



The High Price of Aduhelm's Approval: An Investigation into FDA's Atypical Review Process and Biogen's Aggressive Launch Plans

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Reform and Committee on Energy and Commerce

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EXECUTIVE SUMMARY

This staff report presents the findings of an 18-month investigation conducted by the Committees on Oversight and Reform, and Energy and Commerce (the Committees) into the regulatory review and approval, pricing, and marketing of biotechnology company Biogen Inc.’s Alzheimer’s disease drug, aducanumab, known more commonly by its trade name, Aduhelm.

More than six million people in the United States live with Alzheimer’s disease, a number projected to increase to as many as 14 million people by 2060.¹ To best support patients and families impacted by Alzheimer’s disease, advance brain health equity, and eradicate this devastating disease, treatments must be effective, safe, accessible to patients, and affordable for federal health care programs.

The Food and Drug Administration (FDA) granted accelerated approval for Aduhelm on the basis that the drug reduces amyloid beta plaque in the brain. The FDA’s action came despite the fact that Biogen cancelled clinical trials for Aduhelm in March 2019 due to an independent report indicating the drug was unlikely to effectively slow cognitive and functional impairment and that further clinical study would be futile.²

In June 2019, FDA and Biogen began a “working group” collaboration to examine data from Biogen’s failed clinical trials.³ New evidence obtained by the Committees shows that the FDA-Biogen working group engaged in at least 115 meetings, calls, and substantive email discussions over the course of a year, from July 2019 to July 2020, including convening more than 40 meetings to guide Aduhelm’s potential approval.

In November 2020, FDA and Biogen prepared and presented a joint briefing document to FDA’s Peripheral and Central Nervous Systems Drugs Advisory Committee (PCNS Advisory Committee)—a joint process that had previously only been used for oncological drugs under

¹ Centers for Disease Control and Prevention, *The Truth About Aging and Dementia* (online at www.cdc.gov/aging/publications/features/dementia-not-normal-aging.html) (accessed Dec. 1, 2022). Centers for Disease Control and Prevention, *Minorities and Women Are at Greater Risk for Alzheimer’s Disease* (online at www.cdc.gov/aging/publications/features/Alz-Greater-Risk.html) (accessed Dec. 1, 2022).

² The Food and Drug Administration’s accelerated approval program allows for earlier approval of drugs that treat serious conditions and fulfill an unmet medical need based on an effect on a surrogate endpoint that is “thought to predict clinical benefit but is not itself a measure of clinical benefit.” 21 U.S.C. § 356(c); Food and Drug Administration, *Accelerated Approval Program* (Oct. 26, 2020) (online at www.fda.gov/drugs/information-health-care-professionals-drugs/accelerated-approval-program). Food and Drug Administration, *Press Release: FDA Grants Accelerated Approval for Alzheimer’s Drug* (June 7, 2021) (online at www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug); Biogen, *Press Release: Biogen and Eisai to Discontinue Phase 3 ENGAGE and EMERGE Trials of Aducanumab in Alzheimer’s Disease* (Mar. 21, 2019) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-and-eisai-discontinue-phase-3-engage-and-emerge-trials>).

³ Food and Drug Administration, *Administrative and Correspondence Documents*, at Page 70 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

circumstances of broad consensus.⁴ None of the empaneled PCNS Advisory Committee members voted to recommend traditional approval for Aduhelm.⁵ Despite the PCNS Advisory Committee's lack of recommendation, and internal concerns raised by experts in FDA's Center for Drug Evaluation and Research's (CDER) Office of Biostatistics (OB) about the inconsistency of the drug's clinical data, the agency granted accelerated approval to Aduhelm on June 7, 2021.⁶

Oversight and Reform Committee Chairwoman Carolyn B. Maloney and Energy and Commerce Committee Chairman Frank Pallone, Jr., announced a joint investigation of the approval and pricing of Aduhelm on June 25, 2021, following concerns about FDA's review of Aduhelm, significant questions about the drug's clinical benefit, and the high price of Aduhelm set by Biogen.⁷

This report is intended to provide policymakers, relevant agencies, and the public with an understanding of Aduhelm's approval process and Biogen's pricing of Aduhelm. This report also provides recommendations intended to ensure and increase public confidence in the continued safety, efficacy, and affordability of FDA-approved drugs.

Over the course of the investigation, the Committees' staff held multiple briefings with FDA and reviewed more than 500,000 pages of documents and information from FDA and Biogen, including internal Biogen strategy documents; Biogen's Board of Directors materials and launch plans; communications among and between senior Biogen and FDA leaders; and internal FDA correspondence and materials. These materials included FDA's internal review of its interactions with Biogen in preparation for and during the PCNS Advisory Committee meeting, which was conducted in the Spring of 2021 and resulted in a report dated May 30, 2021. Though the internal review concluded the interactions between FDA and Biogen prior to the PCNS Advisory Committee meeting were appropriate, it presented three findings of atypical

⁴ Food and Drug Administration, *Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee Meeting: Combined FDA and Applicant PCNS Drugs Advisory Committee Briefing Document* (Nov. 6, 2020) (online at www.fda.gov/media/143502/download); Briefing by Patricia Cavazzoni, M.D., Director, Office of New Drugs, Center for Drug Evaluation and Research; Food and Drug Administration et al., to Staff, Committee on Energy and Commerce and Committee on Oversight and Reform (Apr. 7, 2022).

⁵ Food and Drug Administration, *FDA's Decision to Approve New Treatment for Alzheimer's Disease* (June 7, 2021) (online at fda.gov/drugs/news-events-human-drugs/fdas-decision-approve-new-treatment-alzheimers-disease).

⁶ Food and Drug Administration, Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Page 12 (May 30, 2021); *Press Release: FDA Grants Accelerated Approval for Alzheimer's Drug* (June 7, 2021) (online at www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug).

⁷ Committee on Energy and Commerce, *Press Release: Chairs Pallone and Maloney Announce Investigation of Biogen's Alzheimer's Drug Aduhelm* (June 25, 2021) (online at energycommerce.house.gov/newsroom/press-releases/chairs-pallone-and-maloney-announce-investigation-of-biogen-s-alzheimer-s); Committee on Oversight and Reform, *Press Release: Chairs Maloney and Pallone Announce Investigation of Biogen's Alzheimer's Drug Aduhelm* (June 25, 2021) (online at oversight.house.gov/news/press-releases/chairs-maloney-and-pallone-announce-investigation-of-biogen-s-alzheimer-s-drug).

processes, and four recommendations for improvement to prevent the situation that prompted the internal review moving forward.⁸

The Committees' review of these materials reveals that FDA's review and approval of Aduhelm consisted of atypical procedures and deviated from the agency's own guidance. These materials also reveal that Biogen had aggressive launch plans for Aduhelm—including in its label and pricing—despite concerns about efficacy, safety, and affordability.

The Committees' investigation found:

- **FDA's Interactions with Biogen Were Atypical and Failed to Follow the Agency's Own Documentation Protocol:** Documents obtained by the Committees show that FDA staff and Biogen engaged in at least 115 meetings, calls, and substantive email exchanges over a 12-month period beginning in July 2019. These exchanges included at least 40 FDA-Biogen "working group" meetings. FDA's own internal review of the agency's approval process for Aduhelm found that the extent of collaboration between FDA and Biogen was atypical and "exceeded the norm in some respects." FDA confirmed that the total number of meetings between FDA staff and Biogen during this time is unknown because FDA lacked a "clear record" of the informal meetings and other interactions between agency staff and Biogen. Of the more than 40 working group meetings between FDA staff and Biogen that were memorialized, not all were properly documented according to internal FDA procedures. The Committees identified an additional 66 calls and substantive email exchanges among the subgroups of the working group that were not memorialized.
- **FDA and Biogen Inappropriately Collaborated on a Joint Briefing Document for the PCNS Advisory Committee That Did Not Adequately Represent Differing Views Within FDA:** The Committees obtained evidence that FDA and Biogen staff worked closely for several months ahead of the November 6, 2020, PCNS Advisory Committee meeting to prepare the joint briefing document for the Committee's review. Documents show that using a joint briefing document afforded Biogen advance insight into FDA's responses and direct guidance from the agency in drafting the company's own sections. For example, in an exchange of the draft briefing document on October 9, 2020, FDA staff asked Biogen to move a paragraph drafted by the agency into Biogen's section of the memorandum—a change reflected when the document was finalized. FDA's internal review determined that the Office of Neuroscience (ON) within CDER's Office of New Drugs (OND) had failed to obtain internal OND consensus on FDA's position prior to working with Biogen on the document. The review concluded that "the use of the joint briefing document was not an appropriate

⁸ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA, Findings and Analysis*, at Pages 11–16 (May 30, 2021) (Food and Drug Administration began this internal assessment in early 2021 after receiving letters from Public Citizen on December 9, 2020, and January 28, 2021, regarding the interactions between Food and Drug Administration staff and Biogen). *Id.*, at Pages 1–2.

approach in this instance” given the substantial disagreement between FDA offices.

- **FDA Pivoted to Using the Accelerated Approval Pathway for Aduhelm on a Substantially Abbreviated Timeline:** Despite considering Aduhelm under the traditional approval pathway for nine months, documents and information obtained by the Committees show that FDA abruptly changed course and granted approval under the accelerated approval pathway—which allows the use of surrogate clinical endpoints to demonstrate effectiveness—after just three weeks of review. According to senior FDA leadership, the shift in approval pathway from traditional approval to accelerated approval only occurred after an FDA expert council meeting on April 7, 2021, resulted in unfavorable feedback for Aduhelm’s traditional approval. Meeting minutes and FDA’s responses to the Committees show FDA informed Biogen on April 28, 2021, that Aduhelm would be considered under the accelerated approval pathway.
- **FDA Approved and Biogen Accepted a Broad Label Indication for Aduhelm Despite Lack of Clinical Data on All Alzheimer’s Disease Stages and Biogen’s Reservations:** FDA approved Aduhelm for treatment of “people with Alzheimer’s disease”—a far broader population than Biogen studied in its clinical trials. Materials obtained by the Committees demonstrate that FDA recommended this broad label indication despite the lack of clinical data on disease stages other than mild cognitive impairment (MCI) and mild dementia stage of disease. Internal documents obtained by the Committees show that Biogen accepted this broad indication statement for Aduhelm despite internal reservations about the lack of evidence of clinical benefit for patients at disease stages outside of the clinical trials and an unknown safety profile. In documents, Biogen’s Alzheimer’s disease team leaders expressed concern that the company could lose credibility by advocating for a broad label that exceeded the clinical trial population, and the company even developed a communications strategy to deal with the anticipated fallout. However, company materials noted that Biogen had “NO plan to push back on broad label indication internally or with the regulators,” and Biogen only sought a label update to clarify the appropriate patient population after patient and provider confusion and public criticism when the drug came to market.
- **Biogen Set an Unjustifiably High Price for Aduhelm to “Make History” for the Company Despite the Impact on Patients and the Medicare Program:** Documents obtained by the Committees show that Biogen viewed Aduhelm as an unprecedented financial opportunity—estimating a potential peak revenue of \$18 billion per year—and developed aggressive launch and marketing plans to maximize revenue throughout the drug’s lifecycle. These internal documents show that Biogen initially set Aduhelm’s price at \$56,000 per year despite a lack of demonstrated clinical benefit in a broad patient population, and the anticipated financial impact on patients and the Medicare program. A September 2020

presentation to the Board stated, “Our ambition is to make history” and “establish ADUHELM as one of the top pharmaceutical launches of all time.” Documents provided to the Committees show that Biogen fully expected the high price would spur “pushback” from providers and payers and that, in anticipation of this backlash, Biogen developed an external narrative about the drug’s value to sell to patients and the public.

- **Biogen Expected Aduhelm to Be a Burden to Medicare and Costly to Patients:** Internal company documents show that Biogen was aware that the financial burden of its high price for Aduhelm would fall primarily on Medicare. Documents show that Biogen projected Medicare would account for more than 85 percent of the drug’s target patient population at the time of its launch—and that government programs would collectively account for 90 percent of the patient population. A November 2020 presentation to the Board noted, “Aducanumab has the potential to be a significant part of the Medicare Part B budget” and calculated that Aduhelm could cost Medicare \$12 billion in one year—representing 36 percent of Medicare’s 2018 Part B budget. Internal company documents also show that Biogen knew based off of previous pricing models that some Medicare patients would struggle to afford Aduhelm. Analyses conducted by Biogen estimated that some Medicare patients could face out-of-pocket costs for Aduhelm of up to 20 percent of their income.
- **Biogen Planned to Spend Billions to Market Aduhelm Despite the Financial Impact on Patients and the Health Care System:** Internal documents show that Biogen planned an aggressive outreach and marketing campaign to launch Aduhelm, focusing on direct outreach to providers, patients, patient advocacy groups, payers, and even policymakers. In some long-range plans, Biogen anticipated spending more than \$3.3 billion on sales and marketing for Aduhelm from 2020 to 2024—more than two and a half times what Biogen spent in total development costs for aducanumab from 2007 until approval in June 2021. In September 2020, Biogen anticipated spending between \$500 million and \$600 million to build out its sales force, with a focus on targeting physicians. Biogen also aimed to activate patients directly through a variety of strategies, including marketing, media, and patient services.

Given these findings, the Committees recommend FDA take three immediate actions to help restore the American people’s trust in the agency’s processes and assurances of drug safety and efficacy:

1. Ensure that all substantive FDA interactions with drug sponsors are properly memorialized;
2. Establish a protocol for joint FDA-Drug Sponsor Briefing Documents for Advisory Committees; and

3. Update its *Guidance for Industry Regarding Development and Review of New Alzheimer's Drugs*.

While FDA's own internal review conclusions in May 2021 consisted of similar recommendations related to meeting memorialization and use of joint briefing documents, as of August 2022, FDA reported to the Committees that it is still in the process of implementing these recommendations.⁹

In addition, as a result of the Committees' findings, the Committees also recommend actions that Biogen, and other drug sponsors, take in the future to fulfill their responsibility to the patients and families who may come to rely on their treatments. Biogen and other drug sponsors should:

1. Communicate safety and efficacy concerns clearly to FDA; and
2. Consider the value assessment made by outside experts, including patient access, when setting drug prices.

The American people rely on FDA for assurance on the safety and efficacy of the medications they take. The number of patients and families impacted by Alzheimer's disease will continue to increase, and it is crucial that FDA and drug companies adhere to established procedures and conduct themselves with the transparency necessary to earn public trust. The Committees urge FDA, Biogen, and other drug sponsors seeking to develop treatments for Alzheimer's disease and other diseases to follow guidance and protocols, provide transparency into the drug evaluation process and drug pricing, and work to better ensure public trust in future drug approvals.

⁹ Food and Drug Administration, *FDA Response to Clarifying Questions from Energy and Commerce and Oversight and Reform Staff*, at Page 4 (Aug. 11, 2022).

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I. BACKGROUND

Aducanumab (Aduhelm) is an amyloid beta-directed antibody—meaning it is designed to target certain plaque build-up in the brain associated with Alzheimer’s disease.¹⁰ Aduhelm is administered by infusion and was developed by Biogen as part of its Alzheimer’s disease portfolio.¹¹ In August 2015, Biogen initiated two Phase 3 trials for Aduhelm, Study 301 and 302, with the first patients enrolled beginning on September 8, 2015.¹² Three-and-a-half years later, on March 21, 2019, Biogen announced it was discontinuing the Phase 3 trials “based on results of a futility analysis conducted by an independent data monitoring committee, which indicated the trials were unlikely to meet their primary endpoint upon completion.”¹³

Two months after these trials were halted, Dr. Billy Dunn, Director of FDA’s ON, within the CDER OND, and Dr. Alfred Sandrock, Biogen’s then-Head of Research and Development, discussed the status of Aduhelm’s terminated trials at a neurology conference in Philadelphia.¹⁴ In this conversation, Dr. Sandrock shared findings from the terminated trials with Dr. Dunn, who suggested that Biogen schedule a Type C meeting—one of four types of formal meetings between CDER and drug sponsors in the drug application process—to further discuss the data.¹⁵

¹⁰ Food and Drug Administration, *Aducanumab (marked as Aduhelm) Information* (July 8, 2021) (online at www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/aducanumab-marketed-aduhelm-information).

