



# Aduhelm Investigation

Biogen

*Selected Investigation Documents*

Committee on Oversight and Reform and Committee on  
Energy and Commerce  
U.S. House of Representatives  
December 2022

<b>Document #</b>	<b>Citation</b>	<b>Short Description</b>
<b>1</b>	BIIB_HCOR_EC_0023329	September 2020 Board of Directors Meeting Materials (Selected Pages)
<b>2</b>	BIIB_HCOR_EC_0126698	Aduhelm Clinical Information Amendment for Labeling
<b>3</b>	BIIB_HCOR_EC_0128260	April 2020 Presentation and Final Report (Selected Pages)
<b>4</b>	BIIB_HCOR_EC_0187343	July 2020 Presentation (Selected Pages)
<b>5</b>	BIIB_HCOR_EC_0204143	November 2020 Presentation (Selected Pages)
<b>6</b>	BIIB_HCOR_EC_0260447	April 2020 Presentation (Selected Pages)
<b>7</b>	BIIB_HCOR_EC_0427521	May 2020 Presentation (Selected Pages)
<b>8</b>	BIIB_HCOR_EC_0427773	April 2021 Presentation (Selected Pages)
<b>9</b>	BIIB_HCOR_EC_0429470	December 2019 Presentation (Selected Pages)
<b>10</b>	BIIB_HCOR_EC_0434630	June 2020 Presentation (Selected Pages)
<b>11</b>	BIIB_HCOR_EC_0442081	White Paper on Positioning/Promoting Aducanumab for the Clinical Trial Population
<b>12</b>	BIIB_HCOR_EC_0448531	November 2020 Presentation (Selected Pages)
<b>13</b>	BIIB_HCOR_EC_0523820	May 2020 Presentation (Selected Pages)



<b>14</b>	BIIB_HCOR_EC_0526003	September 2020 Presentation (Selected Pages)
<b>15</b>	BIIB_HCOR_EC_0616631	April 2021 Presentation (Selected Pages)
<b>16</b>	BIIB_HCOR_EC_0623390	July 2020 Presentation
<b>17</b>	BIIB_HCOR_EC_0642217	March 2020 Presentation (Selected Pages)

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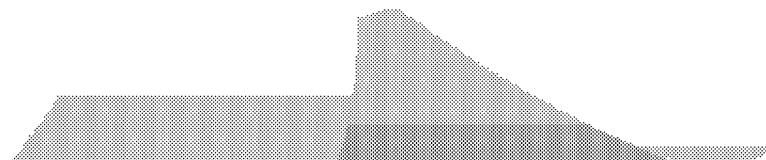


# Aducanumab Value Story

September 30, 2020



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Presentation to the Board of Directors

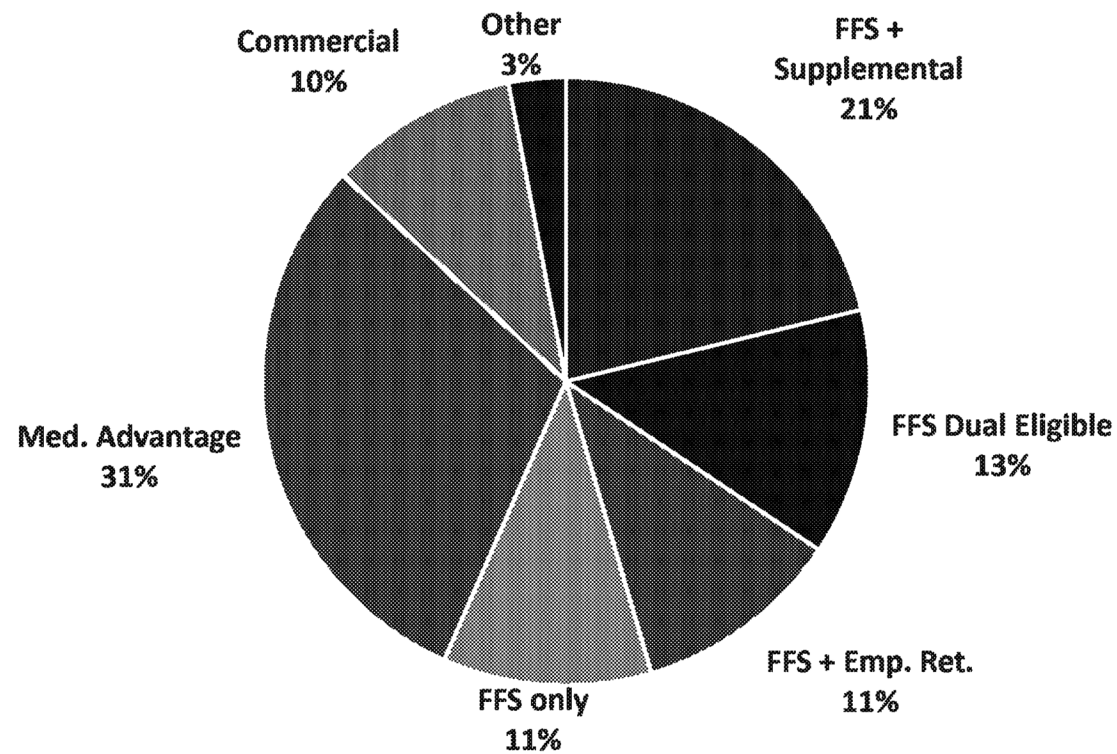


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**Medicare is anticipated to account for >85% of patients at the time of launch**



Source: claims analysis for currently diagnosed AD and MCI patients

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# Aducanumab U.S. Launch Update

[REDACTED] US Organization  
[REDACTED] Alzheimer's Franchise US  
[REDACTED] Alzheimer's Medical US & Global Medical  
[REDACTED] [REDACTED] Alzheimer's Marketing US

September 30, 2020



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Presentation to the Board of Directors

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## 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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**ADUHELM (aducanumab-avwa)  
BLA 761178**

**Clinical Information Amendment  
to Support a Labeling Prior Approval Supplement**

BLA 761178

## 1.11.3 Clinical Information Amendment

**1. BACKGROUND AND RATIONALE**

The objective of this Clinical Information Amendment is to support the proposed update of the Aduhelm USPI and summarizes the following

- Rationale for changes to Section 1 – Indications and Usage
- Rationale for changes to the Medication Guide

Biogen believes the most appropriate patients for Aduhelm treatment are patients who are either at the mild cognitive impairment or mild dementia stages of Alzheimer’s disease. This is consistent with the population studied in our clinical trials and is outlined in Section 14 of the USPI.

We have heard from health care providers (HCPs) that 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 Aduhelm. Absence of information on disease stage, for example, could be viewed as a suggestion that the initiation of Aduhelm treatment at any stage, including patients at stages appreciably beyond those studied, is indicated. In particular, in our engagements with prescribers we heard that it was considered most important to clarify in the label whether Aduhelm can be initiated in patients at stages more advanced than those assessed in our studies.

**1.1 INDICATION AND USAGE**

In an effort to provide greater clarity, and mitigate confusion in the HCP community, we are proposing changes to the indication statement. These proposed changes appear in red text below:

“ADUHELM is indicated for the treatment of Alzheimer’s disease. ADUHELM was assessed in patients with mild cognitive impairment or mild dementia stage of the disease. There are no data on initiating treatment at earlier or later stages of the disease than were studied. This indication is approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with ADUHELM [*see Clinical Studies (14)*]. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).”

