Recent strategic re-alignment generates cost savings of ~$150 million in 2024 and ~$200 million in 2025
Lean, fit-for-purpose structure	Tuned organization with sole focus on Abecma growth	Streamlined cost structure and financial profile; 2Q24 operating expenses reduced approx. 43% ($28M) vs. 1Q24

Strategic realignment successfully executed in 1H 2024: sale of R&D assets to Regeneron and Novo Nordisk

- **Completed sale of R&D business to Regeneron in April 2024:** sold oncology and autoimmune research and development programs
- **Completed sale of R&D program to Novo Nordisk in June 2024:** sold Hemophilia A program and gene editing technology for up to $40 million
- **2seventy focused exclusively on development and commercialization of *Abecma*,** creating path to financial sustainability
- **New company structure and leadership** aligns with go-forward business needs; streamlined team of ~60-70 employees
- **Transaction maximizes value for shareholders** and best positions Abecma to deliver for patients

KarMMa-3 supports the totality of *Abecma*'s competitive profile in a population of patients with high unmet need

***Abecma* is now available for the treatment of adult patients with relapsed or refractory multiple myeloma earlier in their treatment journey**

SUPERIOR EFFICACY VS. STANDARD REGIMENS

3x longer mPFS

8x higher percentage of ≥CR

20.7-mos mPFS in bridged patients with reduced tumor burden[1]

ESTABLISHED SAFETY PROFILE

Generally predictable CRS & NT

No parkinsonism or Guillain-Barre syndrome in registration trials[2]

RELIABLE MANUFACTURING

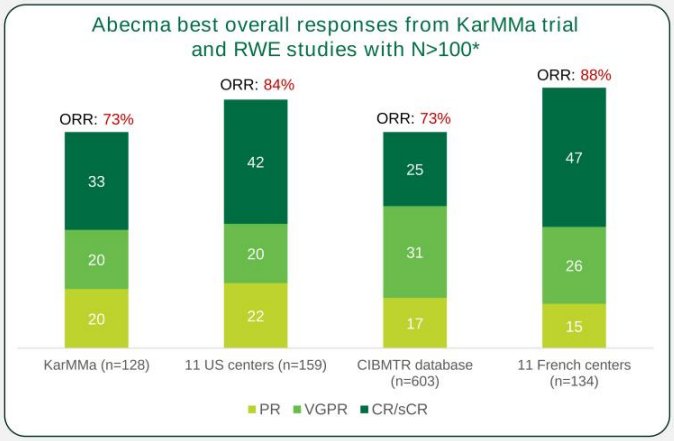
Unlimited slot availability

Highest number of locations

94% US commercial manufacturing success rate

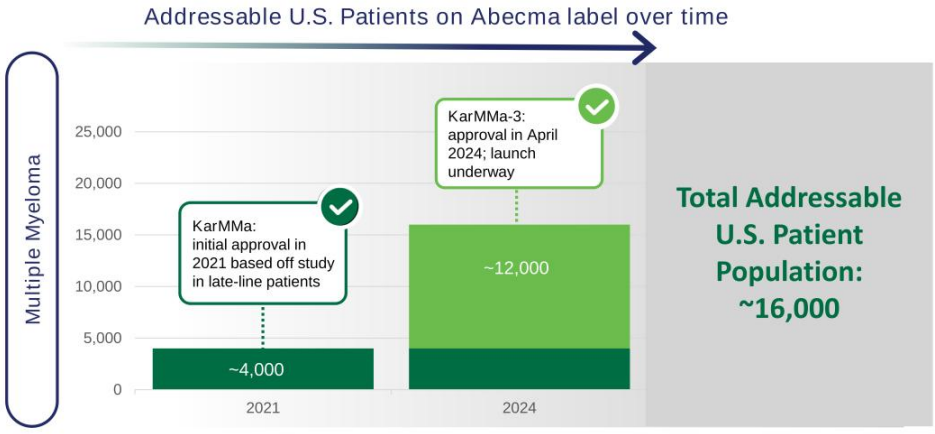
[1]While in an unpowered subgroup where these findings should be interpreted with caution
[2]Grade 3 myelitis and Grade 3 parkinsonism mentioned in USPI have occurred after treatment with *Abecma* in another study in multiple myeloma

Abecma real world experience shows consistent outcomes with the KarMMa pivotal study despite sicker patient population