¹¹ Food and Drug Administration, *Highlights of Prescribing Information: ADUHELM* (online at www.accessdata.fda.gov/drugsatfda_docs/label/2021/761178s003lbl.pdf) (accessed Dec. 1, 2022). Biogen entered into a collaboration agreement with Japanese pharmaceutical company Eisai Co., agreed to jointly develop and commercialize Aduhelm. Biogen, *Biogen and Eisai Expand Existing Collaboration Agreement to Develop and Commercialize Investigational Alzheimer’s Disease Treatments Including Phase 3 Aducanumab* (Oct. 23, 2017) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-and-eisai-expand-existing-collaboration-agreement-develop>). This agreement was amended in March 2022 to give Biogen sole decision making and commercial rights with respect to Aduhelm. Biogen, *Biogen and Eisai Amend Collaboration Agreements on Alzheimer’s Disease Treatments* (Mar. 14, 2022) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-and-eisai-amend-collaboration-agreements-alzheimers>).

¹² Biogen, *Press Release: Biogen Enrolls First Patient in Global Phase 3 Study of Investigational Treatment Aducanumab (BIIB037) for Early Alzheimer’s Disease* (Sept. 8, 2015) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-enrolls-first-patient-global-phase-3-study>). Phase 3 trials are typically large trials to confirm a drug’s effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug to be used safely, and are the last phase of testing before a drug is submitted to the regulatory authorities for marketing approval. Food and Drug Administration, *What Are the Different Types of Research?* (Jan. 4, 2018) (online at www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research).

¹³ Biogen, *Press Release: Biogen and Eisai to Discontinue Phase 3 ENGAGE and EMERGE Trials of Aducanumab in Alzheimer’s Disease* (Mar. 21, 2019) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-and-eisai-discontinue-phase-3-engage-and-emerge-trials>).

¹⁴ *Inside “Project Onyx”: How Biogen Used an FDA Back Channel to Win Approval of its Polarizing Alzheimer’s Drug*, STAT (June 29, 2021) (online at www.statnews.com/2021/06/29/biogen-fda-alzheimers-drug-approval-aduhelm-project-onyx/).

¹⁵ Briefing by Patricia Cavazzoni, M.D., Director; Office of New Drugs, Center for Drug Evaluation and Research; Food and Drug Administration et al., to Staff, Committee on Energy and Commerce and Committee on

Documents obtained from FDA show that following the meeting in Philadelphia, Biogen re-engaged in conversations with the agency, seeking to demonstrate that further post-hoc analysis of the data from the two incomplete Phase 3 trials could demonstrate clinical benefit.¹⁶ After a June 14, 2019, Type C meeting, FDA and Biogen agreed that further analyses of the data were needed, and FDA stated in the meeting minutes that, “those further analyses would best be conducted as part of a bilateral effort involving the agency and sponsor, i.e., through a ‘workstream’ or ‘working group’ collaboration.”¹⁷ After a year of working group collaboration, involving numerous meetings and exchanges of data analysis between Biogen and FDA, on July 7, 2020, Biogen completed its submission of a Biologics License Application (BLA) to FDA for the approval of Aduhelm for the treatment of Alzheimer’s disease.¹⁸

On November 6, 2020, FDA convened the PCNS Advisory Committee to review the clinical trial data and discuss the evidence supporting the Aduhelm application.¹⁹ Advisory committees provide FDA with independent opinions from outside experts on the safety, efficacy, and appropriate use of products and drugs, and FDA generally follows an advisory committee’s recommendation, although it is not bound to do so.²⁰ None of the 11 empaneled members of the PCNS Advisory Committee recommended approval, as Committee members “did not agree that it was reasonable to consider the clinical benefit of the one successful trial as the primary

Oversight and Reform (Apr. 7, 2022). There are four types of formal meetings defined in the Prescription Drug User Fee Act that occur between requesters and Food and Drug Administration staff with established best practices for documentation: (1) Type A; (2) Type B; (3) Type B (end of phase); and (4) Type C. Type C meetings allow sponsors to engage with Center for Drug Evaluation and Research on a wide range of topics, whereas Type A and Type B meetings are reserved for specific situations, such as resolving stalled drug development programs or to discuss a new application. Food and Drug Administration, *Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants* (May 2009) (online at www.fda.gov/media/72253/download).

¹⁶ Food and Drug Administration, *Administrative and Correspondence Documents*, at Pages 65–66 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

¹⁷ *Id.*, at Page 70.

¹⁸ Biogen, *Press Release: Biogen Completes Submission of Biologics License Application to FDA for Aducanumab as a Treatment for Alzheimer’s Disease* (July 8, 2020) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-completes-submission-biologics-license-application-fda>).

¹⁹ Food and Drug Administration, *November 6, 2020: Meeting of the Peripheral and Central Nervous System Drugs Advisory Committee Meeting Announcement* (Feb. 5, 2021) (www.fda.gov/advisory-committees/advisory-committee-calendar/november-6-2020-meeting-peripheral-and-central-nervous-system-drugs-advisory-committee-meeting#event-information).

²⁰ Food and Drug Administration, *Advisory Committees Give FDA Critical Advice and the Public a Voice* (Sept. 21, 2022) (online at www.fda.gov/consumers/consumer-updates/advisory-committees-give-fda-critical-advice-and-public-voice). “The marketing applications include data to show the safety and effectiveness of human drugs, and the outside experts receive summary information about the applications and copies of FDA’s review of the application documents. Based on this information, advisory committees may recommend approval or disapproval of a drug’s marketing application.” Food and Drug Administration, *Human Drug Advisory Committees* (Oct. 5, 2017) (online at www.fda.gov/advisory-committees/committees-and-meeting-materials/human-drug-advisory-committees).

evidence supporting approval.”²¹ The question of accelerated approval was never posed to the PCNS Advisory Committee for discussion or vote.²²

Following letters from Public Citizen (a non-profit consumer rights advocacy group) to FDA—sent December 9, 2020, and January 28, 2021—both expressing concern of close collaboration between the agency and Biogen and calling for an investigation, in the spring of 2021, FDA’s Office of Medical Policy (OMP) initiated an internal review of FDA’s and Biogen’s interactions in preparation for and during the PCNS Advisory Committee meeting.²³ According to FDA, OMP officials reviewed available documentation for meetings between FDA and Biogen representatives and interviewed six representatives from ON, OB, and the Office of Oncologic Diseases (OOD).²⁴

The internal review report, obtained by the Committees and not previously released, was completed on May 30, 2021, and included three findings and four recommendations.²⁵ After noting that FDA “has often used incremental resources and efforts to further the development of treatments for diseases such as Alzheimer’s that have unmet medical needs,” the review concluded that, “There is no evidence that these interactions with the sponsor in advance of filing were anything but appropriate in this situation.”²⁶ However, the internal review presented three findings of atypical processes: (1) FDA’s and Biogen’s collaboration “exceeded the norm in some respects”; (2) the internal scientific dispute “was not addressed early enough in the process”; and (3) the preparation of joint agency and drug sponsor briefing document “may have

²¹ Food and Drug Administration, *FDA’s Decision to Approve New Treatment for Alzheimer’s Disease* (June 7, 2021) (online at www.fda.gov/drugs/news-events-human-drugs/fdas-decision-approve-new-treatment-alzheimers-disease); Food and Drug Administration, *Peripheral and Central Nervous System Drugs Advisory Committee (PCNS) Meeting* (Nov. 6, 2020) (online at www.fda.gov/media/145691/download).

²² Food and Drug Administration, *Peripheral and Central Nervous System Drugs Advisory Committee (PCNS) Meeting* (Nov. 6, 2020) (online at www.fda.gov/media/145691/download).

²³ Letter from Michael A. Carome, M.D., Director, Public Citizen’s Health Research Group, to Stephen M. Hahn, M.D., Commissioner, Food and Drug Administration, and Patrizia Cavazzoni, M.D., Acting Director, Center for Drug Evaluation and Research; Food and Drug Administration (Dec. 9, 2020) (online at www.citizen.org/wp-content/uploads/201209_Letter-to-FDA-RE-Aducanumab-BLA-Review_FINAL-WITH-ENCLOSURE.pdf); Letter from Michael A. Carome, M.D., Director, Public Citizen’s Health Research Group, to Janet Woodcock, M.D., Acting Commissioner, Food and Drug Administration (Jan. 28, 2021) (online at <https://mkus3lurbh3lbztg254fzode-wpengine.netdna-ssl.com/wp-content/uploads/2566.pdf>); *How an Unproven Alzheimer’s Drug Got Approved*, New York Times (July 19, 2021) (updated Oct. 20, 2021) (online at www.nytimes.com/2021/07/19/health/alzheimers-drug-aduhelm-fda.html); Briefing by Food and Drug Administration, to Staff, Committee on Energy and Commerce and Committee on Oversight and Reform (July 23, 2021); Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Pages 1–2 (May 30, 2021).

²⁴ Food and Drug Administration, *FDA Response to Clarifying Questions from Energy and Commerce and Oversight and Reform Staff*, at Page 9 (Aug. 11, 2022).

²⁵ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis* (May 30, 2021).

²⁶ *Id.*, at Page 11.

contributed to the impression by Public Citizen that FDA’s objectivity may have been compromised.”²⁷

The internal review report also identified four recommendations: (1) engage CDER leadership for further discussions regarding whether Aduhelm was “an isolated issue” or reflects a need for further education about how to incorporate scientific and/or regulatory differences within the review process; (2) brief Office Directors in a timely manner to allow escalation of any issues (such as discordant views or complex applications) before a PCNS Advisory Committee meeting; (3) use an FDA and drug sponsor joint briefing document for the PCNS Advisory Committee “only when there is a unified FDA perspective on the data”; and (4) maintain documentation of interactions between the sponsor and FDA, outside of Type C meetings, in FDA’s document archival system.²⁸

Over the next five weeks, OND Director Dr. Peter Stein reviewed and discussed these findings and recommendations with the Directors of the Office of Translational Sciences, the Office of Surveillance and Epidemiology, and OMP. On July 6, 2021, Dr. Stein submitted an “After Action Plan” to CDER Director Dr. Patrizia Cavazzoni, including steps that had been taken and proposing additional actions to address the internal review recommendations. The plan proposed that OND develop best practices for preparation for PCNS Advisory Committee meetings, including the use of joint briefing documents and guidelines for handling scientific differences of opinion. In addition, the After Action Plan proposed that: CDER organize an internal workshop for leaders on handling differences in scientific opinion within a team culture; OND review its processes for its staff to brief Senior Offices leadership on controversial, challenging, or noteworthy issues taken to an Advisory Committee meeting; and OND develop a training plan “to assure that staff are consistently and regularly trained” on how to document interactions between the agency and drug sponsors.²⁹

On June 7, 2021, following an FDA Medical Policy and Program Review Council (MPPRC) meeting on April 7, 2021, and a Center Director Briefing on April 26, 2021, FDA granted accelerated approval to aducanumab under the trade name Aduhelm without additional input from the PCNS Advisory Committee.³⁰ FDA’s use of this approval pathway was based on the statutory standard for efficacy relying on a surrogate endpoint that is reasonably likely to

²⁷ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Pages 4–11 (May 30, 2021).

²⁸ *Id.*, at Pages 13–16.

²⁹ Food and Drug Administration, *After Action Plan*, at Pages 1–2 (July 6, 2021).

³⁰ Medical Policy and Program Review Council, *Medical Policy and Program Review Council Meeting: BLA 761178, Aducanumab for the Treatment of Alzheimer’s Disease* (Mar. 31 and Apr. 7, 2021) (meeting minutes). Food and Drug Administration, *Summary Memorandum*, at Page 56 (June 7, 2021) (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/Aducanumab_BLA761178_Dunn_2021_06_07.pdf); Food and Drug Administration, *Press Release: FDA Grants Accelerated Approval for Alzheimer’s Drug* (June 7, 2021) (online at www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug).

predict clinical benefit.³¹ In the case of Aduhelm’s accelerated approval, FDA relied on the reduction of amyloid beta plaque in the brain as the surrogate endpoint in determining that it would be “reasonably likely to predict a clinical benefit to patients” of delaying cognitive decline.³²

Aduhelm’s initial label indication for use was “for the treatment of Alzheimer’s disease.”³³ On July 7, 2021, however, following concern about the drug’s initial broad label, the drug’s indication was revised and narrowed to clarify that “[t]reatment with ADUHELM should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in clinical trials.”³⁴ Under accelerated approval, drug companies are required to conduct studies—known as Phase 4 confirmatory trials—to confirm the drug’s anticipated clinical benefit. FDA gave Biogen almost nine years, until August 2029, to complete the confirmatory trial for Aduhelm and until February 2030 to submit its report to FDA.³⁵

The research and medical communities immediately responded to FDA’s approval of Aduhelm with furor, concern, and confusion.³⁶ Experts noted that prior to Aduhelm’s approval, “FDA had not indicated that it considered beta-amyloid a valid pharmacodynamic biomarker, much less an acceptable surrogate endpoint for clinical trials.”³⁷ Within weeks of FDA’s approval of Aduhelm, three members of the PCNS Advisory Committee resigned publicly in protest, with one writing that the approval of Aduhelm was “probably the worst drug approval

³¹ 21 U.S.C. § 356(c); Food and Drug Administration, *Press Release: FDA Grants Accelerated Approval for Alzheimer’s Drug* (June 7, 2021) (online at www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug).

³² Food and Drug Administration, *FDA’s Decision to Approve New Treatment for Alzheimer’s Disease* (June 7, 2021) (online at www.fda.gov/drugs/news-events-human-drugs/fdas-decision-approve-new-treatment-alzheimers-disease).

³³ Food and Drug Administration, *Highlights of Prescribing Information: ADUHELM* (online at www.accessdata.fda.gov/drugsatfda_docs/label/2021/761178s003lbl.pdf) (accessed Dec. 1, 2022); See also *In Reversal, F.D.A. Calls for Limits on Who Gets Alzheimer’s Drug*, New York Times (July 8, 2021) (online at www.nytimes.com/2021/07/08/health/aduhelm-alzheimers-fda.html).

³⁴ Food and Drug Administration, *Highlights of Prescribing Information: ADUHELM* (online at www.accessdata.fda.gov/drugsatfda_docs/label/2021/761178s003lbl.pdf) (accessed Dec. 1, 2022).

³⁵ Letter from Billy Dunn, M.D., Director; Office of Neuroscience, Center for Drug Evaluation and Research; Food and Drug Administration, to Biogen, at Page 3 (June 7, 2021) (online at www.accessdata.fda.gov/drugsatfda_docs/appletter/2021/761178Orig1s000ltr.pdf).

³⁶ See e.g., *Furor Rages Over FDA Approval of Controversial Alzheimer’s Drug*, Washington Post (June 17, 2021) (online at www.washingtonpost.com/health/2021/06/17/alzheimers-drug-controversy/); *Alzheimer’s Drug Approved Despite Doubts About Effectiveness*, Science Insider (June 7, 2021) (online at www.science.org/content/article/alzheimer-s-drug-approved-despite-doubts-about-effectiveness).

³⁷ G. Caleb Alexander, M.D. et al., *Revisiting FDA Approval of Aducanumab*, New England Journal of Medicine (Aug. 26, 2021) (online at www.nejm.org/doi/full/10.1056/NEJMp2110468).

decision in recent U.S. history.”³⁸ In the months that followed, several major medical centers, insurance companies, and the U.S. Department of Veterans Affairs decided not to add Aduhelm to their formularies.³⁹ The common concern raised by experts centered on the lack of evidence of benefits related to the surrogate endpoint used to support Aduhelm’s approval, along with known safety risks to patients.⁴⁰ Even among patients facing the disease, there was uncertainty and controversy regarding the drug’s approval.⁴¹

At the time of Aduhelm’s launch, Biogen announced that the list price of the drug for the average-weight patient would be \$56,000 per year—which Biogen’s then-CEO called a “fair” price.⁴² The company subsequently reduced the price of the drug, announcing in December 2021 that the yearly price of the average maintenance dose would be reduced to \$28,200 effective January 1, 2022.⁴³ In February 2022, Biogen released its 2021 earnings, which showed only \$3 million in revenue from Aduhelm for all of 2021.⁴⁴ On April 7, 2022, the Centers for Medicare & Medicaid Services (CMS) finalized its National Coverage Determination, which provided that Aduhelm would only be covered by Medicare for participants in studies approved or supported by FDA, CMS, or the National Institutes of Health.⁴⁵ On April 22, 2022, Biogen announced that

³⁸ *Three F.D.A. Advisors Resign Over Agency’s Approval of Alzheimer’s Drug*, New York Times (June 10, 2021) (online at www.nytimes.com/2021/06/10/health/aduhelm-fda-resign-alzheimers.html); Letter from Aaron Kesselheim, M.D., J.D., M.P.H., Professor of Medicine, Harvard Medical School, to Janet Woodcock, M.D., Acting Commissioner, Food and Drug Administration (June 10, 2021) (online at <https://pbs.twimg.com/media/E3jKN4GWYAUGj9U.png>).