Our proposal is to retain the current indication statement “For the treatment of Alzheimer’s disease”, and augment with information to clarify who are the most appropriate patients to be treated with Aduhelm:

1. Add the stages of disease for the population studied in the clinical trials.
2. Add a statement to clarify the stages of disease for which there is currently no data available on the initiation of treatment with Aduhelm.

**Rationale**

- Keeping the current indication statement retains the description of the disease for which Aduhelm is indicated. Alzheimer’s disease is a progressive neurological disorder, understood today to be continuum along which patients inevitably progress.

BLA 761178

## 1.11.3 Clinical Information Amendment

- Addition of the stages of disease in which Aduhelm was assessed in the clinical trials [Mild Cognitive Impairment or mild dementia stage of the disease] will support understanding the stages of disease where data are currently available, and therefore will advise on the most appropriate stage of Alzheimer's disease in which to initiate the treatment of Aduhelm.
- Addition of a statement to clarify the stages of disease for which there are currently no data available on the initiation of treatment with Aduhelm: [There are no data on initiating treatment at earlier or later stages of the disease than were studied]. This will clarify that at present there is no data on initiating treatment at these stages of disease and therefore that the effect of Aduhelm is unknown if initiated at these stages.
- The use of 'initiating treatment' in this statement is intentional rather than using 'There are no data on treatment'. In the clinical trials patients continued to progress along the disease continuum. Some patients while on treatment will have achieved cognitive scores that could over time classify them as 'at later stages' of disease. We have no data to inform that treatment is no longer effective in this setting and want to avoid potential confusion regarding stopping treatment at later stages. We aim to be clear in addressing the HCP feedback that we do not have data on the *initiation* of treatment.
- We have suggested changes to be consistent with the current medical lexicon. We assessed and dismissed options that had potential to further confuse, e.g. through introduction of less used terminology. Specifically, we considered "treatment in early symptomatic Alzheimer's Disease" and concluded that 'early symptomatic' is not widely or consistently used by the Alzheimer's disease HCPs and may lead to greater confusion.

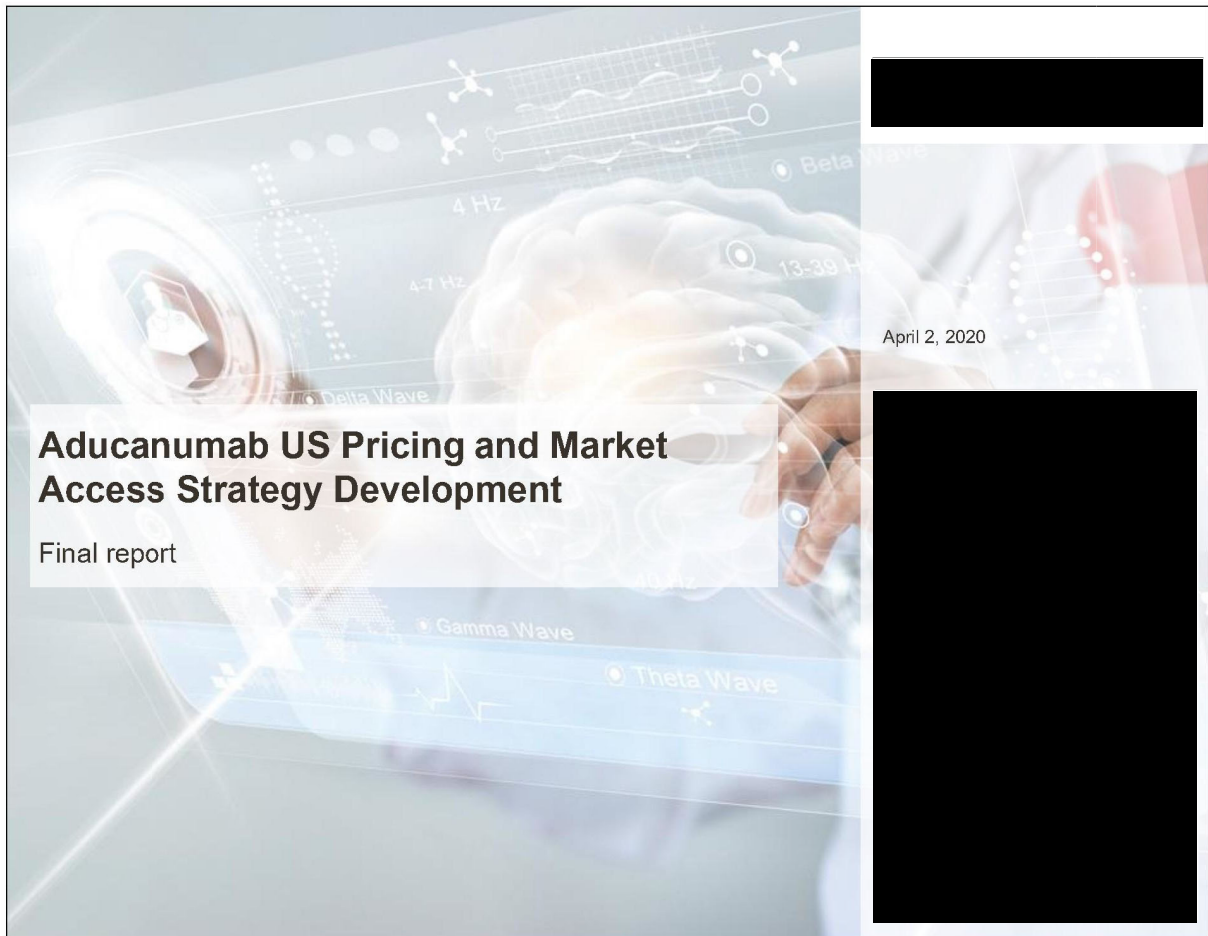
## 1.2 MEDICATION GUIDE

To be consistent with the proposed update to the indication statement, Biogen has reviewed the Medication Guide and suggests the following proposed edit to ensure clarity in communication with their HCP:

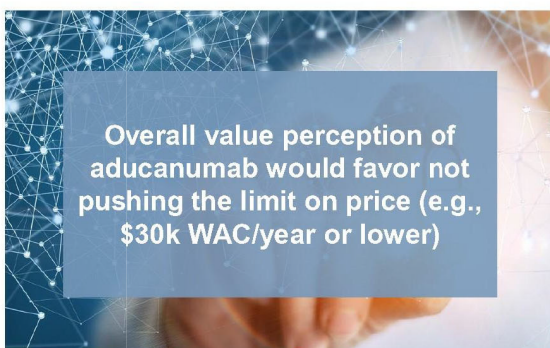
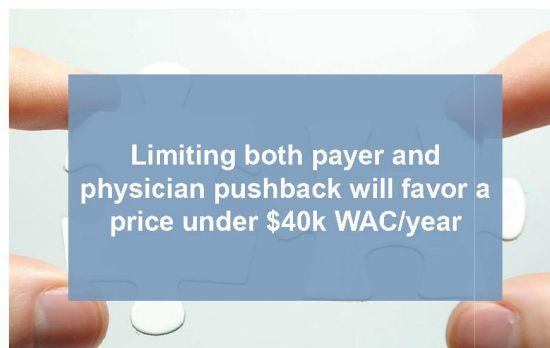
**What is ADUHELM?**

- ADUHELM is a prescription medicine used to treat people with Alzheimer's disease. Your doctor can advise if ADUHELM is right for you.
- It is not known if ADUHELM is safe and effective in children.