- **Several large global studies show *Abecma* efficacy in the real world is consistent or better than the KarMMa study**
- **Many RWE patients across all studies would not have met the eligibility criteria for KarMMa**
- **Safety data similar to KarMMa with no new safety signals; limited Parkinsonism and Guillain-Barre and low non-relapse mortality***

KarMMa-3 study has the potential to drive label expansion into broad U.S. market opportunity



Key questions on *Abecma* in earlier lines

What did we learn from KarMMa-3 in terms of OS?	• OS confounded by patient-centric design which allowed for crossover. Imbalance in early deaths driven by patients untreated with ide-cel • No difference between *Abecma* and SOC in ITT; when adjusted for crossover, OS favors *Abecma* arm
What does this mean for *Abecma* in the 3L+ commercial setting?	• 3x mPFS benefit over standard of care in heavily pretreated, triple class exposed* patient population • Importance of bridging therapy, especially in high-risk patients
What are you doing to shift the dynamics in the market?	• Educating market on *Abecma's* competitive profile • BMS driving education on KarMMa-3 label including patient population, real world evidence, treatment sequencing and use of bridging
What other evidence generation strategies are you pursuing?	• KarMMa-2 cohort 2c data demonstrate the potential of *Abecma* in NDMM. Of note, **all patients who received maintenance with lenalidomide are still in response. ISRs with maintenance post *Abecma* are underway.** • New cohort in KarMMa-2 is investigating optimized bridging strategy

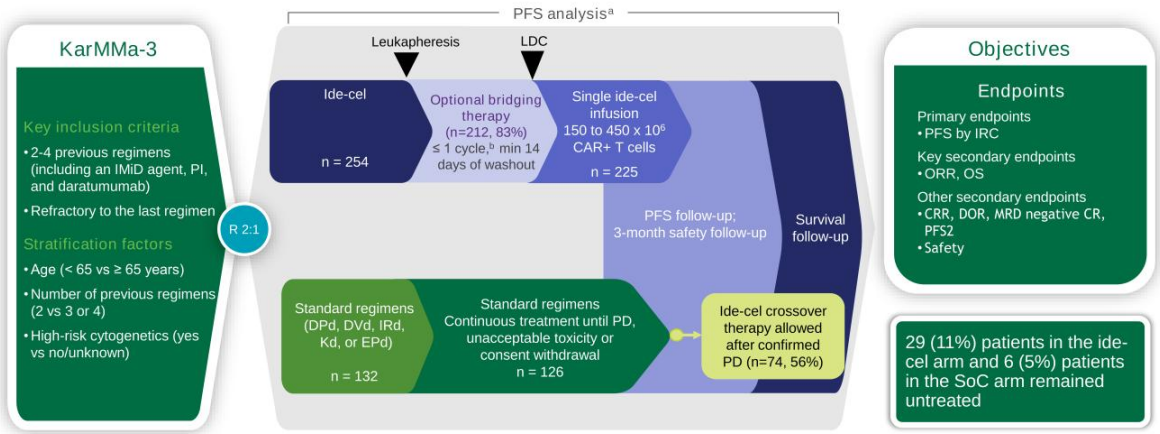
*Patients who received an immunomodulatory agent, a PI, and an anti-monoclonal antibody. ISR = Investigator sponsored research

KarMMa-3

2seventybio

Rodriguez-Otero P, et al. ASH 2023 Abstract 1028

KarMMa-3 study design (NCT03651128)



[a]Time from randomization to the first occurrence of disease progression or death from any cause according to IMWG criteria; [b]Up to 1 cycle of DPd, DVd, IRd, Kd, or EPd may be given as bridging
AE, adverse event; DPd, daratumumab/pomalidomide/dexamethasone; DVd, daratumumab/bortezomib/dexamethasone; EPd, elotuzumab/pomalidomide/dexamethasone; IRC, Independent Response Committee; IRd, ixazomib/lenalidomide/dexamethasone; Kd, carfilzomib/dexamethasone; LDC, lymphodepleting chemotherapy; min, minimum; MRD, minimal residual disease; PD, progressive disease; PFS2, progression-free survival on next line of therapy; PROs, patient-reported outcomes; PS, performance status; R, randomization