³⁹ *Cleveland Clinic and Mount Sinai Won’t Administer Aduhelm to Patients*, New York Times (July 14, 2021) (online at www.nytimes.com/2021/07/14/health/cleveland-clinic-aduhelm.html); *Insurers Balk at Paying for Biogen’s \$56,000-a-Year Alzheimer’s Treatment*, Bloomberg News (Nov. 18, 2021) (online at www.bloomberg.com/news/articles/2021-11-18/insurers-balk-at-paying-for-biogen-alzheimer-s-treatment); *U.S. Veterans Health Administration Turns Down Biogen Alzheimer’s Drug*, Reuters (Aug. 11, 2021) (online at www.reuters.com/business/healthcare-pharmaceuticals/us-veterans-health-administration-turns-down-biogen-alzheimers-drug-2021-08-11/).

⁴⁰ See e.g., Aaron S. Kesselheim and Jerry Avorn, *The F.D.A. Has Reached a New Low*, New York Times (June 15, 2021) (online at www.nytimes.com/2021/06/15/opinion/alzheimers-drug-aducanumab-fda.html).

⁴¹ *As Debate on Alzheimer’s Drug Heats Up, Dementia Patients Are Torn*, U.S. News & World Report (Mar. 4, 2022) (online at www.usnews.com/news/health-news/articles/2022-03-04/dementia-patients-divided-over-alzheimers-drug-aduhelm).

⁴² *Biogen CEO Says \$56,000 Annually for Alzheimer’s Drug is “Fair,” Promises Not to Hike Price for at Least 4 Years*, CNBC (June 7, 2021) (online at www.cnbc.com/2021/06/07/biogen-ceo-says-56000-annually-for-alzheimers-drug-is-fair-promises-not-to-hike-price-for-at-least-4-years.html).

⁴³ Biogen, *Press Release: Biogen Announces Reduced Price for ADUHELM to Improve Access for Patients with Early Alzheimer’s Disease* (Dec. 20, 2021) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-announces-reduced-price-aduhelm-improve-access-patients>).

⁴⁴ Biogen, *Press Release: Q4 and Full Year 2021: Financial Results and Business Update*, at Page 30 (Feb. 3, 2022) (online at <https://investors.biogen.com/static-files/019bc8a4-527e-4565-a58b-91ef680630c1>).

⁴⁵ Centers for Medicare & Medicaid Services, *Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer’s Disease (AD)* (Apr. 7, 2022) (CAG-00460N) (online at www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=375&ncdver=1).

it was withdrawing its application to market Aduhelm in the European Union.⁴⁶ On May 3, 2022, Biogen informed investors that it was “[s]ubstantially eliminating commercial infrastructure” supporting Aduhelm following CMS’s National Coverage Determination.⁴⁷

On August 4, 2021, the Department of Health and Human Services’ (HHS) Office of Inspector General (OIG) announced it would be conducting a related investigation into, among other matters, “how the FDA implements the accelerated approval pathway.”⁴⁸ HHS OIG issued the first of its related reports in September 2022, which examined in part the delays in confirmatory trials for drugs granted accelerated approval and has indicated that its complete findings may not be available until 2023.⁴⁹

In the meantime, several similar anti-amyloid beta drugs for Alzheimer’s disease are already in FDA’s review pipeline, including: lecanemab, another drug developed by Biogen and Eisai, for which FDA granted priority review and a decision is expected by January 2023; Eli Lilly & Company’s donanemab, for which FDA has accepted expedited review and a decision is expected in February 2023; and Roche’s gantenerumab, which received breakthrough therapy designation from FDA in October 2021.⁵⁰

⁴⁶ Biogen, *Press Release: Update on Regulatory Submission for Aducanumab in the European Union* (Apr. 22, 2022) (online at <https://investors.biogen.com/news-releases/news-release-details/update-regulatory-submission-aducanumab-european-union-0>).

⁴⁷ Biogen, *Press Release: First Quarter 2022: Financial Results and Business Update*, at Page 6 (May 3, 2022) (online at <https://investors.biogen.com/static-files/d71367a7-5c59-46d9-a043-f5db8a885abe>).

⁴⁸ Department of Health and Human Services, Office of Inspector General, *Review of the FDA’s Accelerated Approval Pathway* (online at <https://oig.hhs.gov/reports-and-publications/workplan/summary/wp-summary-0000608.asp>) (accessed Dec. 1, 2022).

⁴⁹ *Id.* Department of Health and Human Services, Office of Inspector General, *Delays in Confirmatory Trials for Drug Applications Granted FDA’s Accelerated Approval Raise Concerns* (Sept. 29, 2022) (online at <https://oig.hhs.gov/oei/reports/OEI-01-21-00401.pdf>).

⁵⁰ *FDA, Under Fire for Aduhelm Approval, Starts Review of Another Alzheimer’s Drug*, BioPharma Dive (July 6, 2022) (online at www.biopharmadive.com/news/fda-under-fire-for-aduhelm-approval-starts-review-of-another-alzheimers/626649/); Lilly, *Press Release: Lilly’s Donanemab Receives U.S. FDA’s Breakthrough Therapy Designation for Treatment of Alzheimer’s Disease* (June 24, 2021) (online at <https://investor.lilly.com/news-releases/news-release-details/lillys-donanemab-receives-us-fdas-breakthrough-therapy>). In September 2022, Biogen and Eisai announced that a study of lecanemab demonstrated clinical benefits associated with the use of lecanemab to reduce amyloid beta plaque and indicated plans to submit lecanemab for traditional FDA approval by the end of March 2023. Biogen, *Press Release: Lecanemab Confirmatory Phase 3 Clarity AD Study Met Primary Endpoint, Showing Highly Statistically Significant Reduction of Clinical Decline in Large Global Clinical Study of 1,795 Participants with Early Alzheimer’s Disease* (Sept. 27, 2022) (online at <https://investors.biogen.com/news-releases/news-release-details/lecanemab-confirmatory-phase-3-clarity-ad-study-met-primary>); *Genentech’s Anti-Amyloid Beta Antibody Gantenerumab Granted FDA Breakthrough Therapy Designation in Alzheimer’s Disease*, Business Wire (Oct. 8, 2021) (online at www.businesswire.com/news/home/20211008005371/en/Genentech%E2%80%99s-Anti-Amyloid-Beta-Antibody-Gantenerumab-Granted-FDA-Breakthrough-Therapy-Designation-in-Alzheimer%E2%80%99s-Disease); *Roche’s Experimental Alzheimer’s Treatment Fails to Slow Cognitive Decline Across Two Clinical Trials*, STAT (Nov. 14, 2022) (online at www.statnews.com/2022/11/14/roches-experimental-alzheimers-treatment-fails-to-slow-cognitive-decline-across-two-clinical-trials/).

II. FDA’S APPROVAL PROCESS WAS RIFE WITH IRREGULARITIES

Documents and information obtained by the Committees, including FDA’s own internal review, show that the agency’s review and approval process for Aduhelm was highly atypical and deviated from FDA’s guidance and procedures in significant respects.

A. Atypical Collaboration and Interactions Between FDA and Biogen

On June 14, 2019, approximately three months after Biogen terminated its Aduhelm trials due to futility, FDA and Biogen senior leaders convened a Type C meeting and agreed to collaborate on a review of data from the incomplete trials.⁵¹ This formal meeting occurred roughly one month after the meeting between Dr. Sandrock and Dr. Dunn, in Philadelphia—a conversation that raised questions of propriety in the media and among stakeholders, but that FDA stated to Committee staffs was commonplace when agency staff and sponsor staff routinely attend scientific conferences.⁵² In the formal, memorialized, Type C meeting that followed, both FDA and Biogen decided to conduct further analyses of the “large but incomplete, complicated, and partially discordant data set” from Biogen’s two clinical trials, and work together “through a ‘workstream’ or ‘working group’ collaboration.”⁵³

Following subsequent meetings between Drs. Dunn and Samantha Budd Haeberlein, Biogen’s then Vice President for Clinical Development, on July 2, 2019, FDA and Biogen representatives met and confirmed an approach for completing collaborative data analyses, and agreed to meet multiple times per week to “define” and “align” work.⁵⁴ Documents obtained from FDA and Biogen show that as Biogen worked to complete and submit its BLA over the next 12 months, FDA and Biogen engaged in at least 115 meetings, calls, and substantive email exchanges concerning the application process. These included at least 45 collaborative workstream meetings that included Drs. Dunn and Budd Haeberlein, seven collaborative workstream meetings involving the rest of the team but without Drs. Dunn and Budd Haeberlein,

⁵¹ Food and Drug Administration, *Administrative and Correspondence Documents*, at Pages 65 and 70 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

⁵² *Inside ‘Project Onyx’: How Biogen Used An FDA Back Channel to Win Approval of its Polarizing Alzheimer’s Drug*, STAT (June 29, 2021) (online at www.statnews.com/2021/06/29/biogen-fda-alzheimers-drug-approval-aduhelm-project-onyx/); Letter from Michael A. Carome, M.D., Director, Public Citizen’s Health Research Group, to Xavier Becerra, Secretary, Department of Health and Human Services (June 30, 2021) (online at www.citizen.org/wp-content/uploads/2591.pdf); Letter from Michael A. Carome, M.D., Director, Public Citizen’s Health Research Group, to Christi A. Grimm, Principal Deputy Inspector General, Office of Inspector General, Department of Health and Human Services (June 30, 2021) (online at www.citizen.org/wp-content/uploads/2592.pdf); Briefing by Patricia Cavazzoni, M.D., Director, Center for Drug Evaluation and Research; Food and Drug Administration et al., to Staff, Committee on Energy and Commerce and Committee on Oversight and Reform (Apr. 7, 2022).

⁵³ Food and Drug Administration, *Administrative and Correspondence Documents*, at Page 70 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

⁵⁴ Food and Drug Administration and Biogen, *Collaborative Workstream: Meeting Record*, at Page 2 (July 2, 2019) (Meeting Minutes).

and 66 other calls and email exchanges between various members of the collaborative working group.⁵⁵ The exact number of interactions between FDA and Biogen leading up to the PCNS Advisory Committee is unknown. Even FDA’s internal review concluded that, “Review of the Type C meetings did not reveal a clear record of the number and nature of interactions between the sponsor and FDA that occurred outside of Type C meetings.”⁵⁶

FDA guidance for industry and review staff recommends communications between staff and sponsors to provide advice and feedback and considers timely and frequent review team collaboration to be critical to good review management.⁵⁷ However, Biogen considered its BLA for Aduhelm to have “a complex dataset resulting in an atypical filing process requiring [a] high-touch engagement strategy with regulators.”⁵⁸

FDA’s internal review found that the extent of collaboration between FDA and Biogen was atypical and “exceeded the norm in some respects.”⁵⁹ The clinical and statistical reviewers on FDA’s Aduhelm review team acknowledged that the “circumstances surrounding the review of the BLA, as well as the amount of time and effort spent on the review and extent of the collaboration, were atypical.”⁶⁰ These reviewers also noted that meeting regularly with a drug sponsor between Type C meetings was *not* typical of other development programs. However, FDA ultimately concluded that the interactions were consistent with the agency’s public health mission given the potential for the first disease modifying drug for Alzheimer’s disease.⁶¹

The internal review further concluded that “the decision to work proactively with the sponsor, especially given the public health implications (taking into account the large unmet medical need), is consistent with FDA policy,” given Dr. Dunn’s assessment of Study 302 as possibly being “a home run” in terms of demonstrating clinical efficacy and safety of Aduhelm.⁶² This conclusion, however, does not appear to have been supported by the

⁵⁵ The Committees requested that the Food and Drug Administration and Biogen each provide a list of meetings and conversations between the agency and Biogen representatives, since January 2018, as well as all available documentation memorializing the meeting, call, or substantive e-mail exchange. Committee staffs reviewed these lists and documentation to develop a consolidated list and count of all meetings, calls, and substantive e-mail exchanges occurring between July 2019 and June 2020. Letter from Biogen to Chairwoman Carolyn B. Maloney, Committee on Oversight and Reform, and Chairman Frank Pallone, Jr., Committee on Energy and Commerce (Mar. 31, 2022).

⁵⁶ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Page 15 (May 30, 2021).

⁵⁷ Food and Drug Administration, *Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications: Guidance for Industry and Review Staff*, at Page 9 (Sept. 2018) (online at www.fda.gov/media/72259/download).

⁵⁸ BIIB_HCOR_EC_0023329, at Page 192.

⁵⁹ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Page 4 (May 30, 2021).

⁶⁰ *Id.*, at Page 5.

⁶¹ *Id.*, at Pages 4–6.

⁶² *Id.*, at Page 5.

information FDA had available at the time it agreed to work collaboratively with Biogen on its approval. The decision to proceed with a bilateral collaborative workstream was made at the June 14, 2019, Type C meeting—before FDA and Biogen conducted additional analyses of Biogen’s “incomplete, complicated, and partially discordant data set,” which were necessary to understand the overall results.⁶³ At the initial Type C meeting on June 14, FDA officials noted that more analysis was needed to determine whether the results supported approval.⁶⁴ The lack of analysis and other major questions FDA raised about the data at this meeting were not sufficiently answered until the end of September 2019 when, following additional analyses by FDA and Biogen, Dr. Dunn concluded that FDA had the information it needed “to coalesce on a path forward.”⁶⁵

B. FDA Failed to Follow Its Own Documentation Protocol

FDA’s internal review found that not all interactions between FDA and Biogen were properly documented or archived in FDA’s Document Archiving Reporting and Regulatory Tracking System (DARRTS), per FDA documentation protocol. FDA guidance stresses the importance of communication between the FDA review team and the sponsor to ensure transparency and clarity during the BLA review process.⁶⁶ However, FDA guidance also encourages communications to be well documented and archived. *CDER’s 21st Century Review Process Desk Reference Guide* notes briefly that it is the regulatory project manager (RPM) and the review team’s role to jointly prepare and archive minutes for meetings other than the post mid-cycle communication and the late-cycle meeting.⁶⁷ The RPM is also responsible for documenting and archiving ‘substantive’ calls with sponsors, though the guide does not specify criteria for whether an interaction is substantive and should be documented.⁶⁸ Although FDA guidance is not binding, the failure to maintain a complete record of meetings between a drug sponsor and FDA’s review team runs counter to the agency’s apparent goal of ensuring transparency and clarity in the review process.

FDA’s internal review found that many of the workstream meetings between FDA staff and Biogen officials outside the formal meeting process were not documented or archived into DARRTS, noting that “documentation from those meetings was not consistently maintained in

⁶³ Food and Drug Administration, *Administrative and Correspondence Documents*, at Page 70 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

⁶⁴ Food and Drug Administration, *Administrative and Correspondence Documents*, at Pages 68–70 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

⁶⁵ BIIB_HCOR_EC_0118271.

⁶⁶ Food and Drug Administration, *Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications: Guidance for Industry and Review Staff*, at Page 9 (Sept. 2018) (online at www.fda.gov/media/72259/download).

⁶⁷ Food and Drug Administration, *CDER 21st Century Review Process Desk Reference Guide*, at Page 31 (online at www.fda.gov/media/78941/download) (accessed Dec. 1, 2022).

⁶⁸ *Id.*

FDA's document archival system."⁶⁹ According to a clinical reviewer in FDA's Division of Neurology, Biogen kept the records of these workstream meetings and provided them to FDA in emails documenting the meetings.⁷⁰ In a letter to the Committees, FDA reported that of the more than 40 collaborative workstream meetings between FDA staff and Biogen that were memorialized (some meetings were not memorialized), not all were entered into DARRTS prior to Aduhelm's approval.⁷¹ Committees' staff identified at least four additional collaborative workstream meetings that may not have been memorialized and were therefore also not entered into DARRTS.⁷²

Other than the scheduling emails indicating that conversations took place, there was no official memorialization of at least 66 calls or substantive email exchanges among the subgroups of the collaborative workstream team—a fact that was apparently overlooked by FDA's review team until the internal review was initiated. Moreover, because FDA's internal review could not ascertain a clear record of the number and nature of interactions between Biogen and FDA, the total remaining undocumented interactions not included in DARRTS remains unknown.

FDA's internal review ultimately included a recommendation to maintain documentation of interactions between the drug sponsor and FDA outside of Type C meetings in FDA's document archival system.⁷³ Specifically, the internal review determined,

If there are frequent interactions that are organized around joint analyses of the data on an ongoing basis, it may be advisable to either have the Type C meeting minutes generally describe the number and nature of the interactions since the last Type C meeting or maintain informal notes, even if just a bulleted email summary, that can be placed into DARRTS [sic].⁷⁴

⁶⁹ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Page 5 (May 30, 2021). Food and Drug Administration's (FDA) *Formal Meetings Guidance* states that FDA should maintain and share formal meeting minutes with the sponsor 30 days after the meeting, indicating that FDA, and not the sponsor, should be responsible for recording meeting minutes. Food and Drug Administration, *Formal Meetings Between the FDA and Drug Sponsors or Applicants of PDUFA Products: Guidance for Industry*, at Pages 17–18 (Dec. 2017) (online at www.fda.gov/media/109951/download). FDA was not able to confirm the exact number of interactions that were not documented or archived.