## Executive summary



Source:

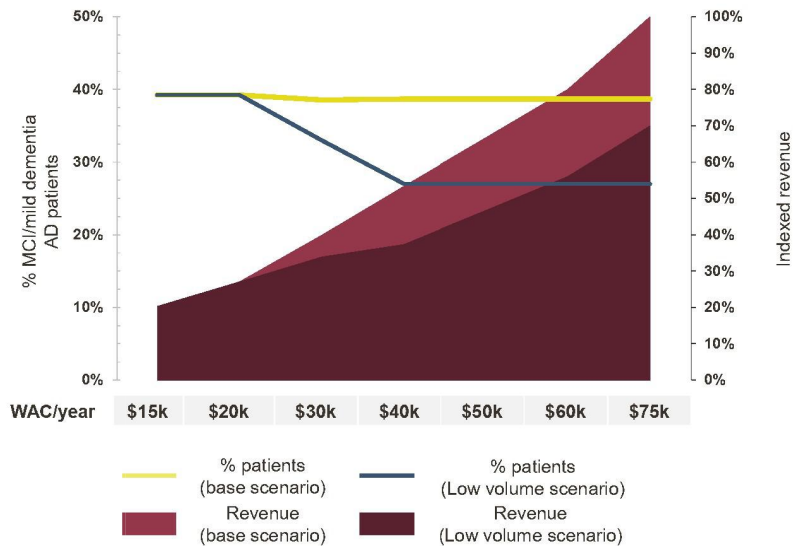
Biogen | Aducanumab Pricing and Launch Strategy | Final report

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## Revenue favors higher aducanumab prices



### Aducanumab indexed revenue and market share



**NOTE:** Reduced uptake of PCSK9s 3 years post-launch vs. forecast at launch was used as proxy for a lower volume scenario for aducanumab

Source: [REDACTED] UM, utilization management; n = 25 US payers; n = 122 US neurologists; \*Impact of public scrutiny on uptake was calculated using PCSK9 prescribing as proxy. Estimated uptake of PCSK9s forecasted in 2018 ~128k patients, Actual/realized uptake in 2018: ~90k patients. (Factor of 0.3 used to calculate reduced impact on prescribing).

Biogen | Aducanumab Pricing and Launch Strategy | Final report

> \$40k WAC/year

### Section takeaways

#### 6 Limited changes in UM relative to price leads to a largely flat volume curve unless public scrutiny reduces volume

- At all prices, payers desire to limit access as much as is clinically appropriate, thereby leaving prescribing unchanged
- Public scrutiny at higher prices can have a negative impact on volume; driven by frequent payer coverage denials and neurologist reluctance to pushback on payers

#### 7 Both potential volume curves lead to greater revenue at higher prices

- This assumes the current environment stays as is
- Public scrutiny results in lower revenue potential compared base case, yet higher prices still likely favor higher revenue



# **Broad Indication Statement Scenario Discussion & Next Steps**

**PDC Meeting**

July 29, 2020

# Disclaimer

This deck is a draft and is intended to be used internally only and for planning purposes. The contents of this deck are based on a range of assumptions regarding future events, including with respect to product approvals, regulatory requirements, patients, prescribers, payors, pricing and reimbursement, other product entrants, etc. To the extent those assumptions prove to be incorrect, the proposed approaches and conclusions will not apply.





## Purpose of this document

**The following Live Capture notes were taken during breakout sessions at the Aducanumab Label Scenario Advisory Board on Friday, July 24, 2020.**

During the advisory board, advisors were split into breakout groups to discuss the implications of two possible label scenarios for aducanumab: 1) Broad label: For the treatment of Alzheimer's disease, and 2) Narrow label: For the treatment of patients with MCI due to AD, and mild AD, with required AB confirmation.

Live Capture notes will inform live synthesis following the advisory board.



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# 1 Initial reactions and patient identification

BREAKOUT ACTIVITY LIVE CAPTURE

**GROUP 1 – BROAD** “For the treatment of Alzheimer’s Disease”

What are the **pros** and **cons** of this potential label in terms of patient identification?

Surprised/cynical x 3!

If this occurs... this opens the door broadly to a large range of patients

(-) A lot of challenges to the system; unable to manage the capacity. Create pressure for identify the “right” patient. Concerns of overwhelming the system

(-) Does this exclude MCI, or complicate MCI as a diagnosis?

(-) Difficult managing expectations and demand: level set and honesty of expectations

Strong push for opinion leaders to define need for amyloid confirmation. Significant pressure on clinicians from patients and caregivers. Would this include preclinical? Before onset, APOE4 carriers...

(+) Probable/possible who have been excluded, broader indication enables treatment for them

(+) DMT will drive a lot of efficiency gains and system improvements

(+) Building awareness and identification will be purposeful ...

(+/-) Broad label will make it more specialist; more interpretive, encourage referral rather than making decision to treat

There may be geographic and regional differences... e.g.: where there may be high levels of specialized care (Rhode Island) vs general care (less urban / rural)

POINTS OF CLARIFICATION

» Do you think your opinion is representative of your peers?

Based on this potential label, how do you identify the right patients to treat? How do you define a non-appropriate patient? How would you manage a non-appropriate patient?

Current clinical criteria would continue to be acceptable.

- Worry about defining who would not benefit/too advanced

Remain relative conservative regarding patient selection.

Would want to include amyloid confirmation.

- But if patient had to pay out of pocket, it will be difficult
- Shift to CSF ...

---- PCP focused training: who’s at risk, how to work up and screen, how to manage and how to refer to specialists. Pragmatic approaches to help find patients and identify for treatment.

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BREAKOUT ACTIVITY LIVE CAPTURE

## 3 Treatment and monitoring implications

GROUP 1 – BROAD

*“For the treatment of Alzheimer’s Disease”*

POINTS OF CLARIFICATION

- » How do you confirm that we have the right patients for therapy?
- » In the absence of a biomarker test, what will guide you to start and stop treatment?

**1 How might we manage safety monitoring? (e.g. safety)**

- Protocols – follow the study protocol
  - Assumption: less in real world
  - Maybe only use MRI for suspicious symptoms
- How might you control for other comorbidities?
  - Concern regarding high risk of ARIA for more advanced patients ...
  - More regular checkups for the first year
- Other concerns from ARIA?
  - Patients on anticoagulants --- not an absolutely exclusion? Patient level discussion.
    - tPA example
  - Uncontrolled hypertension / diabetes / other risk factors for cerebrovascular complications

OTHER: use of ports for drug delivery and long term treatment management?

**2 How long will patients be treated? (e.g. stopping criteria)**

- What do we know about continued treatment?
  - Lack of data: Clearing of amyloid? Do you stop and wait for accumulation?
  - Slow down frequency of treatment?

Potential stopping criteria

- Stop if poor toleration
- Showers of micro hem
- Issues with infusion

Burden/benefit discussion based on a patient treatment burden and response

- MMSE measurement of progression may be enough
  - E.g.: even pill burden may drive a patient to ask if it is truly beneficial
  - Lack of perceived benefit with MMSE decline might trigger a conversation
- Note: As patients progress it is possible for reduced tolerance for MRIs and resistance

Biogen-65520

**3 How might we measure treatment response?**

- Team decision to determine assessment approaches for different stages of disease

- MOCA for earlier
- MMSE for moderate
- Like RBAN, but unlikely – would need to use something that medical extenders are trained in
- Goal attainment scaling: conversation with patient and caregiver: “what bothers the most...”