Heavily Pretreated, Triple Class Exposed* Patient Population

Characteristic	Ide-cel (n = 254)	Standard regimens (n = 132)
Median (range) age, years	63 (30–81)	63 (42–83)
Median (range) time from diagnosis to screening, years	4.1 (0.6–21.8)	4.0 (0.7–17.7)
Previous autologous HSCT	214 (84)	114 (86)
R-ISS disease stage		
I	50 (20)	26 (20)
II	150 (59)	82 (62)
III	31 (12)	14 (11)
EMP	61 (24)	32 (24)
High tumor burden[a]	71 (28)	34 (26)
High-risk cytogenetics[b]	166 (65)	82 (62)
del(17p)	66 (26)	42 (32)
t(4;14)	43 (17)	18 (14)
t(14;16)	8 (3)	4 (3)
1q gain/amplification	124 (49)	51 (39)
Ultra-high–risk cytogenetics[c]	67 (26)	29 (22)
Median (range) time to progression on last prior antimyeloma therapy, months	7.1 (0.7–67.7)	6.9 (0.4–66.0)
Daratumumab refractory	242 (95)	123 (93)
Triple-class–refractory[d]	164 (65)	89 (67)

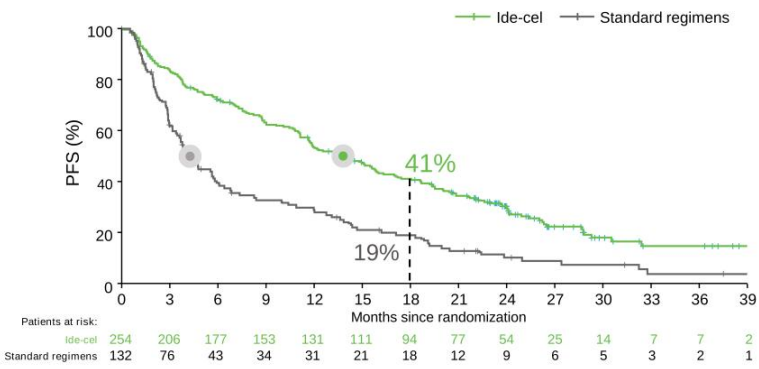
Baseline characteristics were generally balanced between treatment arms
Overall, 66% of patients had triple-class refractory RRMM and 95% were daratumumab refractory, indicating a difficult-to-treat patient population

Adapted from Rodriguez-Otero P, et al. *N Engl J Med* 2023;388:1002–1014.
Data are n (%) unless otherwise stated. [a]≥ 50% CD138+ plasma cells in bone marrow; [b]Included del(17p), t(4;14), t(14;16), or 1q gain/amplification; [c]≥ 2 of del (17p), t(4;14), t(14;16), t(14;20), or 1q gain/amplification; [d]Refractory to ≥ 1 each of an IMiD agent, a PI, and an anti-CD38 antibody. EMP, extramedullary plasmacytoma; HSCT, hematopoietic stem cell transplantation; R-ISS, revised International Staging System.

*Patients who received an immunomodulatory agent, a PI, and an anti-monoclonal antibody

Rodríguez-Otero P, et al. ASH 2023 Abstract 1028

Significant benefit with ide-cel at final PFS analysis (ITT population)



Median PFS[a]

13.8 months

4.4 months

Hazard ratio[b]

HR 0.49

(95% CI, 0.38–0.63)

18-month PFS rate

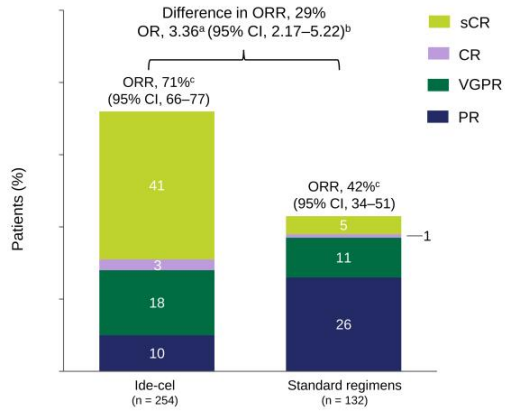
41% | 19%

- Ide-cel continued to show longer PFS than standard regimens, with a 51% reduction in risk of PD or death, consistent with the KarMMa-3 interim analysis[1]
- With extended follow-up, the safety profile of ide-cel was consistent with prior reports with no new safety signals identified[2-4]

PFS was analyzed in the ITT population of all randomized patients in both arms and included early PFS events occurring between randomization and ide-cel infusion. PFS based on IMWG criteria per IRC. [a]Based on Kaplan-Meier approach; [b]Statified HR based on univariate Cox proportional hazard model. CI is two-sided. IMWG, International Myeloma Working Group; mITT, modified intent-to-treat; SE, standard error.