⁷⁰ Briefing by Patricia Cavazzoni, M.D., Director; Office of New Drugs, Center for Drug Evaluation and Research; Food and Drug Administration et al., to Staff, Committee on Energy and Commerce and Committee on Oversight and Reform (Apr. 7, 2022).

⁷¹ Food and Drug Administration, *FDA Response to Clarifying Questions from Energy and Commerce and Oversight and Reform Staff*, at Page 11 (Jan. 3, 2022).

⁷² Specifically, the Committees identified four meetings that were referred to in other documents provided by the agency or Biogen, but FDA could not produce a summary of the discussion or other record of the meeting.

⁷³ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Page 15 (May 30, 2021).

⁷⁴ *Id.*, at Pages 15–16.

C. FDA and Biogen Inappropriately Collaborated on a Joint Briefing Document for the PCNS Advisory Committee That Did Not Adequately Represent Differing Views Within FDA

Following their workstream meetings, FDA and Biogen prepared a joint briefing document in preparation for the November 6, 2020, PCNS Advisory Committee meeting.⁷⁵ Briefing materials, which include the briefing document, refer to the package of information prepared by FDA and the sponsor and provided to advisory committee members before and during a meeting. These briefing materials include information such as a summary of clinical and non-clinical safety and effectiveness data, adverse drug reaction data, and statistical protocols and analyses.⁷⁶

According to FDA officials, a joint briefing document approach had previously only been utilized by FDA nine times, specifically by OOD, as FDA has generally taken the position that the briefing materials and presentations of FDA and drug sponsors should be independent and separate documents.⁷⁷ For example, a prior PCNS Advisory Committee meeting in April 2018 utilized separate sponsor and agency briefing documents—one prepared by the drug sponsor and submitted to FDA before submitting materials to the PCNS Advisory Committee, and another document prepared by FDA reviewers summarizing their preliminary observations.⁷⁸ In contrast, Aduhelm’s joint briefing document contained both Biogen’s and FDA’s sections that were drafted through a collaborative process, which made distinguishing between the agency’s and the sponsor’s respective analyses and positions challenging. At least one point attributed to Biogen was, for instance, written by FDA, while, at the same time, the briefing document also included FDA response sections ostensibly intended to depict the agency’s objective responses to Biogen’s analysis.

Documents obtained by the Committees show that the FDA review team and Biogen representatives worked closely for several months ahead of the November 2020 PCNS Advisory Committee meeting to prepare text for Biogen’s sections of the briefing document. In addition,

⁷⁵ Food and Drug Administration, *Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee Meeting: Combined FDA and Applicant PCNS Drugs Advisory Committee Briefing Document* (Nov. 6, 2020) (online at www.fda.gov/media/143502/download).

⁷⁶ Food and Drug Administration, *Guidance for Industry, Advisory Committee Meetings—Preparation and Public Availability of Information Given to Advisory Committee Members* (Aug. 2008) (online at www.fda.gov/media/75436/download).

⁷⁷ Briefing by Patricia Cavazzoni, M.D., Director; Office of New Drugs, Center for Drug Evaluation and Research; Food and Drug Administration et al., to Staff, Committee on Energy and Commerce and Committee on Oversight and Reform (Apr. 7, 2022); Letters from Food and Drug Administration, to Chairman Frank Pallone, Jr., Committee on Energy and Commerce, and Chairwoman Carolyn B. Maloney, Committee on Oversight and Reform, at Page 17 (Oct. 22, 2021).

⁷⁸ Food and Drug Administration, *Briefing Information for the April 19, 2018, Meeting of the Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee* (Apr. 16, 2018) (online at <https://public4.pagefreezer.com/browse/FDA/04-03-2022T19:30/https://www.fda.gov/advisory-committees/peripheral-and-central-nervous-system-drugs-advisory-committee/briefing-information-april-19-2018-meeting-peripheral-and-central-nervous-system-pcns-drugs-advisory>).

FDA provided Biogen with draft text of FDA’s own responses. This approach afforded Biogen advance insight into FDA’s responses and direct guidance from the agency in drafting the company’s own sections. For example, in an exchange of the draft briefing document on October 9, 2020, FDA asked Biogen to move a paragraph previously drafted by the agency for its own response section of the document into the preceding Biogen section—a change reflected when the document was finalized.⁷⁹

In preparing a joint briefing document for Aduhelm, FDA’s ON process differed from that previously used by OOD—notably, by not obtaining internal consensus on FDA’s position prior to joint briefing documents being developed. In the case of Aduhelm, while certain members of the FDA review team worked closely with Biogen to prepare a joint briefing document for the PCNS Advisory Committee meeting, staff from the Division of Biometrics I—the FDA division that does statistical review to ensure the safety and effectiveness of new drugs and that had concerns about the Aduhelm post-hoc analyses and data—were initially excluded from the process and were only given limited time to review and comment on the joint briefing document late in the revision process.⁸⁰ Specifically, the Division of Biometrics I only became aware of the joint briefing document when it received a draft “two to three days before comments were needed” and at least one month after Division of Neurology I staff and others within the ON and Biogen staff started drafting joint briefing materials.⁸¹ According to FDA’s internal review, the Division of Biometrics I had not expected the use of a joint briefing document for the PCNS Advisory Committee meeting because it had not previously been discussed during inter-divisional meetings.⁸²

During the joint briefing document drafting process, there were internal disagreements regarding the significance of trial results and post-hoc analyses between FDA’s Division of Neurology I and the Division of Biometrics I. The agency’s internal review noted that while there were attempts to resolve the disagreement between the divisions, the ON Director determined in October 2020 that resolving apparent differences was not feasible without delaying the scheduled PCNS Advisory Committee meeting. In addition, while the ON Director reported meeting with Division of Biometrics I leadership to discuss the statistical review and resolve the internal dispute shortly before the deadline to submit a joint briefing document for

⁷⁹ BIIIB_HCOR_EC_0005178, at Pages 84–85; Food and Drug Administration, *Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee Meeting: Combined FDA and Applicant PCNS Drugs Advisory Committee Briefing Document*, at Page 82 (Nov. 6, 2020) (online at www.fda.gov/media/143502/download).

⁸⁰ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Page 10 (May 30, 2021). While the Division of Biometrics was initially involved in the working group, starting in around October 2019, after they raised concerns about the analyses, they were not invited to further working group meetings and were not consulted on final details of models used. In a September 2019 meeting, the statistical reviewer in the Division of Biometrics presented about aducanumab at an internal Office of Biostatistics Round and concluded that “substantial evidence of effectiveness was not met.” The Division of Biometrics conveyed their reservations regarding the evidence to the Division of Neurology I and Biogen in Type C meetings. *Id.*, at Page 7.

⁸¹ *Id.*, at Pages 8 and 10.

⁸² Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Page 10 (May 30, 2021).

the PCNS Advisory Committee meeting, the Director of the Division of Biometrics I did not recall any such meeting.⁸³

Although ON's Division of Neurology I noted that several changes were made to the document in response to the Division of Biometrics I's comments, FDA's internal review found that the joint document did not give equal weight to the divisions' divergent perspectives and appeared to offer a more favorable perspective for approval.⁸⁴ During FDA's internal review, OOD noted that they would have been hesitant to use a joint briefing document in situations involving internal disagreements among FDA reviewers.⁸⁵ In contrast, ON proceeded developing joint briefing documents even though the FDA review team was not in alignment on key substantive issues.⁸⁶ FDA's own internal review found that this approach for the PCNS Advisory Committee was inappropriate, concluding that "the use of the joint briefing document was not an appropriate approach in this instance" given the substantial disagreement between FDA reviewers.⁸⁷

D. FDA Pivoted to Using the Accelerated Approval Pathway for Aduhelm on a Substantially Abbreviated Timeline

Documents and information obtained by the Committees show that, for nine months, FDA originally considered Aduhelm under the traditional approval pathway used for most drugs. However, after just a three-week period following negative internal FDA feedback about Aduhelm's lack of demonstrated clinical benefit necessary for traditional approval, the agency abruptly changed course, granting approval under the accelerated approval pathway—which allows the use of surrogate clinical endpoints to demonstrate effectiveness.

From the time Biogen submitted the BLA for Aduhelm to FDA on July 7, 2020, through the second meeting of the MPPRC—which FDA described to the Committee as a body in the CDER Office of Medical Policy that "routinely discusses and provides advice on complex regulatory decisions"—on April 7, 2021, FDA considered Aduhelm for potential approval through the traditional approval pathway.⁸⁸ While the use of the accelerated approval pathway was included as one of multiple options for approval pathway consideration in the first Type C meeting between Biogen and FDA on June 14, 2019, it does not appear to have been seriously

⁸³ Food and Drug Administration, *Internal Review of FDA-Biogen Interactions for Aducanumab BLA Findings and Analysis*, at Pages 8–9 (May 30, 2021).

⁸⁴ *Id.*, at Page 10.

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ *Id.*, at Page 12.

⁸⁸ Letters from Food and Drug Administration to Chairman Frank Pallone, Jr., Committee on Energy and Commerce, and Chairwoman Carolyn B. Maloney, Committee on Oversight and Reform, at Page 6 (Oct. 22, 2021).

considered as a pathway until after April 7, 2021.⁸⁹ According to CDER leadership, the shift in approval pathway from traditional approval to accelerated approval only occurred shortly after the second of the two MPPRC meetings on April 7, 2021, at which FDA experts provided unfavorable feedback for Aduhelm's approval.⁹⁰ According to FDA officials, sometime after that meeting, substantive discussions regarding utilizing the accelerated approval pathway for Aduhelm began within FDA's OND, and CDER Director Dr. Cavazzoni requested a decisional briefing.⁹¹

FDA issued its accelerated approval for Aduhelm without having put the question of the appropriateness of accelerated approval before any external advisory body or internal expert group. While FDA is not required to do so, it is a particularly notable lapse in this instance given that Dr. Dunn stated at the PCNS Advisory Committee meeting in November 2020 that FDA was "not using the amyloid as a surrogate for efficacy" at that point, and the meeting transcript shows that there were no further discussions of whether this approach may be appropriate.⁹² Even after FDA decided to review Aduhelm under the accelerated approval pathway, the agency did not reconvene the PCNS Advisory Committee to consider approval under this new pathway. In addition, accelerated approval was not put before MPPRC on March 31, 2021, nor April 7, 2021.⁹³ The MPPRC's meeting minutes demonstrate that the merits of the accelerated approval pathway were not raised "as this option had not been presented or otherwise discussed."⁹⁴ At the time of FDA's accelerated approval of Aduhelm on the basis of a surrogate endpoint, and still to date, FDA's applicable guidance, *Early Alzheimer's Disease: Developing Drugs for Treatment, Guidance for Industry*, had last been issued in February 2018. This guidance states that there is "no sufficiently reliable evidence that any observed treatment effect on such biomarker measures [beta-amyloid as a surrogate endpoint] would be reasonably likely to predict clinical benefit."⁹⁵

⁸⁹ Food and Drug Administration, *Administrative and Correspondence Documents*, at Pages 64 and 70 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

⁹⁰ Medical Policy and Program Review Council, *Medical Policy and Program Review Council Meeting: BLA 761178, Aducanumab for the Treatment of Alzheimer's Disease*, at Page 8 (Mar. 31 and Apr. 7, 2021) (meeting minutes).

⁹¹ Food and Drug Administration, *FDA Response to Clarifying Questions from Energy and Commerce and Oversight and Reform Staff*, at Pages 2–3 (Jan. 3, 2022); Letters from Food and Drug Administration to Chairman Frank Pallone, Jr., Committee on Energy and Commerce, and Chairwoman Carolyn B. Maloney, Committee on Oversight and Reform, at Page 6 (Oct. 22, 2021).

⁹² Food and Drug Administration, *Peripheral and Central Nervous System (PCNS) Drugs Advisory Committee Meeting Transcript*, at Pages 140: 15–17 (Nov. 6, 2020) (online at www.fda.gov/media/145691/download).

⁹³ Medical Policy and Program Review Council, *Medical Policy and Program Review Council Meeting: BLA 761178, Aducanumab for the Treatment of Alzheimer's Disease*, at Page 8 (Mar. 31 and Apr. 7, 2021) (meeting minutes).

⁹⁴ *Id.*

⁹⁵ Food and Drug Administration, *Early Alzheimer's Disease: Developing Drugs for Treatment, Guidance for Industry*, at Page 6 (Feb. 2018) (online at www.fda.gov/media/110903/download).

FDA reported to the Committees that in deciding to use beta-amyloid plaque reduction as a surrogate endpoint, the agency relied on data from three different clinical development programs that were not all available at the time of the PCNS Advisory Committee meeting, and which reported clinical benefit associated with reductions in amyloid plaque.⁹⁶ These clinical programs included Biogen’s Aduhelm, Biogen-Eisai’s lecanemab, and Eli Lilly & Company’s donanemab—the latter two currently under review by FDA.⁹⁷ In addition, FDA told the Committees in January 2022 that the agency is in the process of updating its February 2018 guidance, but could not provide a concrete timeframe for its revision—officials said they would “work to ensure it is [updated] by 2023.”⁹⁸

On April 26, 2021, the decisional briefing was held with CDER Director Dr. Cavazzoni to discuss the potential approval of Aduhelm.⁹⁹ At this briefing, CDER senior leadership, as well as Dr. Peter Marks, Director of the Center for Biologics Evaluation and Research, and Dr. Rick Pazdur, Director of the Oncology Center of Excellence, reviewed the OND and the ON recommendation to approve Aduhelm through the accelerated approval pathway. This approach was supported by Dr. Cavazzoni, Dr. Marks, Dr. Pazdur, and the CDER Office Directors for Clinical Pharmacology and Medical Policy. The OB Director dissented, noting that there was insufficient evidence to support accelerated or any other type of approval.¹⁰⁰

⁹⁶ Food and Drug Administration, *FDA Response to Clarifying Questions from Energy and Commerce and Oversight and Reform Staff*, at Pages 1 and 3 (Jan. 3, 2022).

⁹⁷ *Id.*, at Page 3. The lecanemab trial data was made public in a 2018 abstract and published in full in April 2021. Biogen, *Press Release: Eisai and Biogen Announce Detailed Results of Phase II Clinical Study of BAN2401 in Early Alzheimer’s Disease at Alzheimer’s Association International Conference (AAIC) 2018* (July 25, 2018) (online at <https://investors.biogen.com/news-releases/news-release-details/eisai-and-biogen-announce-detailed-results-phase-ii-clinical>); Swanson et al., *A Randomized, Double-Blind, Phase 2b Proof-of-Concept Clinical Trial in Early Alzheimer’s Disease Lecanemab, An Anti-Aβ Protofibril Antibody*, *BioMed Central* (Apr. 17, 2021) (online at <https://alzres.biomedcentral.com/articles/10.1186/s13195-021-00813-8>). The data from the donanemab trial was announced in a press release in January 2021 and published online in March 2021. Lilly, *Press Release: Lilly’s Donanemab Slows Clinical Decline of Alzheimer’s Disease in Positive Phase 2 Trial* (Jan. 11, 2021) (online at <https://investor.lilly.com/news-releases/news-release-details/lillys-donanemab-slows-clinical-decline-alzheimers-disease>); Minton et al., *Donanemab in Early Alzheimer’s Disease*, *New England Journal of Medicine* (Mar. 31, 2021) (online at <https://pubmed.ncbi.nlm.nih.gov/33720637/>). On July 5, 2022, Biogen-Eisai reported that the Food and Drug Administration had accepted lecanemab for the accelerated approval pathway and expects to release a decision by January 6, 2023. Biogen, *Press Release: The U.S. FDA Accepts and Grants Priority Review for EISAI’s Biologics License Application of Lecanemab for Early Alzheimer’s Disease Under the Accelerated Approval Pathway* (July 5, 2022) (online at <https://investors.biogen.com/news-releases/news-release-details/us-fda-accepts-and-grants-priority-review-eisais-biologics>). Eli Lilly & Company also reported in August 2022 that FDA accepted donanemab for the accelerated approval pathway. Lilly, *Press Release: Lilly Reports Second-Quarter Financial Results, Highlights Momentum of New Medicines and Pipeline Advancements* (Aug. 4, 2022) (online at <https://investor.lilly.com/news-releases/news-release-details/lilly-reports-second-quarter-financial-results-highlights>).