- MMSE – due to commonality/comfort (used with communication to patients)
- Category Fluency (not communicated to patients)

- MMSE, MOCA back and forth, Category Fluency

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## Patient Advocacy Groups general feedback

### - A broad label scenario brings both benefits and challenges

- Benefits:

- Concept is easier for broader community to understand; may be less of a need to be as extensive in educating about MCI due to AD and mild AD dementia
- More inclusive of patients
- Underserved populations, often screened later, may have a better chance to get access earlier
- Can provide hope to patients and caregivers that have been living with disease

- Challenges:

- May increase stigma associated with a broad AD diagnosis and may reduce the urgency for a diagnosis
- Increased demand may overwhelm healthcare system capacity
- Patients most likely to benefit may not have access if demand/urgency is higher from more progressed patients
- There may be backlash among patients who don't see benefit, without an understanding that drug is not a cure



Global Alzheimer's Disease Advocacy Steering Committee

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## Key steering committee insights

- Having Alzheimer's Disease on the label, without specific mention of MCI due to AD/mild AD dementia may increase stigma around diagnosis
- There may be an opportunity, with a broad label, for providers to focus on pre-clinical patients and enhance education on A $\beta$  confirmation
- There may be an opportunity to frame aducanumab as an amyloid drug versus an Alzheimer's drug, which could help address stigma concerns
- Education about the appropriate patient based on trials data (ie, with MCI due to AD or mild AD dementia) is an appropriate approach, regardless of the label, as these patients stand the best chance to benefit the most
- PCPs play an important role, particularly in areas and among communities with limited access to specialists, and require education in order to support patient screening and treatment
- Narrative around new treatment should not be solely tied to aducanumab, as there are multiple reasons to be hopeful and seek diagnosis (eg, lifestyle interventions, symptomatic treatments, the prospect of science delivering additional new treatments)
- The complicated treatment pathway may prohibit/limit access for underserved populations in areas with less established health systems
- Income inequality may be a primary driver of treatment seeking, as those with means may be among the first to seek treatment
- Patient advocacy groups are playing an active role in communicating and educating the AD community; the group expressed a willingness to align communication with label scenario, if approved



Global Alzheimer's Disease Advocacy Steering Committee

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# Payer Advisors Discussions

- Access restrictions
  - The broader the label, the higher the probability of payers creating policies and hurdles to minimize utilization
  - “Payers will require confirmation of amyloid beta in many geographies, even if the label doesn’t”
- Patient experience – disappointment for those turned away
- Physician experience – management of patients without clear guidance, strained relationships
- Cost to Medicare – major impact on Medicare budget and “would be scrutinized very aggressively.”
- Potential impact on price



## ECP considerations on broad label scenario\*

### ➤ Value & Access implications:

- Prolonged pricing and reimbursement negotiations due to limited data in populations being requested, hence slower uptake than LRP
- Wider access than study populations will be met with demand for lower net prices and / or delayed negotiations, which can not be compensated for by additional volume due to diagnostic pathway bottlenecks
- Overburden healthcare system putting pressure on payers to limit access to ADU

### ➤ Health care system considerations: broad label further supports current lack of urgency for early AD diagnosis

- Lack of urgency to make changes on protocols, guidelines, policies, processes to facilitate early diagnosis
- Current infrastructure is already a potential major bottleneck, a broad label might discourage public health care systems to make the required investments to shorten patient journey.
- CSF confirmation of beta amyloid pathology and MRI monitoring for titration not feasible or very challenging for advanced AD patients

### ➤ Business considerations: Broad label inconsistent with target patient profile (early AD)

- Risk of downsize ADU potential: in the absence of disease state limitation for prescription, the lack of urgency to treat may challenge forecasted uptake.
- Additionally, broader indication is not expected to result in greater number of patients being treated due to infrastructure required to identify, treat and monitor patients, and changes required to facilitate earlier diagnosis
- Clinical experience with ADU at launch will be heterogenous → Risk of ADU not meeting expectations in real world setting and increased skepticism about ADU efficacy
- Risk of focussing on "managing the tsunami" instead driving the right patients to the healthcare system



## ECP considerations on broad label scenario\* (cont.)

- **Projected low likelihood of regulatory success for CDS position based on EMA feedback to date**
  - Other aspects of the dossier that may be more critical will become deprioritised while pursuing broad indication claim
  - Limited data across all stages of disease expected to increase scope of post-marketing studies
  - May require conditional approval to obtain Broad label - fallback to narrower indication of MCI/mild due to AD is recognised as standalone indication by EMA
- **Competitive considerations:**
  - Broad label not always a competitive advantage for first mover: aiming for the entire AD market creates the risk of not truly owning any segment before competition arrives
  - Future DMT entrants (BAN2401, gantenerumab) likely to have targeted label in ECP region. In that situation there is the risk competition being preferred for early AD patients
  - Extended payer negotiations leading to potential delays on launches will limit our 1st mover advantage in many ECP markets (smaller window of opportunity until competition comes to the market)
- **Reputational risk for Biogen:**
  - Early positive experiences and perceptions in the real world are key to meet expectations and preserve Biogen reputation in neurosciences.
  - Biogen risk to lose credibility by arguing for access to sub-populations where we have neither data nor powered endpoints
  - Additional reputational risk if we would have to restrict reimbursed segment in order to 1) avoid low prices and/ or 2) Avoid lengthy negotiations.
  - Risk that external stakeholders (regulators, payers) define the ADU target patient



\*These scenarios are for planning purposes only and are based on certain assumptions that may prove to be inaccurate

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# Aducanumab US Pricing: Strategic Considerations

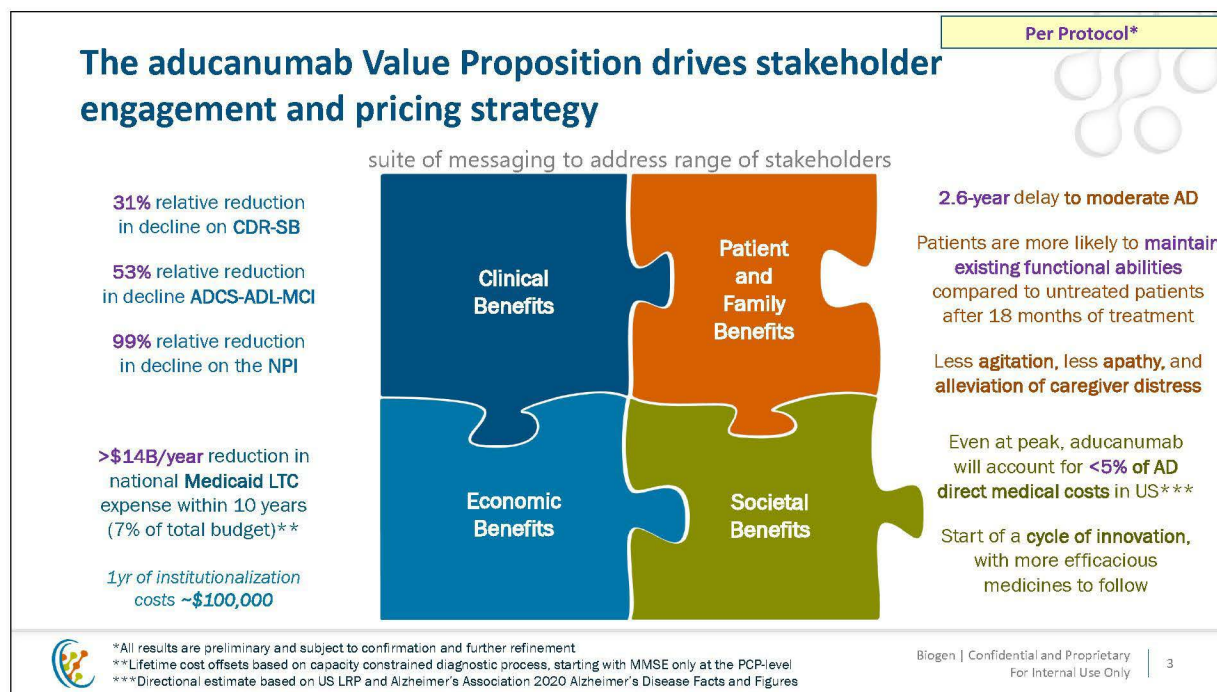
## Presentation to the Board of Directors