1. Rodriguez-Otero P, et al. N Engl J Med 2021;384:705-716. 2. Rodriguez-Otero P, et al. N Engl J Med 2021;384:705-716; 3. Munshi NC, et al. N Engl J Med 2021;384:705-716; 4. Raje N, et al. N Engl J Med 2019;380:1726-1737.

Statistically significant, deep and durable responses with ide-cel



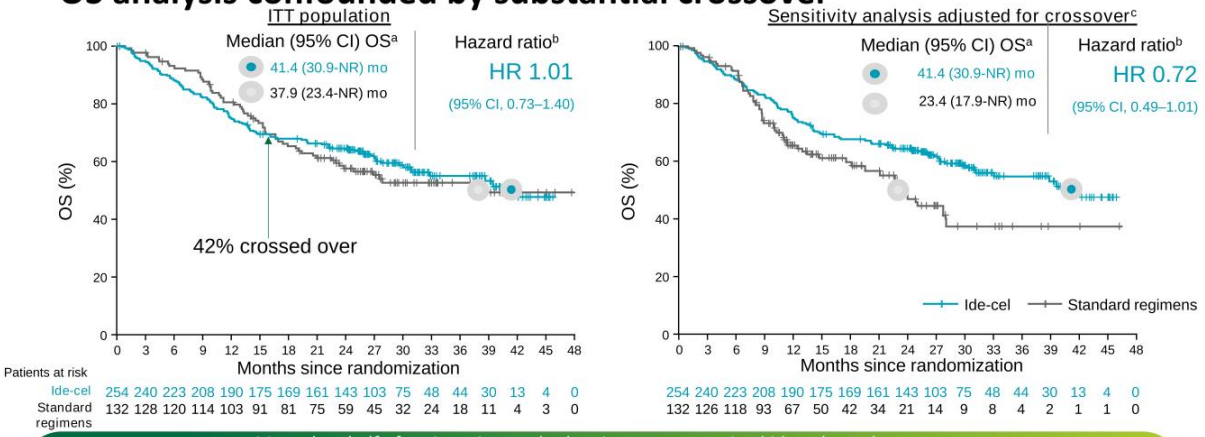
	Ide-cel (n = 254)	Standard regimens (n = 132)
CR rate, % (95% CI)[d]	44 (38–50)	5 (2–9)
MRD-negative CR rate, n/N (%) (95% CI)[e]	57/163 (35) (28–42)	1/54 (2) (0–5)
Median (95% CI) DOR, months	16.6 (12.1–19.6)	9.7 (5.5–16.1)
Median PFS2, months	23.5	16.7
HR (95% CI)	0.79 (0.60–1.04)	

- With extended follow-up, ide-cel continued to demonstrate higher ORR versus standard regimens[1]
- CR rate increased by 5% in the ide-cel arm but was unchanged for standard regimens
- Ide-cel continued to demonstrate durable, statistically significant and clinically meaningful improvements in patient-reported outcomes[2]

Per IMWG criteria. Individual responses may not sum to ORR due to rounding.
[a]OR is for ORR, calculated based on the observed response rate with two-sided Wald CI; [b]Two-sided Wald interval; [c]Patients with ≥ PR; [d]Patients with CR or sCR; [e]≥ 1 negative MRD value within 3 months prior to achieving ≥ CR until PD or death. MRD was assessed by NGS at a sensitivity of 10^{-5} per IMWG Uniform Response Criteria and as specified by the protocol. 95% CI was calculated using 2-sided Wald interval. OR, odds ratio; NGS, next generation sequencing; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.
1. Rodriguez-Otero P, et al. N Engl J Med 2023;388:705-716. 2. Hansen et al, ASH 2023

Rodriguez-Otero P, et al. ASH 2023 Abstract 1028

OS analysis confounded by substantial crossover



More than half of patients in standard regimens arm received ide-cel as subsequent therapy upon confirmed PD and the majority received ide-cel within 3–16 months of randomization

Prespecified crossover-adjusted analysis shows OS benefit of ide-cel

Information fraction for OS was 74% (n = 164/222 required events). [a]Based on Kaplan–Meier approach; [b]Stratified HR is based on the univariate Cox proportional hazards model. CI is 2-sided and calculated by bootstrap method; [c]Two-stage Weibull model without recensoring (prespecified analysis). NR, not reached.