⁹⁸ Food and Drug Administration, *FDA Response to Clarifying Questions from Energy and Commerce and Oversight and Reform Staff*, at Page 3 (Jan. 3, 2022).

⁹⁹ Food and Drug Administration, *Summary Memorandum*, at Page 56 (June 7, 2021) (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/Aducanumab_BLA761178_Dunn_2021_06_07.pdf).

¹⁰⁰ *Id.*

According to email correspondence from Biogen to FDA, and confirmation from the agency, FDA officials told Biogen at an April 28, 2021, meeting that they were considering the accelerated approval pathway for Aduhelm.¹⁰¹ FDA publicly announced Aduhelm’s accelerated approval five weeks later, on June 7, 2021.¹⁰²

E. FDA Issued Initial Approval with an Unexpectedly Broad Label Indication

Documents reviewed by the Committees indicate that FDA recommended and later approved a broad label indication for Aduhelm—beyond the stages of the disease studied under the clinical trials.¹⁰³ FDA’s initial approval of Aduhelm on June 7, 2021, included a statement that Aduhelm is “indicated for the treatment of Alzheimer’s disease.”¹⁰⁴ The broadness of this initial label was criticized by medical experts and physicians because the trials on which Aduhelm’s approval were based only enrolled a particular subset of Alzheimer’s patients—individuals with mild cognitive impairment due to Alzheimer’s disease or mild Alzheimer’s disease.¹⁰⁵ Following criticism from medical experts and confusion from health care providers, one month after approval, Biogen requested that FDA update Aduhelm’s label to include an addition to the “Indications and Usage Section” to emphasize the drug should be initiated in populations studied in the clinical trials—patients with MCI due to Alzheimer’s disease or mild dementia stage of disease.¹⁰⁶

Documents obtained by the Committees appear to show that, despite a lack of clinical data for populations beyond those who participated in the trials themselves, FDA recommended Biogen pursue a broad indication statement for Aduhelm. During a June 17, 2020, Type C Meeting, for instance, Biogen asked FDA to “advise which patient population would be most appropriate” for Aduhelm.¹⁰⁷ FDA responded that while “commenting definitively” is

¹⁰¹ BIIB_HCOR_EC_0126816.

¹⁰² See Food and Drug Administration, *Press Release: FDA Grants Accelerated Approval for Alzheimer’s Drug* (June 2021) (online at www.fda.gov/news-events/press-announcements/fda-grants-accelerated-approval-alzheimers-drug).

¹⁰³ The Committees could not determine who within the Food and Drug Administration recommended this approach, nor whether it was a consensus decision or if there was disagreement among agency staff.

¹⁰⁴ Food and Drug Administration, *Summary Memorandum*, at Page 1 (June 7, 2021) (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/Aducanumab_BLA761178_Dunn_2021_06_07.pdf).

¹⁰⁵ *Furor Rages Over FDA Approval of Controversial Alzheimer’s Drug*, Washington Post (June 17, 2021) (online at www.washingtonpost.com/health/2021/06/17/alzheimers-drug-controversy/); Sam Gandy, *6 Ways The FDA’s Approval of Aduhelm Does More Harm Than Good*, STAT (June 15, 2021) (online at www.statnews.com/2021/06/15/6-ways-fda-approval-aduhelm-does-more-harm-than-good/); Aaron S. Kesselheim and Jerry Avorn, *The FDA Has Reached a New Low*, New York Times (June 15, 2021) (online at www.nytimes.com/2021/06/15/opinion/alzheimers-drug-aducanumab-fda.html).

¹⁰⁶ Biogen, *Press Release: FDA Approves Updated Aduhelm Prescribing Information to Emphasize Population Studied in Clinical Trial* (July 8, 2021) (online at <https://investors.biogen.com/news-releases/news-release-details/fda-approves-updated-aduhelmtm-prescribing-information-emphasize>).

¹⁰⁷ Food and Drug Administration, *Administrative and Correspondence Documents*, at Page 34 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

“premature,” a “reasonable approach to take for your draft labeling is to structure your labeling proposal based on an indication statement for the treatment of patients with Alzheimer’s disease.”¹⁰⁸

Although leaders in Biogen’s Alzheimer’s program identified concerns internally about a broad label (discussed in Section III), in materials reviewed by the Committees, it appears that Biogen did not directly communicate those concerns to FDA. Meanwhile, communications from FDA to Biogen obtained by the Committees continued to refer to a broad indication statement. For example, a May 2021 email from FDA to Biogen proposed an indication statement to say “ADUHELM is indicated for the treatment of Alzheimer’s disease.”¹⁰⁹ In response to related questions from the Committees, FDA stated that it supported the broad label for several reasons, including that: (1) even though the studies were in early stages of the disease, “there is no reason to think that aducanumab would only bind to [beta] amyloid in those stages of the disease”; and (2) it was expected that, even with treatment with the drug, patients would experience some disease progression so those who started with MCI could then find themselves no longer within the indication if their disease progressed.¹¹⁰

III. BIOGEN AIMED TO MAXIMIZE PROFITS WITH A BROAD LABEL, HIGH PRICE, AND AGGRESSIVE MARKETING—DESPITE LACK OF CLINICAL DATA ON ALL ALZHEIMER’S PATIENTS AND KNOWN FINANCIAL IMPACT

A. Biogen Applied for a Broad Label for Aduhelm Despite a Lack of Clinical Data on All Alzheimer’s Disease Stages

On June 7, 2021, FDA granted accelerated approval to Aduhelm with a drug label indicating its use to treat “people with Alzheimer’s disease,” a broad category of patients that far exceeded the patient population studied in clinical trials.¹¹¹ Internal documents obtained by the

¹⁰⁸ Food and Drug Administration, *Administrative and Correspondence Documents*, at Page 34 (online at www.accessdata.fda.gov/drugsatfda_docs/nda/2021/761178Orig1s000AdminCorres.pdf) (accessed Dec. 1, 2022).

¹⁰⁹ BIIB_HC0R_EC_0122764, at Pages 1–2. In a May 2021 email from FDA’s then-Senior Regulatory Health Project Manager and part of the review team to a leader of Biogen’s regulatory sciences, FDA changed Biogen’s draft language for the “Indications and Usage” section of Aduhelm’s label from “ADUHELM is indicated to delay clinical decline in patients with Alzheimer’s disease” to “ADUHELM is indicated for the treatment of Alzheimer’s disease.”

¹¹⁰ Letters from Food and Drug Administration to Chairman Frank Pallone, Jr., Committee on Energy and Commerce, and Chairwoman Carolyn B. Maloney, Committee on Oversight and Reform, at Page 18 (Oct. 22, 2021).

¹¹¹ Biogen, *Press Release: FDA Grants Accelerated Approval for ADUHELM as the First and Only Alzheimer’s Disease Treatment to Address a Defining Pathology of the Disease* (June 7, 2021) (online at <https://investors.biogen.com/news-releases/news-release-details/fda-grants-accelerated-approval-aduhelmtm-first-and-only>). “INDICATION: ADUHELM is a prescription medicine used to treat people with Alzheimer’s disease.” *Id.* See also Letter from Dr. Billy Dunn, M.D., Director; Office of Neuroscience, Center for Drug Evaluation and Research; Food and Drug Administration, to Biogen Inc.; re “BLA Accelerated Approval” (June 7, 2021) (online at www.accessdata.fda.gov/drugsatfda_docs/applletter/2021/761178Orig1s000ltr.pdf).

Committees show that Biogen sought the broad indication despite a lack of evidence of clinical benefit for patients at different disease stages, an unknown safety profile, and analyses concluding that a broad label could cause patient and provider confusion and challenge health system capacity.¹¹² Internal Biogen documents indicate that Biogen’s Alzheimer’s team leaders expressed concern the company could lose credibility by advocating for a broad label indication that exceeded the clinical trial population, and the company even developed a communications strategy to deal with the anticipated fallout.¹¹³ Despite these concerns, Biogen appears to have been unwilling to disagree with FDA and accepted the broad label indication statement initially proposed by FDA, and only sought a label update to the usage and indications section to clarify the appropriate patient population after public backlash.¹¹⁴

Documents show that as early as March 2020, four months before the formal meeting between FDA and Biogen in July 2020 to discuss Aduhelm’s application, FDA had “signaled that there is a high chance the agency will suggest a ‘broad label’ indication, such as ‘treatment of AD [Alzheimer’s disease]’” for the drug.¹¹⁵ In a “Broad label” scenario, Biogen anticipated an indication statement that Aduhelm was appropriate for “the treatment of Alzheimer’s disease.”¹¹⁶ In what Biogen referred to as a “Narrow label” scenario, Aduhelm would be indicated for a sub-population of Alzheimer’s patients that more closely reflected the population of its clinical trials—patients with MCI due to Alzheimer’s disease and mild dementia stage of disease, with confirmed amyloid beta plaque.¹¹⁷ In evaluating the potential labels, Biogen sought feedback from various external stakeholders, including medical experts, patient advocacy groups, and payers.

Internal company documents indicate that Biogen’s own leaders and outside stakeholders raised concerns over a potential broad label, including the lack of efficacy and safety information about the use of Aduhelm by individuals outside of the disease stages studied in the trials,

¹¹² The “Indications and Usage” section of a drug’s label states, “the disease or condition, or manifestation or symptoms thereof, for which the drug is approved, as well as whether the drug is indicated for the treatment, prevention, mitigation, cure, or diagnosis of that disease or condition[.]” It is meant to “enable healthcare practitioners to readily identify appropriate therapies for patients by clearly communicating the drug’s approved indication(s).” Food and Drug Administration, *Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products—Content and Format: Guidance for Industry* (July 2018) (online at www.fda.gov/files/drugs/published/Indications-and-Usage-Section-of-Labeling-for-Human-Prescription-Drug-and-Biological-Products-%E2%80%94Content-and-Format-Guidance-for-Industry.pdf).

¹¹³ See BIIB_HCOR_EC_0187343, at Page 27.

¹¹⁴ See BIIB_HCOR_EC_0623390, at Page 1. Aducanumab Product Development and Commercialization team meeting minutes noting, “EC [Executive Committee] supports the recommendation of filing with the broad label consistent with the Core Data Sheet (CDS) and global position”) (July 29, 2020); Biogen, *Press Release: FDA Approves Updated ADUHELM Prescribing Information to Emphasize Population Studied in Clinical Trial* (July 8, 2021) (online at <https://investors.biogen.com/news-releases/news-release-details/fda-approvs-updated-aduhelmtm-prescribing-information-emphasize>) (accessed Dec. 1, 2022).

¹¹⁵ See e.g., BIIB_HCOR_EC_0642217, at Page 3 (Mar. 4, 2020, presentation titled, “Label Scenario Considerations,” which analyzed four label scenarios).

¹¹⁶ BIIB_HCOR_EC_0187343, at Page 6.

¹¹⁷ *Id.*

potential limits on health system capacity, and challenges in ensuring access to Aduhelm for those who would benefit most.¹¹⁸

i. Biogen Considered Concerns That a Broad Label Indication Was Not Supported by Efficacy or Safety Data

Documents obtained by the Committees reveal that Biogen had early warnings about the potential risks associated with a label for Aduhelm beyond the clinical trial population, which was limited to patients with MCI due to Alzheimer’s disease and mild Alzheimer’s disease dementia. In a March 2020 presentation for Biogen’s Executive Committee, Aduhelm’s Product Development and Commercialization team (PDC) recommended that the label for Aduhelm include a diagnostic component to confirm the presence of amyloid beta plaque—a characteristic of patients studied in the clinical trials. The presentation stated: “Efficacy is dependent on appropriate diagnosis” and recommended, “Safety profile of the product to include a diagnostic to ensure only the right patients receive treatment.”¹¹⁹

In July 2020, the Biogen “Aducanumab Label Scenario Advisory Board” met to weigh the benefits and risks of a broad label versus a narrow label. At that meeting, Biogen staff (including some leaders of the Alzheimer’s program) were split into groups to discuss the implications of two possible labels.¹²⁰ Notes from the “Broad Label Scenario” group raised several potential concerns about a broad label, including that it would: (1) open the door to a wide range of patients; (2) create challenges in identifying the “right” patient for whom the drug would be an appropriate therapy; (3) raise questions about who would not benefit from treatment; and (4) raise challenges around “managing expectations” for efficacy of the drug and ability to meet demand.¹²¹ The presentation also noted treatment implications for a broader patient population, such as the lack of data about when to stop treatment and the impact of treatment as patients progress.¹²² The presentation concluded with concern that Biogen could risk losing credibility if it advocated that Aduhelm be used by Alzheimer’s patients that did not have the same disease characteristics as those who participated in the clinical trials.¹²³

¹¹⁸ See e.g., BIIB_HCOR_EC_0642217; BIIB_HCOR_EC_0187343; BIIB_HCOR_EC_0623390; BIIB_HCOR_EC_0442081; BIIB_HCOR_EC_0427521.

¹¹⁹ BIIB_HCOR_EC_0642217, at Page 2.

¹²⁰ BIIB_HCOR_EC_0187343, at Pages 4–7 (“Broad Indication Statement Scenario Discussion & Next Steps” presentation draft used for internal planning purposes).

¹²¹ *Id.*, at Page 9.

¹²² *Id.*, at Page 11.

¹²³ *Id.*, at Page 27. The presentation also identified a number of concerns under a narrow label scenario. For example, the group that considered a possible narrow label that required confirmation of mild Alzheimer’s disease and the presence of amyloid beta plaque for treatment with Aduhelm discussed how to educate non-specialists like primary care physicians on the signs a patient might be a candidate for Aduhelm, the difficulty of differentiating between mild and moderate Alzheimer’s disease, the number of people who might be excluded from confirmatory testing for the presence of amyloid plaque due to the cost of those tests or medical contraindications, and the geographic, socioeconomic, and cultural barriers that might hinder access to confirmatory testing. See *Id.*, at Pages 14–17.

A March 2020 presentation by the PDC titled, “Label Scenario Considerations: Confidential: Aducanumab PDC Feedback,” included details on the medical and commercial implications of a broad label. Among the medical considerations, the PDC noted the risk of a “[h]igh discontinuation rate based on potential smaller benefits in changing the course of the disease in more advanced patients,” and “[p]otential consequences on safety profile if drug used in a broader, clinically more impaired patient population.”¹²⁴ This presentation also warned that a broad label could lead to “high discontinuation due to perceived lack of benefit and potential change in safety profile” compared to the patient population studied in trials, and that a “[n]egative experience’ with the efficacy of aducanumab” and the “unknown safety profile” for Aduhelm in a broad population of all patients with Alzheimer’s disease could negatively affect long-term use of the drug.¹²⁵

These concerns were echoed by external stakeholders. A July 2020 white paper titled, “Positioning/Promoting Aducanumab for the Clinical Trial Population,” sent from an outside consultant to a senior marketing leader at Biogen at the time, described feedback from a Key Stakeholder Forum where clinician, advocate, and payer representatives expressed support for promoting Aduhelm to patients similar to the clinical trial population.¹²⁶ In describing the reasons that stakeholders supported this approach, the consultant wrote that “positioning or promoting aducanumab for patients with moderate-to-severe AD introduces risk to the patient without known clinical benefit,” would “not be in the best interest of patients,” and would “likely be giving **false hope** to patients **desperate** for anything that might slow the progression of the disease.”¹²⁷ The stakeholders’ rationales for promoting Aduhelm for patients consistent with the clinical trial population included that doing so “[e]nsures that the product will be **targeted only for patients** where there is a **known clinical benefit**: patients with early-stage Alzheimer’s disease (MCI to mild AD) and confirmed amyloid beta pathology” and that “limiting the positioning and promotion of aducanumab to the clinical trial population **optimizes the risk-benefit calculation for patients.**”¹²⁸

ii. *Biogen Considered Concerns That a Broad Label Could Challenge Health Care System Capacity and Limit Patient Access*

In addition to potential efficacy and safety concerns, Biogen executives considered concerns that a broad label could challenge health care system capacity and limit access to those likely to most benefit from the drug. For example, in the July 2020 PDC presentation, leaders of Biogen’s Alzheimer’s disease program expressed concern that, with a broad label, health care providers might face challenges “managing expectations and demand” for the drug, warning that desire for Aduhelm could “overwhelm the system.”¹²⁹ By contrast, under a narrow label, the

¹²⁴ BIIB_HCOR_EC_0642217, at Page 13.

¹²⁵ *Id.*, at Page 7.

¹²⁶ BIIB_HCOR_EC_0442080; BIIB_HCOR_EC_0442081.