November 13, 2020



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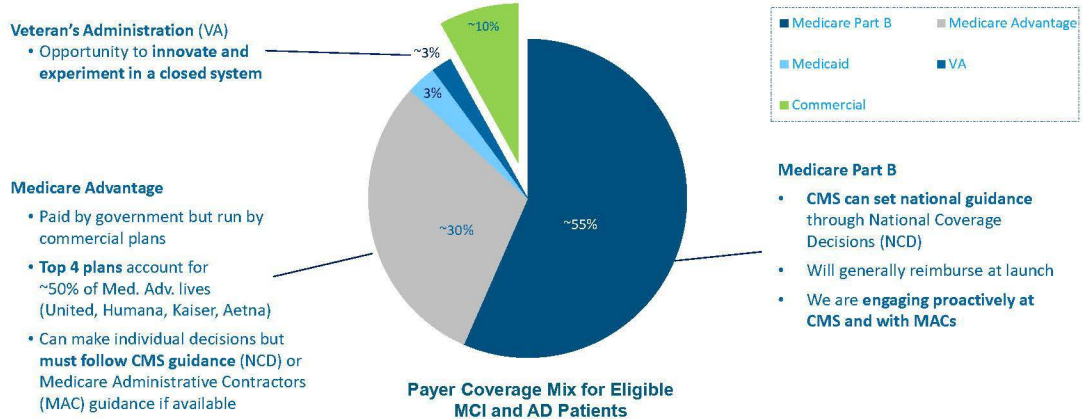




53% (Per Protocol): 3.3 million fewer, 159K peak in 2037, 5% lower average Medicaid spend, 760 billion cumulative savings in Medicaid spend by 2050 or \$14 bn annually by 2030



## Medicare and other government payers cover ~90% of our patients



**Medicare Part B:** Medical insurance component of Medicare, charging for medical care by service item. Beneficiaries pay monthly premiums and 155% annual deductible and 20% co-insurance based on Medicare approved service cost. 80% of FFS beneficiaries have supplemental insurance to cover the 20% co-insurance costs.

**Medicaid:** State and Federal program providing health insurance for low-income individuals.

**Medicare Advantage:** A type of Medicare health plan offered by a private insurance company that contracts with Medicare to provide both hospital and medical benefits. Beneficiaries have annual out-of-pocket maximums that vary by selected plan.

**Veterans Administration (VA):** Health care benefit provider for individuals who were active in service; services allocated on a priority basis.

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## OneBiogen Team is engaging actively with key stakeholders to solidify value proposition & pricing



### Key Engagement Focus Areas Across Stakeholders

- Value proposition feedback and endorsement
- Economic modeling approach support and validation
- Payer stakeholder environment shaping
- Pricing environment preparation
- Optimizing HTA and payer evidence strategy
- CMS coverage for drug and diagnostics
- ICER Preparation
- Advisory Committee Assistance
- Education on ADLs
- Education on the Importance of Early Diagnosis



## Patient Advocacy Group Value Engagement: Educating about cost & value in AD, ensuring understanding of Biogen's position

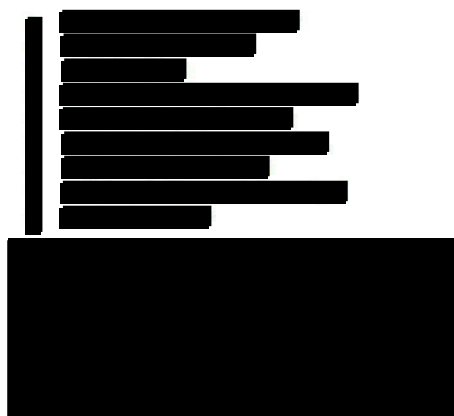
### Goals

- Create awareness for broad understanding of cost & value in AD
- Support PAG understanding of aducanumab data, patient journey, reimbursement process and potential access challenges
- Support a strong patient voice
- Share Biogen's position, as appropriate

### Biogen Strategy

- Engage over time and regularly with PAGs on topics related to value – leverage key PAG platforms (Global steering committee, Readiness Briefings, 1:1 w select PAGs)
- Provide opportunities for PAGs to share views on value to foster holistic perspective (webinars, speaker opportunities)
- Share Biogen's position and provide data briefings, as appropriate
- Inform PAGs about public policy landscape and advocacy opportunities

### Outreach to Key Groups

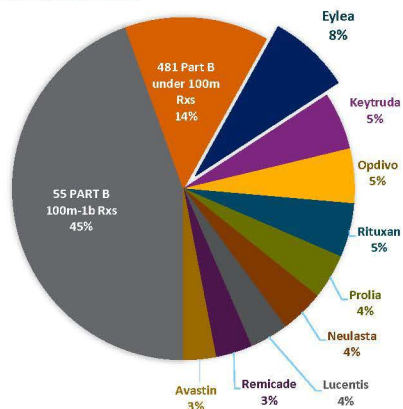


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# As of 2018, Eylea was the largest single contributor to Medicare Part B budget, with ~\$2.6B spent (8% of total)

## MEDICARE PART B BUDGET: 2018 ACTUAL SPEND

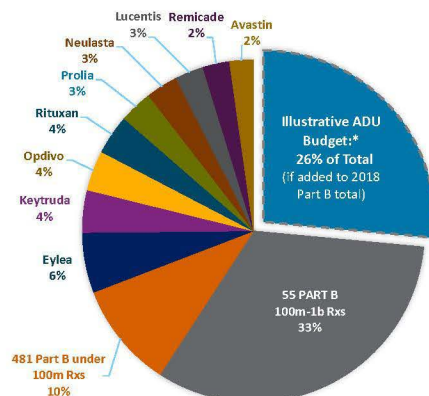
	ANNUAL COST (2018)
Eylea	\$2.6B
Keytruda	\$1.8B
Opdivo	\$1.7B
Rituxan	\$1.7B
Prolia	\$1.4B
Neulasta	\$1.4B
Lucentis	\$1.2B
Remicade	\$1.1B
Avastin	\$1.0B
Total for 55 PART B products with 100M-1B Scripts	\$14.8B
Total for 481 Part B products with under 100M Scripts	\$4.5B
2018 Total (Actual)	~\$33.3B



# 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)
<b>Aducanumab*</b> (Illustrative)	<b>\$12.0B*</b>
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)

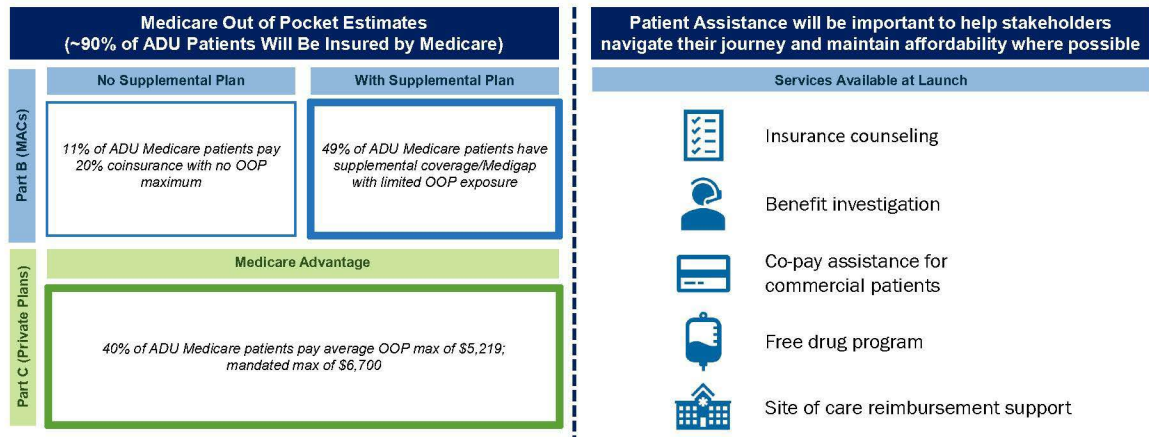
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## Pricing decision-making will account for several considerations in addition to core Value Story



## Most patients will have limited out-of-pocket exposure for aducanumab and ancillary services. Assistance programs will be in place at launch.