Patients who never received ide-cel drive imbalance in early OS events

Patients who died ≤6 months from randomization, n (%)	Ide-cel (n = 254)	Standard regimens (n = 132)
Patients who died	30 (12)	9 (7)
Did not receive study treatment	17 (7)	0
Received study treatment	13 (5)	9 (7)
Primary cause of death		
AEs	8 (3)	3 (2)
Myeloma progression	18 (7)	6 (5)
Other causes[a]	4 (2)	0

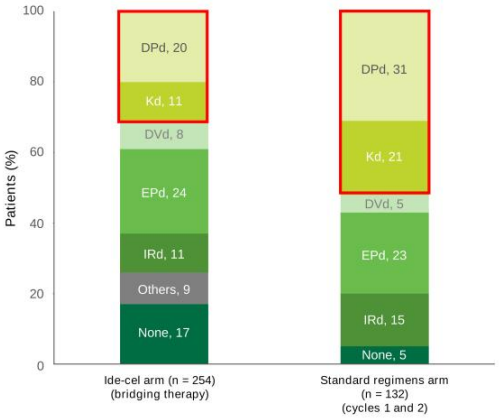
	Ide-cel		Standard regimens	
Baseline characteristic, n (%)	**Deaths ≤ 6** months from randomization (n = 30)	ITT population (n = 254)	**Deaths ≤ 6** months from randomization (n = 9)	ITT population (n = 132)
R-ISS stage III	9 (30)	31 (12)	2 (22)	14 (11)
High-risk cytogenetic abnormalities[b]	21 (70)	107 (42)	6 (67)	61 (46)
EMP	12 (40)	61 (24)	3 (33)	32 (24)
High tumor burden[c]	14 (47)	71 (28)	2 (22)	34 (26)

Early deaths occurred most commonly in patients with multiple high-risk features, mostly due to myeloma progression, and mostly in patients in the investigational arm who never received ide-cel

No differences in death rates due to AEs were observed between treatment arms

[a]All 4 cases of "death from other cause" in the ide-cel arm were reported verbatim as "unknown", which was coded under the system organ class of "general disorder and administration site condition"; [b]Included del17p13 (reflective of del[17p]), t(14;16), or t(4;14); [c]Determined by the higher value between bone marrow aspiration and bone marrow biopsy CD138+ plasma cell. Low tumor burden: < 50%, high tumor burden: ≥ 50%.

Suboptimal bridging therapy



Lower use of effective bridging regimens

- Less use of DPd and Kd in ide-cel arm—the 2 regimens with the most disease burden reduction during bridging therapy[1]

Lower dose intensity bridging therapy in ide-cel arm

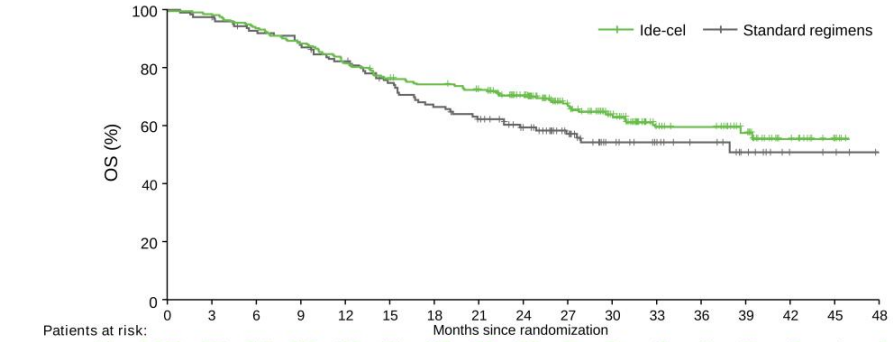
- 17% had no bridging; median 24 day washout period before ide-cel

Median (range) time without therapy within first 60 days

- Ide-cel arm: 26 (1–60) days
- Standard regimens arm: 6 (0–60) days

Cumulative dose during bridging therapy for the ide-cel arm and cycles 1 and 2 for the standard regimens arm was defined as the sum of all doses taken in mg. Dose intensity was defined as the cumulative dose divided by total days. [a]For patients in the ide-cel arm, bridging therapy was considered in the dose intensity calculation: total days in denominator = (earliest date of infusion, death, off-study, last alive, or start of subsequent therapy) − randomization date. For patients in the standard regimens arm, only the cycle 1 and cycle 2 dose were considered in dose intensity calculation. Einsele H et al. IMS 2023.