¹²⁷ BIIB_HCOR_EC_0442081, at Pages 1 and 2 (emphasis in original).

¹²⁸ *Id.*, at Page 1 (emphasis in original).

¹²⁹ BIIB_HCOR_EC_0187343, at Page 9.

Biogen Alzheimer's disease team expected: "Patients with greatest potential for benefit will be identified," noting that a narrow label would "advance identification and improve/slow rate of progression" for those patients.¹³⁰

A May 2020 presentation prepared for the Executive Committee warned: "HCPs [Health Care Providers]/Systems unprepared to screen/treat high volume of AD patients."¹³¹ The presentation noted that with a broad label for all Alzheimer's disease patients, there would be an "enhanced need to educate on system challenges and reinforce appropriate patient and study outcomes to manage potential negative responses regarding system capacity challenges and efficacy."¹³²

Various external stakeholders also shared concerns with Biogen—which the company shared in internal meetings and presentations—that the health care system might not be prepared to respond to a broad label scenario. Minutes from a July 2020 Aducanumab PDC Team Meeting, sent to a Biogen regulatory policy leader, summarize feedback from stakeholders about the different label scenarios.¹³³ Six key medical experts familiar with the clinical trials who served as part of Biogen's "U.S. Medical Ad [Advisory] Board on Label Scenarios" shared the following feedback on the broad label: "Did not find much upside to this scenario; felt that this created a burden for the healthcare centers"; and "[g]eneral surprise that this scenario was being considered."¹³⁴ The group also noted that the "appropriate population to treat are patients that are aligned with the trial patient population" and emphasized the "need to ensure that Biogen is communicating appropriately [to health care providers] about healthcare system capacity and readiness."¹³⁵

Biogen's patient advocacy steering committee also raised concerns about the possibility of demand overwhelming the health care system and making it more difficult for patients most in need to access treatment. In a list of the benefits and challenges of a broad label, the patient advocacy groups noted challenges including: "Increased demand may overwhelm healthcare system capacity," and "[p]atients most likely to benefit may not have access if demand/urgency is higher from more progressed patients," meaning patients whose disease state is more advanced than those studied in the clinical trials.¹³⁶ Another document summarizing this group's feedback noted that a broad label would raise access equity issues, noting:

¹³⁰ *Id.*, at Page 14.

¹³¹ BIIB_HCOR_EC_0427521, at Page 3.

¹³² *Id.*, at Page 115. *See also* BIIB_HCOR_EC_0642217, at Page 4 ("a broad label will add infrastructural pressure and create risk to current GTM ['Go-To-Market'] strategy and assumptions as well as potential confusion for HCPs and patients).

¹³³ BIIB_HCOR_EC_0623358.

¹³⁴ BIIB_HCOR_EC_0623390, at Page 2. These medical leaders also were "[c]urious to know who was driving this scenario and why it was being considered." BIIB_HCOR_EC_0623390, at Page 2.

¹³⁵ *Id.*, at Pages 2–3. The narrow label group also "wondered why Biogen was assessing a broad label." *Id.*, at Page 3.

¹³⁶ BIIB_HCOR_EC_0187343, at Page 20.

PDC Team discussed that while PAG's [Patient Advocacy Groups] may see an opportunity that a broad indication statement may provide access to more patients, access could possibly be limited to those who can afford the medication and know how to navigate the healthcare system.¹³⁷

iii. *Biogen Appears to Have Had "NO Plan to Push Back" on Broad Label for Aduhelm Despite Reservations*

Despite concerns about efficacy, safety, and access related to a broad label raised internally by Aduhelm project leaders and externally by experts, patient advocates, and payers, documents obtained by the Committees indicate that Biogen intended to utilize a broad label if approved by FDA. In the July 2020 Aducanumab PDC Team meeting minutes outlining concerns from Biogen executives and stakeholders about a broad label for Aduhelm, the company noted that it had "NO plan to push back on broad label indication internally or with the regulators."¹³⁸

Other documents indicate that Biogen was unwilling to raise these concerns with FDA directly but considered having others do so. In a May 2020 email exchange between a Biogen leader in global product strategy and an outside advisor summarizing an "Advisory Meeting" held by Biogen, the outside advisor said of the broad label: "I understand the sensitivity around discussions with the FDA, particularly given aducanumab's 'unique' journey through clinical development, and appreciate the desire not to push back when things are going well."¹³⁹ The advisor also suggested these concerns be raised "through the external experts and the representative from the advocacy community" at the FDA's Advisory Committee meeting, rather than by Biogen.¹⁴⁰ The advisor suggested that Biogen could "socialize these issues" with external stakeholders who could express concern to FDA in Biogen's place.¹⁴¹

It appears that, instead of expressing its many concerns about a broad label to FDA or applying for a narrower label, Biogen designed a "go-to-market strategy" for Aduhelm that attempted to limit the patient population utilizing Aduhelm even while the label indicated Aduhelm was appropriate for all people with Alzheimer's disease. As part of this strategy, Biogen would "target getting patients on therap[ies] that are consistent with the clinical trial

¹³⁷ BIIB_HCOR_EC_0623390, at Page 3. Biogen appears to have seen these concerns as widely applicable, even to markets outside the U.S. healthcare system. Regarding the European market, Biogen warned that a broad label could "[o]verburden [the] healthcare system putting pressure on payers to limit access to ADU [Aduhelm]" and could lead to "[p]rolonged pricing and reimbursement negotiations due to limited data in [the] populations being requested, hence slower uptake." BIIB_HCOR_EC_0187343, at Page 26; *See also Id.*, at Page 23 (describing how, "The broader the label, the higher the probability of payers creating policies and hurdles to minimize utilization.").

¹³⁸ BIIB_HCOR_EC_0623390, at Page 4.

¹³⁹ BIIB_HCOR_EC_0173415, at Page 5.

¹⁴⁰ *Id.*, at Page 6.

¹⁴¹ *Id.*

population” by focusing its go-to-market plan on patients with MCI due to Alzheimer’s disease and mild Alzheimer’s disease dementia.¹⁴² Meanwhile, Biogen executives worked on “messaging” to address the expected concerns with a broad label.¹⁴³ For example, Biogen anticipated needing to respond to questions about “what a broad indication statement means, how is [sic] came to be, and how Biogen and the community should prioritize post launch because the healthcare system will not be able to accommodate every potential patient.”¹⁴⁴

Documents show that even as Biogen moved forward with a broad label for Aduhelm, executives expressed concern that the broad label could damage the company’s credibility and were developing plans to manage the fallout by focusing marketing efforts on patients that fit the clinical trial population profile and developing a communications strategy to address potential backlash.¹⁴⁵ In June 2020 meeting minutes, the Aducanumab PDC Team warned that, based on initial feedback from patient advocates, providers, and experts, Biogen would need a plan to mitigate risks to the company’s credibility in the event the broad label was approved:

Based on all feedback received by stakeholders on the broad label scenario, develop a comprehensive plan and specific actions for anticipating broad label scenario (KMEs [key medical experts], PAGs, communications, payer approach), addressing anticipated public surprise and questions, and mitigating risks including risks to company credibility even though the go-to-market strategy remains unchanged to focus on MCI due to AD/mild AD.¹⁴⁶

After Biogen moved forward with the broad label for Aduhelm, the company faced physician and patient confusion and public criticism. Within a month of Aduhelm’s approval, Biogen requested that FDA update the indications and usage section of the label to narrow it to the disease stages studied in the trials.¹⁴⁷ In Biogen’s filing with FDA to support this label clarification, the company explained that the update was necessary because “the current indication statement in Section 1 which lists the disease as ‘Alzheimer’s disease’ without reference to clinical stages is leading to some uncertainty about who should be treated with

¹⁴² BIIB_HCOR_EC_0623390, at Page 5.

¹⁴³ *Id.*, at Page 6.

¹⁴⁴ *Id.*

¹⁴⁵ *Id.*, at Pages 5–6.

¹⁴⁶ *Id.*, at Page 6.

¹⁴⁷ See e.g., *Biogen, FDA Walk Back Controversial Aduhelm Label After Weeks of Fierce Criticism*, Fierce Pharma (July 8, 2021) (online at www.fiercepharma.com/pharma/facing-pushback-biogen-and-fda-agree-to-narrow-aduhelm-s-broad-label); *Updated: Biogen Narrows its Aduhelm Label After FDA Left the Floodgates Open*, Endpoints News (July 8, 2021) (online at <https://endpts.com/biogen-narrows-its-aduhelm-label-after-fda-left-the-flood-gates-open/>); *Biogen, Press Release: FDA Approves Updated Aduhelm Prescribing Information to Emphasize Population Studied in Clinical Trials* (July 8, 2021) (online at <https://investors.biogen.com/news-releases/news-release-details/fda-approves-updated-aduhelmtm-prescribing-information-emphasize>).

Aduhelm.”¹⁴⁸ Biogen asserted that its update would offer “greater clarity, and mitigate confusion” by augmenting the indication statement “to clarify who are the most appropriate patients to be treated with Aduhelm.”¹⁴⁹ Specifically, the update added information on the disease stage of the patients in the Aduhelm clinical trials and clarified the stages of disease on which Biogen had no data for Aduhelm.¹⁵⁰

B. Biogen Set an Unjustifiably High Price for Aduhelm to “Make History” for the Company Despite the Impact on Patients and the Medicare Program

Documents obtained by the Committees show Biogen viewed Aduhelm as an unprecedented financial opportunity—estimating a potential peak revenue of \$18 billion per year—and developed aggressive launch and marketing plans to maximize revenue throughout the drug’s lifecycle. These internal documents show that Biogen set Aduhelm’s price despite a lack of demonstrated clinical benefit in a broad patient population, and without significant regard to the anticipated financial impact on patients and the Medicare program.

Presentations prepared for Biogen’s Board of Directors as early as December 2019 emphasized the company’s goal of breaking industry pricing and revenue records with the launch of Aduhelm. One presentation prepared for Biogen’s Board of Directors in December 2019 titled “Aducanumab US Launch Vision and Priorities” stated that Biogen’s goal was to have a “[b]lockbuster by 2021.”¹⁵¹

Presentations prepared for a September 2020 Board of Directors meeting highlighted the company’s financial expectations for Aduhelm. One presentation—presented on behalf of Biogen senior executives stated: “Our ambition is to make history” and “establish ADUHELM as one of the top pharmaceutical launches of all time.”¹⁵² The presentation emphasized the goal of Aduhelm being a “blockbuster” drug within 12 months of launch and modeled that Aduhelm revenue would reach roughly \$8.7 billion by 2024. This model was based on a number of assumptions, including a launch date of February 2021, a list price of \$55,000 per year, a “net price” of \$47,000 at launch, and a broad indication statement but expectation of low initial use in patients with moderate Alzheimer’s disease due to payer restrictions.¹⁵³ A second presentation from an executive who was at the time leading Biogen’s global product strategy proclaimed that

¹⁴⁸ BIIB_HCOR_EC_0126698, at Page 2. Biogen noted that providers were confused about whether Aduhelm can safely be administered at any stage and, in particular, in patients at more advanced stages.

¹⁴⁹ *Id.*

¹⁵⁰ *Id.*

¹⁵¹ BIIB_HCOR_EC_0429470, at Page 3. A blockbuster drug is commonly understood as one that brings in more than \$1 billion in revenue annually. *See e.g.,* Ravi Gupta, M.D. et al., *Approvals and Timing of New Formulations of Novel Drugs Approved by the U.S. Food and Drug Administration Between 1995 and 2010 and Followed Through 2021*, JAMA Health Forum (May 2022) (online at www.ncbi.nlm.nih.gov/pmc/articles/PMC9123500/).

¹⁵² BIIB_HCOR_EC_0023329, at Page 224.

¹⁵³ *Id.*, at Pages 224–225.

the company would deliver a “transformative launch of aducanumab.”¹⁵⁴ A third presentation predicted that, while Biogen was facing some financial headwinds, “our top and bottom line will quickly rebound with the launch of aducanumab” and that Aduhelm was “potentially a \$18B peak revenue product.”¹⁵⁵

Our ambition is to make history



Turning the tide on AD for patients



61 days until December 1



Blockbuster in 12 months

Our ambitious patient goals for 2021 and beyond will establish ADUHELM as one of the top pharmaceutical launches of all time

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Presentation to the Board of Directors

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In June 2021, Biogen brought Aduhelm to market with a price of \$56,000 per year for an average-weight person.¹⁵⁶ Biogen’s pricing strategy backfired—the company faced significantly lower-than-expected U.S. sales and complaints that the high price of Aduhelm was not worth its benefits.¹⁵⁷ In Biogen’s annual filing with the Securities and Exchange Commission, the

¹⁵⁴ BIIB_HCOR_EC_0023329, at Page 145. Other documents refer to aducanumab’s transformational launch in the context of revolutionizing “the Alzheimer’s disease treatment paradigm.” See e.g., BIIB_HCOR_EC_0434630, at Page 12.

¹⁵⁵ BIIB_HCOR_EC_0023329, at Page 256. This presentation further noted that the successful launch of aducanumab would be a “[c]hange of magnitude for Biogen and humanity.” *Id.*, at Page 257. An earlier presentation from June 2020 titled, “Aducanumab LRP and AD Portfolio Overview,” estimated aducanumab potential peak sales revenue of even higher—\$23 billion. BIIB_HCOR_EC_0434630, at Page 2.

¹⁵⁶ Biogen, *Press Release: Biogen and Eisai Launch Multiple Initiatives to Help Patients with Alzheimer’s Disease Access ADUHELM* (June 7, 2021) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-and-eisai-launch-multiple-initiatives-help-patients>).

¹⁵⁷ See e.g., *Biogen’s Alzheimer’s Drug Sales Remain Slow as Company Warns of Further Cost Cuts*, BioPharma Dive (Feb. 3, 2022) (online at www.biopharmadive.com/news/biogen-aduhelm-sales-slow-cost-cutting-fourth-quarter/618222/); *Biogen’s Reckoning: How the Aduhelm Debacle Pushed a Troubled Company and its Fractured Leadership to the Brink*, STAT (Dec. 8, 2021) (online at www.statnews.com/2021/12/08/biogen-aduhelm-al-sandrock-michel-vounatsos-company-reckoning).

company noted that it brought in only \$3 million in revenue from Aduhelm in 2021, compared to its initial projections of over a billion dollars.¹⁵⁸ Approximately six months later, Biogen lowered the list price, or Wholesale Acquisition Cost (WAC), to about half—\$28,200 for an average-weight person.¹⁵⁹ Biogen’s then-CEO Michel Vounatsos acknowledged that Biogen’s initial aggressive price tag was “wrong.”¹⁶⁰

i. Biogen Set Aduhelm’s Price to Maximize Revenue Despite Knowing It Was Not in Patients’ or the Public’s Best Interests

Documents obtained by the Committees show that Biogen set Aduhelm’s price for purposes of “revenue maximization,” and expected the high price would spur “pushback” from providers, payers, and the public.¹⁶¹ Documents show that in anticipation of this backlash, Biogen developed an external narrative about the drug’s value to sell to patients and the public.

Documents reviewed indicate that, as early as Spring 2020, Biogen engaged third-party consultants to provide strategic guidance on pricing Aduhelm and developing a narrative to support the aspired price. In April 2020, Biogen received a final report from consultants on Aduhelm pricing strategies, with an analysis of the trade-offs of a range of pricing scenarios.¹⁶² The report’s Executive Summary presented the key considerations and takeaways from each scenario, noting that “[r]evenue maximization favors prices greater than \$40k WAC/year” while limiting payer and physician pushback would favor list prices below \$40,000 per year, and maximizing patient volume would favor list prices of \$15,000 to \$20,000 per year.¹⁶³

¹⁵⁸ Biogen, *2021 Form 10k*, at Page 66 (Feb. 3, 2022) (online at <https://investors.biogen.com/static-files/2c625543-a243-4367-8248-af360692e6d2>); BIIB_HCOR_EC_0434630, at Page 29 (June 2020 long range plan anticipated Aduhelm U.S. revenue at over \$1 billion in 2021 and \$4 billion in 2022). Biogen’s annual filing with the Securities and Exchange Commission also noted that its ability to successfully commercialize Aduhelm may be adversely impacted by various factors including, “our ability to maintain a positive reputation among patients, healthcare providers and others in the Alzheimer’s disease community, which may be impacted by pricing and reimbursement decisions relating to Aduhelm.” Biogen, *2021 Form 10k*, at Page 41 (Feb. 3, 2022) (online at <https://investors.biogen.com/static-files/2c625543-a243-4367-8248-af360692e6d2>).