## Core Launch Price Framing Approach

### Three Core Messages

*Preliminary Illustrative Language*

We are pricing aducanumab at **\$Xk per year** (WAC) based on its value as determined by the following...

- 1. Value to patients, caregivers and society at large:** First treatment to meaningfully change the course of Alzheimer's disease, delay disease progression, and help maintain patient's independence longer
- 2. After decades of failed research we have the first disease-modifying treatment in AD: Aducanumab** will catalyze further investments and innovation leading to more competition in Alzheimer's
- 3. The appropriate patient population for aducanumab:** Aducanumab is a targeted treatment requiring specialist visits, accurate diagnosis, A-Beta positivity, monthly infusions, and monitoring.





## Potential Alzheimer's Strategic Pricing Considerations

★ Focus of Today's Discussion	Strategic Consideration
Long-Term Sustainability	★ <b>Price Certainty:</b> <i>No price increases for a period of X years</i> ★ <b>Social Contract:</b> <i>We respect the social contract that allows free pricing of innovation followed by swift entry of biosimilars</i>
Budget Impact Misperceptions	★ <b>Budget Protection:</b> <i>Caps on patient volume to address concerns regarding population size</i>
Launch Price Receptivity	★ <b>Durability:</b> <i>Discounts tied to duration on therapy (e.g., discount after X years)</i>
Patient Affordability	<b>Early Experience Program:</b> <i>Free drug for a period of X months following FDA approval</i> <b>Traditional Patient Support Programs:</b> <i>Co-Pay Assistance* &amp; Free Drug Programs</i>

### Other Programs Under Discussion

- ✓ **Sponsored Diagnostics:** *Sponsored CSF testing while reimbursement is under evaluation*
- ✓ **Selective Outcomes-Based Contracting:** *Ready and willing to partner with payers*



Examples for exploration. Subject to management, legal and regulatory review  
 \*for commercially insured patients

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## Framing Price based on Durability: **Recommendation to not use as Core Narrative in US** (Evaluating selective use and ex-US)

*Illustrative language\**

- What we do know: if used at the target dose, **aducanumab clears amyloid plaque after ~3-5 years** and provides meaningful clinical, economic, and humanistic benefits; **we have no evidence that aducanumab is a lifelong treatment**
- We established price based on the **assumption that patients would have an opportunity to discontinue aducanumab treatment after ~5 years**; we will continue to study this in the real world
- Should the data show that patients require treatment beyond ~5 years, Biogen stands ready to engage in creative payment/reimbursement/financing or rebating options to **ensure that aducanumab remains cost-effective**
- This price reflects the **tremendous value aducanumab brings to Alzheimer's patients, their caregivers, and society at large**

*For example:*

- A patient who **takes ADU for X years will pay \$X for treatment**, yet that patient **may avoid Y years in a nursing home, which alone is worth \$Y in avoided costs**
- This is **just one example** of the massive economic and humanistic benefits that the patient, their caregiver, and society at large will continue to realize



\*Language to be refined with R&D / Clinical Development

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## Potential Alzheimer's Strategic Pricing Considerations

★ Focus of Today's Discussion	Strategic Consideration
Long-Term Sustainability	★ <b>Price Certainty:</b> <i>No price increases for a period of X years</i> ★ <b>Social Contract:</b> <i>We respect the social contract that allows free pricing of innovation followed by swift entry of biosimilars</i>
Budget Impact Misperceptions	★ <b>Budget Protection:</b> <i>Caps on patient volume to address concerns regarding population size</i>
Launch Price Receptivity	★ <b>Durability:</b> <i>Discounts tied to duration on therapy (e.g., discount after X years)</i>
Patient Affordability	<b>Early Experience Program:</b> <i>Free drug for a period of X months following FDA approval</i> <b>Traditional Patient Support Programs:</b> <i>Co-Pay Assistance* &amp; Free Drug Programs</i>

### Other Programs Under Discussion

- ✓ **Sponsored Diagnostics:** *Sponsored CSF testing while reimbursement is under evaluation*
- ✓ **Selective Outcomes-Based Contracting:** *Ready and willing to partner with payers*



Examples for exploration. Subject to management, legal and regulatory review  
 \*for commercially insured patients

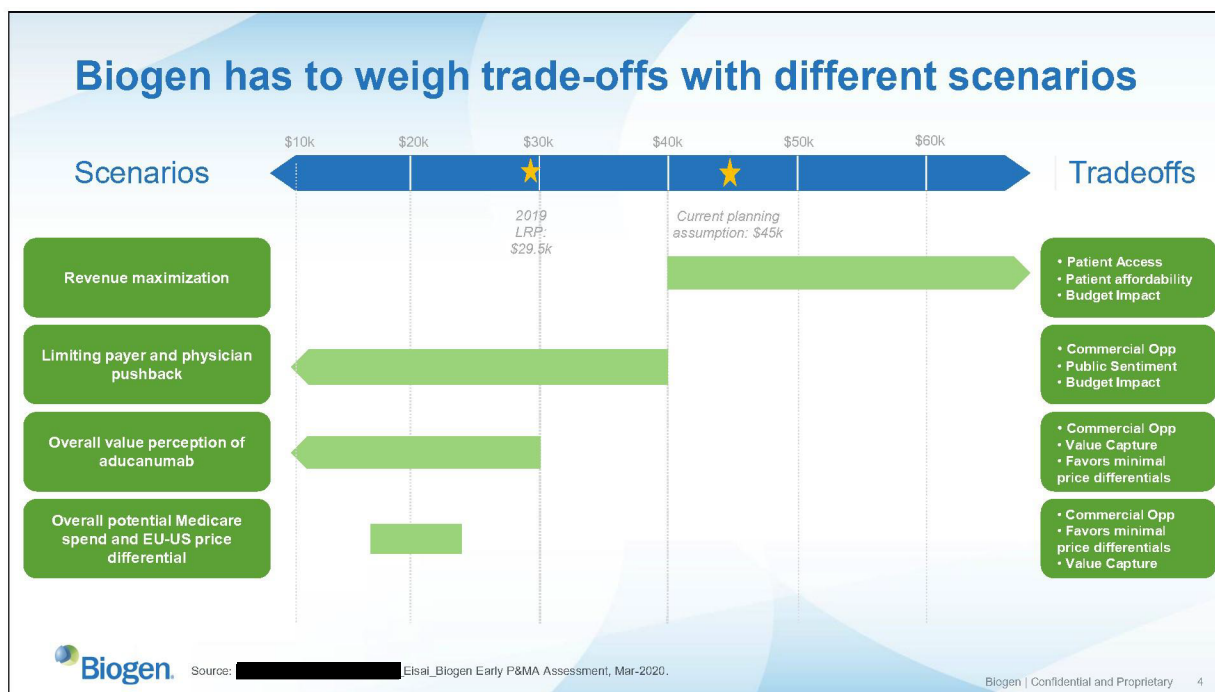
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# Aducanumab US Pricing and Market Access Strategy Development