Trend of OS benefit with ide-cel among treated patients



Patients at risk:

Ide-cel	225	223	212	200	185	171	165	157	139	99	71	45	41	28	13	4	0
Standard regimens	126	123	115	109	101	89	79	73	58	44	31	23	18	11	4	3	0

Median OS[a]

NR

NR

Hazard ratio[b]

HR 0.83

(95% CI, 0.58–1.18)

In the treated population of patients who received the study treatment to which they were randomly assigned, there was a trend toward OS benefit with ide-cel versus standard regimens

[a]Based on Kaplan–Meier approach; [b]Stratified HR based on the univariate Cox proportional hazards model. CI is two-sided.

KarMMa-3 Data Supports the Potential of *Abecma* in Earlier Lines

- KarMMa-3 demonstrates a **significantly longer** and **clinically meaningful improvement** of **PFS** with ide-cel versus standard regimens in patients with early line relapse and triple-class exposed* (TCExp) RRMM across all subgroups[1]
  - 51% reduction in risk of disease progression or death with ide-cel
- Patient-centric KarMMa-3 design allowed crossover, which confounds the OS interpretation
  - 56% of patients in the standard regimens arm crossed over to receive ide-cel
  - A prespecified analysis adjusting for crossover showed **improved OS with ide-cel** versus standard regimens
- Bridging therapy was suboptimal for patients with multiple high-risk features and rapidly progressing disease
  - This highlights the importance of **effective bridging therapy**
- The safety profile of ide-cel was manageable and consistent with previous studies[1-3]
- KarMMa-3 shows a favorable benefit-risk profile with ide-cel, and supports the use of ide-cel in patients with TCExp RRMM, a population with poor survival outcomes with conventional therapies

1. Rodríguez-Otero P, et al. N Engl J Med 2023;388:1002–1014; 2. Munshi NC, et al. N Engl J Med 2021;384:705–716; 3. RajeN, et al. N Engl J Med 2019;380:1726–1737.
*Patients who received an immunomodulatory agent, a PI, and an anti-monoclonal antibody

KarMMa-2c and KarMMa-9

2seventybio

Update on KarMMa-9 Study

The initiation of KarMMa-9 in a NDMM population was based on the positive data generated in **KarMMa-2 cohort 2c** in a similar patient population.

Since that time, NDMM treatment landscape has improved considerably:

- Increasing use of quadruplet therapy induction
- Incorporation of more aggressive consolidation therapies
- Ongoing optimization of maintenance therapy regimens

As a result, there are considerably fewer eligible patients.

We, along with our study sponsor BMS, will **discontinue enrollment in the Phase 3 KarMMa-9 study** and continue to focus on serving patients with a high unmet need who will benefit most from *Abecma*.

With our focus on capital allocation and creating value for all stakeholders, we anticipate this decision will conserve over $80 million in near-term expenditures and accelerate our path to breakeven in 2025.

KarMMa-2c: Deepened responses in patients with inadequate response to frontline ASCT (less than VGPR)

- All treated patients alive at data cut-off with median follow up of 39.4 months; no new safety signals
- ORR: 87.1%; CRR: 77.4%
- At 36 months, DOR was 80.9% and PFS was 76.8%
- Of the 8 patients that received lenalidomide maintenance, progression events have not been observed

CR/sCR
VGPR
PR
MINIMAL RESPONSE
STABLE DISEASE
PD
LEN Maintenance
Ongoing

The bar starts at month 2, day 1 (equivalent to 1 month post ide-cel infusion) and continues to later of last response assessment date or data cutoff date (May 3, 2023). Response was defined as ≥ PR based on IMWG criteria by investigator assessment.
D, day; LEN, lenalidomide; M, month.

THANK YOU

2seventybio