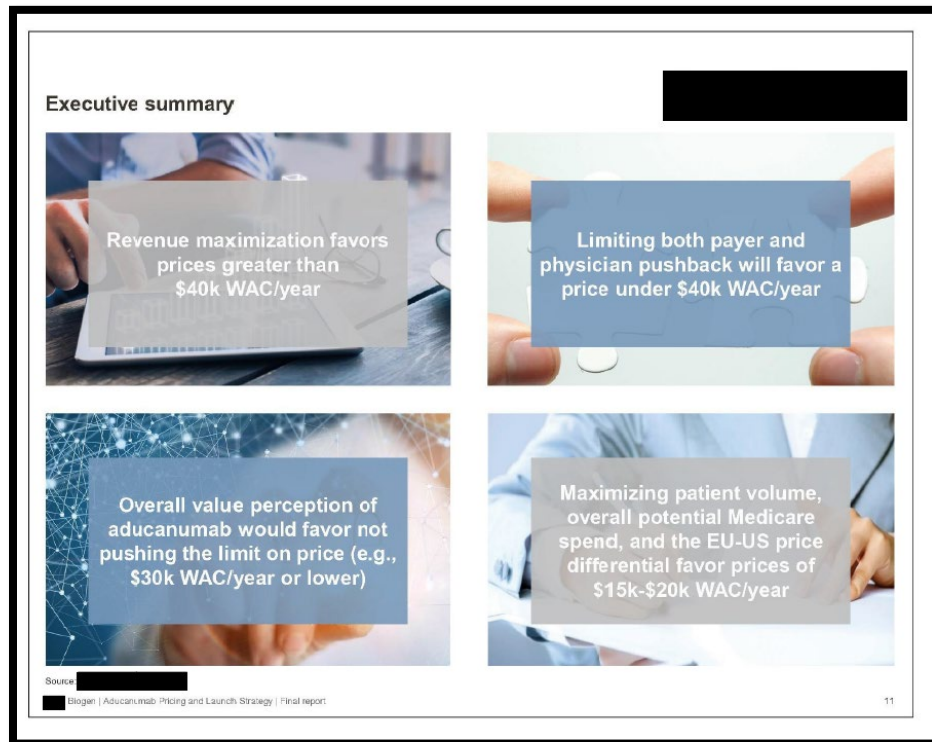
¹⁵⁹ Biogen, *Press Release: Biogen Announces Reduced Price for Aduhelm to Improve Access for Patients with Early Alzheimer’s Disease* (Dec. 20, 2021) (online at <https://investors.biogen.com/news-releases/news-release-details/biogen-announces-reduced-price-aduhelmr-improve-access-patients>).

¹⁶⁰ *Biogen CEO: Company Was “Wrong” About Initial Aduhelm Price, “Courageous” to Lower It*, STAT (Jan. 10, 2022) (online at www.statnews.com/2022/01/10/biogen-ceo-company-was-wrong-about-initial-aduhelm-price-courageous-to-lower-it/). Biogen collected only \$3 million in product revenue from Aduhelm in 2021—significantly below its anticipated revenue of over \$1 billion for 2021. See Biogen, *2021 Form 10k*, at Pages 66 and 69 (Feb. 3, 2022) (online at <https://investors.biogen.com/static-files/2c625543-a243-4367-8248-af360692e6d2>); BIIB_HCOR_EC_0434630, at Page 29 (June 2020 long range plan anticipated Aduhelm’s U.S. revenue at over \$1 billion in 2021 and \$4 billion in 2022).

¹⁶¹ BIIB_HCOR_EC_0128260, at Page 11.

¹⁶² BIIB_HCOR_EC_0128260. The consultants also flagged the importance of narrowing down the list price differential between the United States and the European Union and the “high likelihood that aducanumab’s launch price will be highly scrutinized upon launch.” BIIB_HCOR_EC_0128148, at Page 6.

¹⁶³ BIIB_HCOR_EC_0128260, at Page 11.



This presentation noted that “[r]evenue favors higher aducanumab prices,” while acknowledging that public scrutiny and payer resistance at higher prices could have a negative impact on volume.¹⁶⁴

Biogen’s internal team summarized the third-party research and discussions in an April 2020 draft presentation, titled “Aducanumab US Pricing and Market Access Strategy Development.” The team explained that setting a list price over \$40,000 would maximize revenue but have negative implications in the areas of “[p]atient [a]ccess,” “[p]atient affordability,” and “[b]udget [i]mpact.”¹⁶⁵ The draft presentation noted that Biogen’s “highest rated goals” in setting a U.S. launch price were to: “Align payers’ perception of aducanumab’s value with the price”; “Maximize patient population with access”; and “Maximize the commercial potential.”¹⁶⁶ Less-highly rated factors included, among other factors, ensuring sustainable financing for patients, aligning physicians’ perception of Aduhelm’s value with its price, limiting the price differential between the United States and Europe, and maintaining a positive relationship with payers.¹⁶⁷ Justifications frequently offered by the pharmaceutical

¹⁶⁴ BIIB_HCOR_EC_0128260, at Page 25.

¹⁶⁵ BIIB_HCOR_EC_0260447, at Page 4.

¹⁶⁶ *Id.*, at Page 5.

¹⁶⁷ *Id.*

industry for high launch prices—including research and development, manufacturing and other costs—were not among the factors presented.¹⁶⁸

A draft presentation in September 2020 indicated that the company was continuing to evaluate launch price options and expected pushback from payers and other stakeholders at all prices but increasing scrutiny at prices above \$30,000 to \$40,000 per year.¹⁶⁹ This presentation again listed various considerations in setting the price—including patient affordability and payer and other stakeholder pushback. To the extent Biogen considered pricing factors other than revenue, it appears that it was for the purpose of mitigating the negative implications the consultants described rather than addressing actual impact on patients.¹⁷⁰

Documents reviewed indicate that, following these pricing discussions, Biogen developed an extensive communications campaign to support Aduhelm’s high price tag by emphasizing the drug’s “value.” Biogen’s outward-facing “value story” emphasized clinical, patient and family, economic, and societal benefits of a treatment that would delay the progression of Alzheimer’s disease.¹⁷¹ Two of the “[c]ore [m]essages” Biogen created to support its high price focused on emphasizing the value Aduhelm would bring to patients, their caregivers and society at large, and how Aduhelm would catalyze new research investment in the field.¹⁷² A November 2020 draft presentation for the Board, titled “Aducanumab US Pricing: Strategic Considerations,” emphasized that establishing and defining the value of Aduhelm early and aggressively, and quickly pushing this message on stakeholders, would be important in mitigating pushback against the drug’s price tag.¹⁷³

Biogen’s leadership persisted with its pricing model and launched the drug in June 2021 with a price tag of \$56,000 per average-weight patient, per year. Immediately after launch, investors described Biogen’s pricing as “substantially higher than expected” and “aggressive.”¹⁷⁴ The nonprofit Institute for Clinical and Economic Review (ICER) independently assessed the clinical effectiveness and value of Aduhelm for treating Alzheimer’s disease and concluded that a fair price of Aduhelm would be within \$3,000 to \$8,400 per year, an 85–95 percent discount

¹⁶⁸ See e.g., *Big Pharma Says Drug Prices Reflect R&D Cost. Researchers Call BS*, Wired (Oct. 13, 2022) (online at www.wired.com/story/drug-research-pricing/); *Big Pharma’s Go-To Defense of Soaring Drug Prices Doesn’t Add Up*, The Atlantic (Mar. 23, 2019) (online at www.theatlantic.com/health/archive/2019/03/drug-prices-high-cost-research-and-development/585253/).

¹⁶⁹ BIIB_HCOR_EC_0526003, at Pages 4 and 7.

¹⁷⁰ *Id.*, at Pages 14–19.

¹⁷¹ BIIB_HCOR_EC_0204143, at Pages 3 and 33.

¹⁷² BIIB_HCOR_EC_0204143, at Page 42 (the third “core message” to support Biogen’s pricing focused on an understanding of the appropriate patient population for Aduhelm).

¹⁷³ See e.g., *Id.*, at Page 6.

¹⁷⁴ See e.g., BIIB_HCOR_EC_0044418, at Page 1; BIIB_HCOR_EC_0044430, at Page 1. These investor takeaways were included in a June 9, 2021, email from a Biogen executive titled, “ADUHELM approval—Summary of Sell-side notes,” that summarized key investor sentiment including that, “Price is higher than expected and many wonder if this will impact uptake with payer and/or political pushback.” BIIB_HCOR_EC_0044413, at Pages 1–2.

off of Biogen’s annual list price of \$56,000.¹⁷⁵ ICER recommended that Biogen lower the price of Aduhelm to a “value-based price” that aligned with the benefits to patients and noted that fair pricing by manufacturers is necessary to “avoid financial toxicity that falls hardest on the most vulnerable patients.”¹⁷⁶

ii. *Biogen Expected Aduhelm to Financially Burden Medicare and Be Costly to Patients*

Internal company documents show that Biogen was aware the financial burden of its high price for Aduhelm would fall primarily on Medicare. Documents show that Biogen projected Medicare would account for more than 85 percent of the drug’s target patient population at the time of its launch and that all government programs would collectively account for 90 percent of the patient population.¹⁷⁷ A November 2020 presentation to Biogen’s Board noted, “Aducanumab has the potential to be a significant part of the Medicare Part B budget” and calculated that, with just 250,000 patients at an estimated WAC of \$55,000 per patient, Aduhelm could cost Medicare \$12 billion in one year—and would be 26 percent of Medicare’s Part B budget if added to Medicare’s 2018 total spending.¹⁷⁸ The presentation included a chart estimating that Medicare could spend nearly five times more on Aduhelm than on the costliest drug to Medicare in 2018.¹⁷⁹

¹⁷⁵ Institute for Clinical and Economic Review, *Press Release: ICER Publishes Final Evidence Report and Policy Recommendations on Aducanumab for Alzheimer’s Disease* (Aug. 5, 2021) (online at <https://icer.org/news-insights/press-releases/icer-publishes-final-evidence-report-and-policy-recommendations-on-aducanumab-for-alzheimers-disease/>).

¹⁷⁶ *Id.*

¹⁷⁷ See e.g., BIIB_HCOR_EC_0023329, at Page 208; BIIB_HCOR_EC_0204143, at Page 5 (Biogen further anticipated that all government programs, including Medicaid and the Department of Veterans Affairs would account for roughly 90 percent of targeted patients). Documents indicate that Biogen lobbyists met with Department of Veterans Affairs administrators to discuss the launch of Aduhelm with the goal of ensuring the Department of Veterans Affairs would cover Aduhelm for veterans as soon as the drug came to market. BIIB_HCOR_EC_0623398, at Page 103.

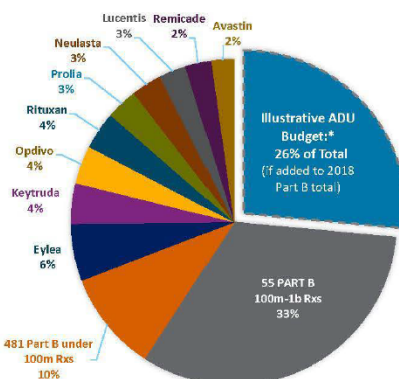
¹⁷⁸ BIIB_HCOR_EC_0204143, at Page 29. Biogen’s projection of \$12 billion represented 36 percent of total Medicare spending for Part B drugs in 2018 (which was \$33.3 billion). Other entities projected that total Medicare spending for Aduhelm in one year could be even higher, and even surpass spending on all other Part B drugs combined. See e.g., Kaiser Family Foundation, *FDA’s Approval of Biogen’s New Alzheimer’s Drug Has Huge Cost Implications for Medicare and Beneficiaries* (June 10, 2021) (online at www.kff.org/medicare/issue-brief/fdas-approval-of-biogens-new-alzheimers-drug-has-huge-cost-implications-for-medicare-and-beneficiaries/).

¹⁷⁹ BIIB_HCOR_EC_0204143, at Pages 28–29.

Aducanumab has the potential to be a significant part of the Medicare Part B budget

MEDICARE PART B BUDGET:
2018 ACTUAL SPEND VS. ILLUSTRATIVE ADU BUDGET

	ANNUAL COST (2018)
Aducanumab* (illustrative)	\$12.0B*
Eylea	\$2.6B
Keytruda	\$1.8B
Opdivo	\$1.7B
Rituxan	\$1.7B
Prolia	\$1.4B
Neulasta	\$1.4B
Lucentis	\$1.2B
Remicade	\$1.1B
Avastin	\$1.0B
Total for 55 PART B products with 100M-1B Scripts	\$14.8B
Total for 481 Part B products with under 100M Scripts	\$4.5B
2018 Total (Actual)	~\$33.3B
Total w/ ADU Added*	~\$45.3B



Engagement Surrounding Budget Impact Perceptions & Misperceptions:

- Field tools to support payer and policymaker discussions
- Objection handlers and education related to **targeted population / patient funnel**
- Narrative talking points related to **uptake analogs** (e.g., PD1s, HCV)



*Illustrative assumptions: estimated **\$48K net per patient** (\$55K WAC) x **250,000 patients** = \$12B (illustration only; does not align to LRP)

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After its launch, outside projections estimated that Medicare spending on Aduhelm could cost Medicare between \$6 billion and \$29 billion per year and that the U.S. government could potentially spend more on Aduhelm than the budgets for the Environmental Protection Agency or the National Aeronautics and Space Administration.¹⁸⁰

Internal company documents also show that Biogen knew from early pricing models that many Medicare patients would face challenges in affording Aduhelm. Analyses conducted by Biogen estimated that some Medicare patients could face out-of-pocket costs for Aduhelm of up to 20 percent of their income.¹⁸¹ One June 2020 presentation noted that Medicare beneficiaries who do not have supplemental coverage—which Biogen estimated in one presentation to be 11 percent of Aduhelm patients—would be required to pay a 20 percent coinsurance on Aduhelm.¹⁸² Information compiled by Biogen’s federal public policy and government affairs team on Aduhelm affordability cautioned, “Over 65 population will face challenges with ability to pay, creating need for appropriate assistance programs.”¹⁸³ The team identified factors that make the Medicare patients at risk for Alzheimer’s disease particularly vulnerable: (1) two-

¹⁸⁰ See e.g., *New Drug Could Cost the Government as Much as It Spends on NASA*, New York Times (June 22, 2021) (online at www.nytimes.com/2021/06/22/upshot/alzheimers-aduhelm-medicare-cost.html).

¹⁸¹ BIIB_HCOR_EC_0616631, at Page 7.

¹⁸² BIIB_HCOR_EC_0623398, at Page 122 (this slide also noted that the drug “will raise affordability concerns for the Medicare program.”). See also BIIB_HCOR_EC_0204143, at Page 39 (noting out-of-pocket expenses for Medicare beneficiaries with and without supplemental plans, and for Medicare Advantage patients).

¹⁸³ BIIB_HCOR_EC_0616631, at Page 10.

thirds have some out-of-pocket exposure; (2) more than 50 percent have income of less than \$50,000 a year; and (3) 35 percent have assets less than \$5,000.¹⁸⁴

Biogen appears to have developed financial assistance programs for eligible patients, including a co-pay assistance program for commercially insured patients and a free drug program for uninsured and underinsured patients.¹⁸⁵ However, these programs leave significant gaps in coverage. For example, Biogen anticipated that Aduhelm would be prohibitively expensive for uninsured patients, noting in one internal analysis that uninsured patients would be expected to “pay full commercial payment rate and WAC for [the] drug.”¹⁸⁶ Yet, to be eligible for Biogen’s “Free Drug Program,” a patient would need to meet certain income and asset criteria, which could exclude many uninsured or underinsured patients.¹⁸⁷ Similarly, although Biogen appears to have developed a co-pay assistance program that would provide financial assistance for the drug, as well as procedure costs for certain patients with lower household income, a patient would need to be commercially insured and meet eligibility criteria to benefit from this program.¹⁸⁸ These programs would not help Medicare beneficiaries, whom Biogen expected would have to pay anywhere “from \$0 to \$9k, stressing fixed income budgets,” as well as additional costs for the required scans and infusion.¹⁸⁹

Companies are not permitted to offer cost-sharing assistance directly to Medicare beneficiaries, because, under the Anti-Kickback statute, it is illegal for drug manufacturers to offer payment that might persuade a patient to purchase something paid for by federal programs, unless certain exceptions apply.¹⁹⁰ Therefore, for Medicare patients, documents indicate that Biogen considered what it described as a “Hail Mary” to provide “cost-sharing assistance” to

¹⁸⁴ BIIB_HCOR_EC_0616631, at Page 10.

¹⁸⁵ BIIB_HCOR_EC_0427773, at Page 37. It is unclear which programs were implemented. Planning documents indicate that the company also planned to explore charitable funding when available to secure financial assistance for out-of-pocket expenses, although it is unclear if this was implemented. BIIB_HCOR_EC_0523820, at Page 9.