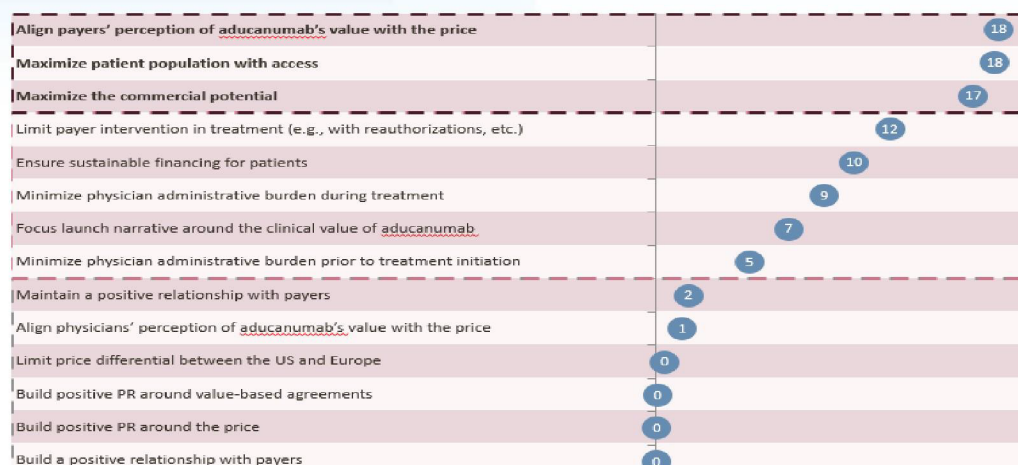
April 9, 2020



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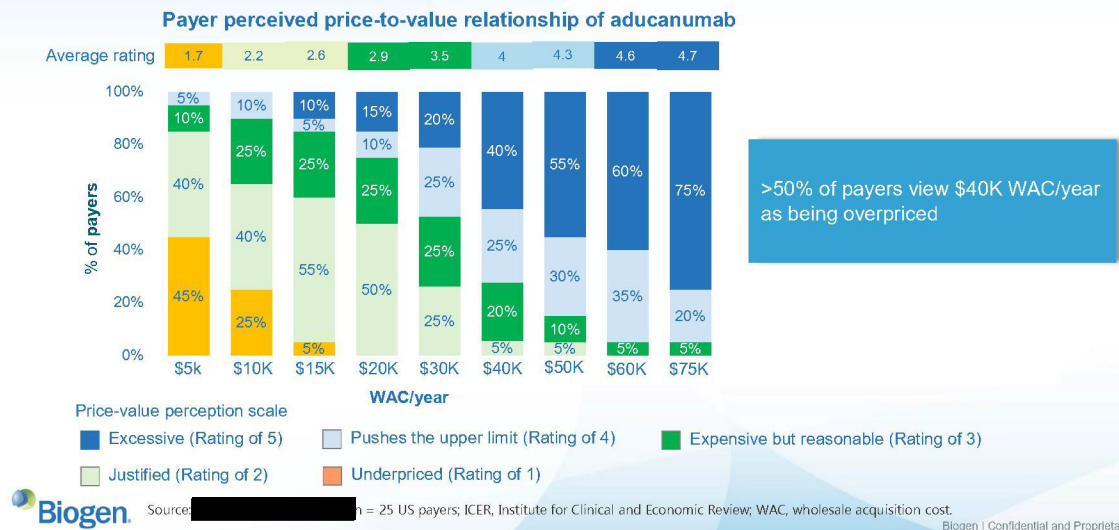
## For the US, the highest rated goals were to align value with price and maximize patient access



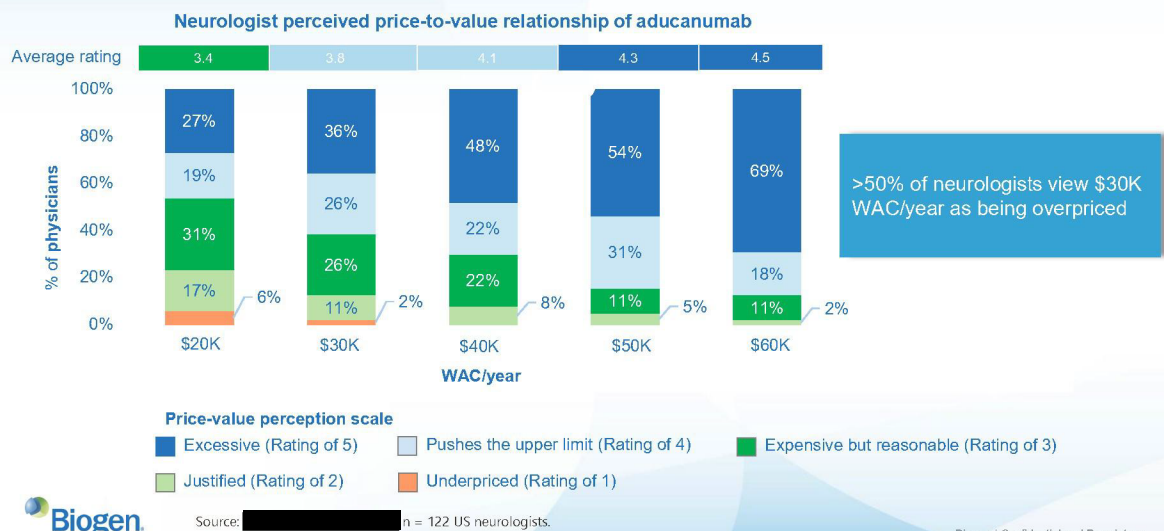
Biogen. Source: [REDACTED] Eisai\_Biogen Early P&MA Assessment, Mar-2020.

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## A \$30k-\$40k WAC/year range represents an upward bound of reflected value for payers



## Assuming awareness, \$20-30K WAC/year represents an upward bound of reflected value for neurologists





# Aducanumab U.S. Launch Update

EC Meeting

May 14, 2020



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# Robust launch plan to address key challenges and maximize potential

## While Aducanumab faces a series of highly complex challenges at launch...

- **Less than ~10k are amyloid confirmed** among ~3.3M clinically diagnosed patients at prioritized sites of care
- **A $\beta$  confirmation constrained** by facility capacity and workflows
- **HCPs/Systems unprepared** to screen/treat high volume of AD patients
- **Buy and bill economics less favorable** in Medicare
- **Questions remain on the value** of treatment
- **Total cost of treatment** with additional cost for diagnostic and monitoring

## ...We have a strong plan in place to address head-on with our strategic imperatives

-  **Enable ecosystem** to support more optimal care & DMT
-  **Drive urgency** to diagnose, confirm & treat
-  **Establish clinical benefit** of delaying disease progression
-  **Partner with community** to prioritize eligible patient population
-  **Build GTM model**, leveraging partners to creating seamless customer journey

Launching Aducanumab optimally right from the beginning is vital to maximizing its full potential over the long-run