¹⁸⁶ BIIB_HCOR_EC_0616631, at Page 6; BIIB_HCOR_EC_0623398, at Page 112.

¹⁸⁷ BIIB_HCOR_EC_0427773, at Pages 18 and 37. These criteria—including income less than \$75,000 per year, household liquid assets under \$25,000, and an income to out-of-pocket ratio of greater than 10 percent—left gaps of patients in need that even Biogen recognized. For example, in planning documents, Biogen noted that more than half of the over 65 population would face challenges in ability to pay and have assets less than \$100,000. BIIB_HCOR_EC_0523820, at Page 5.

¹⁸⁸ BIIB_HCOR_EC_0427773, at Page 38.

¹⁸⁹ BIIB_HCOR_EC_0523820, at Page 4. The Committee on Oversight and Reform has found previously that drug companies often highlight the generosity of their patient assistance programs but internally emphasize the return on investment from these programs in the form of increased sales, and company spending on these programs is often minimal compared to the enormous amount of revenue brought in by the drug. See Majority Staff, Committee on Oversight and Reform, *Drug Pricing Investigation* (Dec. 10, 2021) (online at <https://oversight.house.gov/sites/democrats.oversight.house.gov/files/DRUG%20PRICING%20REPORT%20WITH%20APPENDIX%20v3.pdf>).

¹⁹⁰ 42 U.S.C. § 1320a-7b.

certain Medicare beneficiaries.¹⁹¹ One Biogen presentation proposed cost-sharing assistance to Medicare fee-for-service beneficiaries who do not have supplemental insurance and cannot afford their cost-sharing obligations.¹⁹² However, the presentation noted that this would require an Inspector General opinion and “regulatory relief” due to the Anti-Kickback Statute.¹⁹³ Internal documents show Biogen reached out to CMS on this strategy, but it is unclear whether Biogen further pursued the “Hail Mary” strategy.¹⁹⁴

Internal documents show that Biogen explored the potential financial impact of Aduhelm in its pre-approval discussions with CMS.¹⁹⁵ A November 2020 presentation to Biogen Board of Directors stated: “We understand that aducanumab is being launched at a challenging time in our history, and are prepared to make the following corporate commitments related to the launch of aducanumab.”¹⁹⁶ Biogen considered “strategic pricing considerations”—including a proposal to freeze price increases for a period of four years.¹⁹⁷ Biogen also considered revisiting Aduhelm’s list price in the event of a significant increase in patient volume beyond the targeted patient population or if patients stayed on Aduhelm beyond a few years.¹⁹⁸

As Biogen anticipated, Aduhelm’s launch price had immediate negative impacts on Medicare and beneficiaries. Five months after Aduhelm’s launch, in November 2021, CMS announced that Medicare Part B’s monthly premium for 2022 would increase by 14.5 percent—noting that roughly half of the premium increase reflected the need for additional contingency reserves in anticipation of significantly higher expenditures due to Aduhelm.¹⁹⁹ This amounted to a monthly premium increase of \$21.60 per beneficiary—reportedly the largest dollar increase in the program’s history.²⁰⁰ After Biogen reduced the price of Aduhelm in December 2021, the Secretary of HHS asked CMS to reassess its recommendation for the Part B premium, but CMS

¹⁹¹ BIIB_HCOR_EC_0616631, at Page 14.

¹⁹² *Id.*, at Page 14.

¹⁹³ 42 U.S.C. § 1320a-7b.

¹⁹⁴ BIIB_HCOR_EC_0616631, at Page 14.

¹⁹⁵ See e.g., BIIB_HCOR_EC_0448531, at Page 4 (“Teams continue to engage actively with key stakeholders to solidify value story and pricing” with “CMS & Policymakers” included among key stakeholders).

¹⁹⁶ *Id.*, at Page 11.

¹⁹⁷ BIIB_HCOR_EC_0015885, at Page 5 (June 2021 presentation on “Aduhelm Value, Price, and Patient Access” for internal discussion purposes only); BIIB_HCOR_EC_0204143, at Page 57 (these strategies were explored, and subject to management, legal and regulatory review). See also BIIB_HCOR_EC_0448531, at Page 11; BIIB_HCOR_EC_0616631, at Page 13.

¹⁹⁸ BIIB_HCOR_EC_0204143, at Pages 54–57 (these strategies were explored and subject to management, legal, and regulatory review).

¹⁹⁹ Centers for Medicare & Medicaid Services, *CMS Announces 2022 Medicare Part B Premiums* (Nov. 12, 2021) (online at www.cms.gov/newsroom/press-releases/cms-announces-2022-medicare-part-b-premiums).

²⁰⁰ AARP, *Medicare Part B Premium Increase for 2022 Largest Ever* (Nov. 15, 2021) (online at www.aarp.org/health/medicare-insurance/info-2021/part-b-premiums-increase.html).

stated that a mid-year premium modification was not feasible.²⁰¹ In September 2022, CMS announced that the standard monthly premium for Medicare Part B enrollees for 2023 would decrease—by \$5.20—as a result of the agency’s revised analysis of projected spending on Aduhelm and other services.²⁰²

C. Biogen Planned to Spend Billions to Market Aduhelm Despite Expectations About the Financial Impact on Patients and the Health System

Internal documents show Biogen planned an aggressive outreach and marketing campaign to launch Aduhelm, focusing on direct outreach to stakeholders—providers, patients, patient advocacy groups, payers, and policymakers. A February 2020 letter from Biogen’s then-CEO to the company’s Board explained that a key focus area for the Aduhelm team was to engage a “broad range of external stakeholders,” including patient advocacy organizations and key medical experts.²⁰³ In some long-range plans, Biogen anticipated spending \$3.3 billion on sales and marketing for Aduhelm from 2020 to 2024—more than two and a half times what Biogen spent on aducanumab lifetime development costs from 2007 until approval in June 2021.²⁰⁴

Documents indicate that Biogen was particularly focused on outreach to health care providers. In September 2020, Biogen anticipated spending between \$500 million and \$600 million to build out its sales force, with a focus on targeting primary care physicians.²⁰⁵ A July 2020 email thread with Biogen’s then-CEO contained a discussion about a June 2020 slide deck on “aducanumab readiness”, which addressed outreach to providers and “education and engagement” with key medical experts, or KMEs.²⁰⁶ The deck presented Biogen’s plans for a brand campaign to reach more than 16,000 health care providers. Biogen executives set a goal to deploy 300 key medical experts as advocates for Aduhelm and educate providers at 600 sites about the drug so they could be ready to prescribe at launch, by the end of 2020.²⁰⁷

²⁰¹ Centers for Medicare & Medicaid Services, *CMS Report to the Secretary: Reexamination of the 2022 Medicare Part B Premium* (May 19, 2022) (online at www.cms.gov/files/document/cms-report-secretary-2022-medicare-part-b-premium-reexamination.pdf).

²⁰² Centers for Medicare & Medicaid Services, *2023 Medicare Parts A and B Premiums and Deductibles 2023 Medicare Part D Income-Related Monthly Adjustment Amounts* (Sept. 27, 2022) (online at www.cms.gov/newsroom/fact-sheets/2023-medicare-parts-b-premiums-and-deductibles-2023-medicare-part-d-income-related-monthly).

²⁰³ BIIB_HCOR_EC_0010511, at Pages 11 and 13 (the Committees do not know which, if any, of these marketing plans were implemented).

²⁰⁴ BIIB_HCOR_EC_0023329, at Page 276; Letter from Biogen to Chairwoman Carolyn B. Maloney, Committee on Oversight and Reform, and Chairman Frank Pallone, Jr., Committee on Energy and Commerce (Feb. 15, 2022) (Biogen reported spending a total of \$1.16 billion from 2007 to 2021 on aducanumab development costs, which include Phase 1, Phase 2, Phase 3 clinical trial expenses plus “other program expenses,” such as consulting, regulatory fees, preclinical sampling, and chemistry, manufacturing and controls costs).

²⁰⁵ BIIB_HCOR_EC_0023329, at Page 276.

²⁰⁶ BIIB_HCOR_EC_0623397; BIIB_HCOR_EC_0623398, at Page 6.

²⁰⁷ BIIB_HCOR_EC_0623398, at Page 6.

Biogen also aimed to activate patients directly through a variety of strategies, including by seeking input directly from patient advocacy organizations.²⁰⁸ Documents show a key piece of Biogen’s outreach to patients was to build support for Aduhelm through collaboration with leading Alzheimer’s disease patient advocacy organizations. Biogen’s planned advocacy group engagement was extensive. Documents show Biogen intended these organizations to build support for Aduhelm among other stakeholders and government agencies.²⁰⁹ For example, Biogen aimed to get input from one organization on patient education and another organization on a helpline design to connect patients with Biogen patient services.²¹⁰ Biogen aimed for these groups to “leverage Biogen-provided materials to communicate to their membership.”²¹¹ Documents show Biogen sought to use support for Aduhelm among patient advocates to present Aduhelm as a drug with “value to patients, caregivers and society at large.”²¹²

Biogen’s plans also involved an extensive media campaign directed at patients. This campaign included plans to educate more than 50 journalists on background and connect them with key medical experts to “shape the narrative” around Aduhelm; use “microtargeting to focus media in target markets, starting in areas with high 65+ and expected readiness”; and roll out a consumer disease education campaign through online platforms such as Facebook, WebMD, YouTube, and Twitter.²¹³

Documents show Biogen also developed marketing strategies to target communities of color.²¹⁴ As part of that strategy, Biogen crafted a public narrative that the company promoted health equity and access, and Biogen worked behind the scenes to enlist and build support for Aduhelm among Alzheimer’s disease advocacy organizations that serve people of color. An internal presentation by a Biogen executive for the company’s Executive Committee, dated April 5, 2021, declared that “at launch, we will have a comprehensive health equity offering.”²¹⁵ The presentation recognized that to be meaningful and impactful, Biogen’s health equity program for Aduhelm would need to address “Early Detection, Diagnosis, and Affordability.”²¹⁶

Biogen designed promotional materials targeted at Black and Latino patients and their health care providers. Among other initiatives, Biogen planned to buy advertising slots on Telemundo, Black Entertainment Television, and other networks to reach consumers of color

²⁰⁸ BIIB_HCOR_EC_0623398, at Pages 175–176.

²⁰⁹ BIIB_HCOR_EC_0204143, at Page 11.

²¹⁰ BIIB_HCOR_EC_0023329, at Pages 211 and 221–222 (the Committees do not know how much of these plans were implemented).

²¹¹ *Id.*, at Page 221.

²¹² BIIB_HCOR_EC_0204143, at Page 42.

²¹³ BIIB_HCOR_EC_0623398, at Pages 175–184; BIIB_HCOR_EC_0023329, at Page 223.

²¹⁴ *See e.g.*, BIIB_HCOR_EC_0427773, at Pages 3–4 (noting key barriers to diagnosis for Black and Latino populations).

²¹⁵ BIIB_HCOR_EC_0427773, at Page 2.

²¹⁶ *Id.*, at Page 5.

directly.²¹⁷ In one presentation, the company indicated it could spend upwards of \$3 million on media advertising focusing on patients of color alone and approximately \$1 million on multilingual patient outreach and funding for patient transportation.²¹⁸

However, Biogen's proposed health equity narrative and marketing plans were not supported by Aduhelm's clinical trials. In Biogen's initial Phase 3 clinical trials for Aduhelm, only 3.0 percent were Hispanic, 0.6 percent of participants were Black, and 0.03 percent were American Indian or Alaska Native.²¹⁹ Only after CMS's proposed national coverage decision, which required that patients in CMS-approved trials be representative of the national population diagnosed with Alzheimer's disease, did Biogen promise to increase diversity in its Phase 4 confirmatory trial.²²⁰

IV. CONCLUSION

The findings in this report raise serious concerns about FDA's lapses in protocol and Biogen's disregard of efficacy and access in the approval process for Aduhelm. The findings also justify experts' and stakeholders' concerns about FDA's accelerated approval of Aduhelm. The criticism surrounding Aduhelm's approval may have been avoided had FDA adhered to its own guidance and internal practices. FDA must take swift action to ensure that its processes for reviewing future Alzheimer's disease treatments do not lead to the same doubts about the integrity of FDA's review.²²¹ Biogen, which currently has another Alzheimer's drug under review by FDA, must provide more transparency into its pricing and analyses of clinical benefit to ensure that new drugs are effective and available for those who need them.

Based on the findings of our investigation and FDA's own identified areas for improvement in its internal review, the Committees make the following recommendations for FDA and Biogen, as well as future drug sponsors.

1. FDA Must Fully Implement Its Own Internal Review Recommendation and Ensure All Substantive Interactions with Drug Sponsors Are Properly

²¹⁷ BIIB_HC0R_EC_0427773, at Page 26 (the company may or may not have implemented this strategy).

²¹⁸ *Id.*

²¹⁹ Jennifer Manly and Maria Glymour, *What the Aducanumab Approval Reveals About Alzheimer Disease Research*, JAMA Neurology (Oct. 4, 2021) (online at <https://jamanetwork.com/journals/jamaneurology/article-abstract/2784441>) (noting, "Older Black adults are estimated to have AD incidence up to double the rates in older White people. Despite this, Biogen reported that only 6 Black people were randomized to the treatment dose approved by the FDA").

²²⁰ Centers for Medicare & Medicaid Services, *Proposed Decision: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease* (Jan. 11, 2022) (online at www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=Y&NCAId=305); Biogen, *Update on the Phase 4 Envision Confirmatory Study of Aduhelm* (Jan. 27, 2022) (online at <https://investors.biogen.com/news-releases/news-release-details/update-phase-4-envision-confirmatory-study-aduhelm>) (committing to enroll 18 percent of U.S. participants in the trial "from Black/African American and Latinx populations").

²²¹ Eli Lilly & Company's donanemab and Biogen-Eisai's lecanemab are both undergoing BLA review at the time of this report's publication.

Memorialized. CDER should proceed with all due urgency to finalize its revised internal guidance on the memorialization of sponsor interactions to ensure that all substantive interactions with sponsors are documented, including specifying the limited circumstances in which documentation is not required. In addition, FDA should provide further resources and training for staff on their responsibility to identify and maintain appropriate documentation in the agency's document archiving system regarding the total number, type, and content of interactions with sponsors, including records of all Type C meetings.

2. **FDA Should Follow Through on Its Internal Review Recommendation and Establish a Protocol for Joint FDA-Drug Sponsor Briefing Documents for Advisory Committees.** As the OND workstream efforts continue to evaluate all activities related to Advisory Committee meeting preparation, FDA should establish clear guidance for agency staff and drug sponsors on the use of a joint briefing document, including: whether and when it is appropriate to develop and utilize a joint briefing document; how to develop and utilize a joint briefing document; the necessary degree of consensus among all FDA reviewers for a joint briefing document to be considered appropriate; and the level of collaboration that is appropriate in preparing the document.
3. **FDA Should Provide Updated Guidance for Industry Regarding Development and Review of New Alzheimer's Drugs.** FDA should update the February 2018 draft guidance, *Early Alzheimer's Disease: Developing Drugs for Treatment, Guidance for Industry*, prior to the approval of future Alzheimer's drugs, in order to provide industry and the public with a complete understanding of the agency's current view on how these drugs should be evaluated.
4. **Biogen and Other Drug Sponsors Should Communicate Safety and Efficacy Concerns to FDA.** Drug sponsors should transmit any safety and/or efficacy concerns raised by its scientific experts during BLA review to the FDA review team.
5. **Biogen and Other Drug Sponsors Should Consider Value and Patient Access When Setting Prices.** Drug sponsors should consider the value assessments made by outside experts, in addition to shareholder and company profits, when setting the launch prices for drugs. Companies should consider pricing strategies for new drugs that maximize patient access. The pharmaceutical industry plays an essential role in developing and producing life-saving drugs, but sky-high launch prices for drugs, especially those with unproven benefit, without consideration of patient access and affordability, are an abuse of the public trust.

The American people rely on FDA for assurance on the safety and efficacy of the medications they take, and it is incumbent upon drug companies such as Biogen to ensure that the well-being and safety of patients are prioritized. The number of patients and families impacted by Alzheimer's disease will continue to increase, and it is crucial that FDA and drug

companies adhere to established procedures and conduct themselves with the transparency necessary to earn public trust. The Committees urge FDA, Biogen, and other drug sponsors seeking to develop treatments for Alzheimer's disease and other diseases to follow guidance and protocols, provide transparency into the drug evaluation process and drug pricing, and work to better ensure public trust in future drug approvals.