# Planning for Possible Indications & Developing our Playbook

## SCENARIO #1: LABEL SPECIFIC TO PATIENTS WITH MCI

*FDA approves adu with indication for patients with MCI and early AD; continued need to educate on appropriate patient and highlight services and system support initiatives to mitigate potential backlash regarding access constraints*

- Deploy messages for appropriate audiences on what the indication means
- Define system challenges specific to patients with MCI
- Outline MCI patient pathway to care and pitch to media
- Create issues management plan to address access constraints and show support for caregivers of patients with advanced disease
- Share positive MCI patient stories
- Communicate patient services and system support initiatives

## SCENARIO #2: LABEL FOR ALL PATIENTS WITH AD

*FDA approves adu with broader indication for treatment of patients with AD; 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*

- Deploy messaging on TPP vs indication to frame appropriate patient
- Define system challenges for broad indication
- Outline and promote patient pathway to care for all AD patients
- Create issues management plan to address access constraints and unknowns of treating patient population not included in clinical program
- Communicate patient services and system support initiatives

## PLAYBOOK DEVELOPMENT


- Scenario plans with supporting media statements, Q&As, PAG communications and other materials to support response based on environment
  - Establish a cross-functional issues management team internally to facilitate a coordinated, informed response in the event of an issue
    - Team to include external experts, as appropriate
  - Prepare internal and external spokespeople to address issues on an as needed basis
    - Closely monitor AD social conversation to identify issues early
  - Channel energy from significant demand to highlight clinical meaningfulness
  - Prepare opportunities to expand and/or evolve community commitments





Presenter: [REDACTED]

**At launch,  
we will have a  
comprehensive  
health equity  
offering ...**




This is a complex issue and there is no silver bullet. The cross-functional team has taken a methodical and insight-driven approach

Focused on key areas of the patient journey we believe Biogen can make a difference around Detection, Diagnosis and Affordability

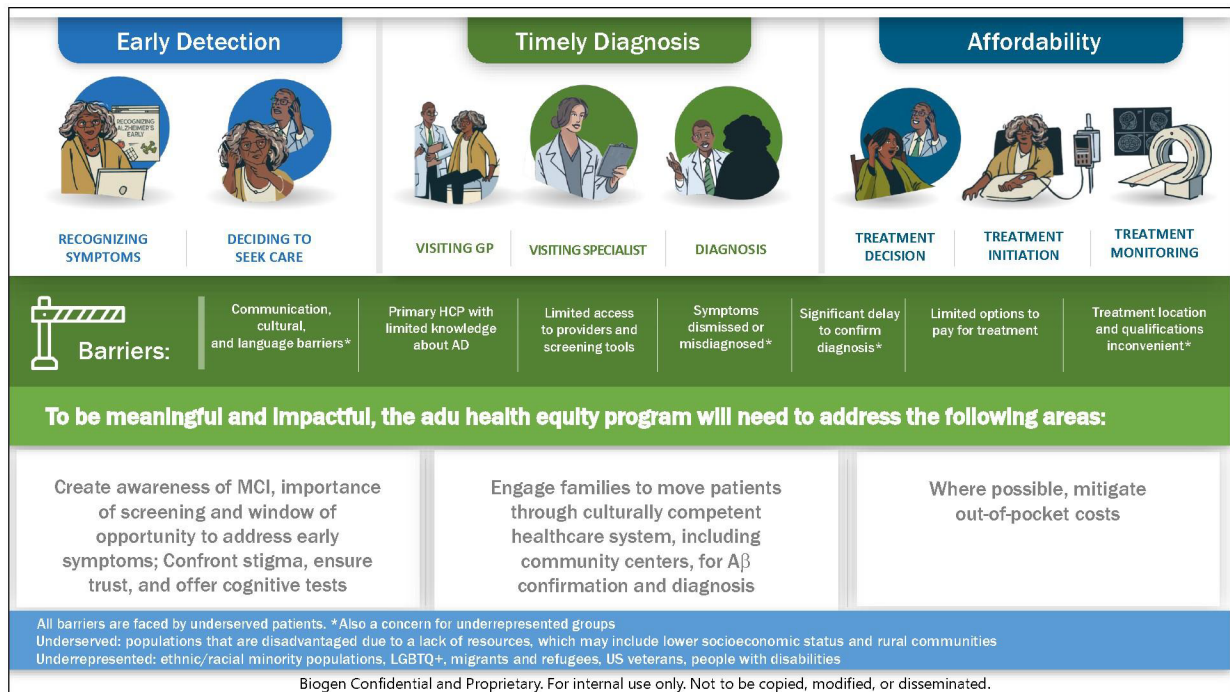
Our approach offers a constellation of solutions toward a comprehensive and deep commitment to health equity in AD

where **science** meets **humanity**

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Presenters: [REDACTED]



Presenter:





# Free Drug Program

Biogen will provide a free drug program as a payer of last resort for uninsured and underinsured patients that has been structured to account for the unique components of the drug and treatment landscape.



## Enroll patients that demonstrate financial need based on the program criteria

- Provide access to therapy for uninsured or underinsured patients
- Included new criteria to allow for better assessment of the patient's financial need
- Aligns with Patient Access Strategy across the Biogen portfolio

## Financial Eligibility Requirements



### Household Income

- Must be <\$75k to be eligible



### Household Liquid Assets

- Must be <\$25k to be eligible



### OOP Cost to Income Ratio

- Must be >10% to be eligible

\*>\$200 annual

## Clinical Criteria\*



- Patient has been diagnosed with mild cognitive impairment (MCI) due to AD or mild dementia due to AD
- Patient has completed beta-amyloid testing

## General Rationale



- True to Biogen's mission – Ensure the right patient has access to the right therapy at the right time
- Simple & Clear – Operationally feasible, Simple to explain to patients and caregivers, and in line with industry standards
- Agile – Start with more restrictive criteria first to allow for future evolution
- Financially Sustainable – Scalable to the size of Alzheimer's disease patient population


where  
**science** meets **humanity**

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 **Biogen**

Presenter: 

# Financial Assistance Programs




## Program Details


- Biogen to offer:
  - Treatment co-pay assistance program**
    - Qualified commercially insured patients will be eligible for adu co-pay assistance as low as \$0 with no income restrictions
  - Infusion co-pay assistance program**
    - Procedure co-pay assistance of \$150 per infusion totaling \$1,950 annual allowance
  - Free Drug Program**
    - Income under \$75K
    - Household liquid Assets under \$25K
    - Income / OOP ratio around 10%

## UP Reach

- Black Medicare beneficiaries are 50% more likely to have no supplemental coverage
- Black and Hispanic Medicare beneficiaries have significantly lower savings and household income




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Field email and print piece talking about health equity  
What is the cross-functional pull through




# Drug & Procedure Co-Pay Assistance




Biogen will provide a copay assistance program for commercially insured patients that has been structured to account for the unique components of the drug & treatment landscape. There are some similarities to [REDACTED] and [REDACTED] programs to provide consistency in our Patient Access Strategy.

Drug Copay Assistance	Procedure Copay Assistance
 <p><b>Copay as low as \$0 patient responsibility with no income restrictions:</b></p> <ul style="list-style-type: none"> <li>Provides an avenue of support for commercial patients prior to consideration for Free Drug enrollment</li> </ul>	 <p><b>\$150 per infusion with \$1,950 annual allowance</b></p> <p><b>No coverage for MRIs</b></p> <ul style="list-style-type: none"> <li>MRI costs are expected to be generally well covered and are not anticipated to create a barrier to treatment</li> <li>Discussion may continue as label is finalized and if there are new coverage insights post launch</li> </ul>
<p><b>Clinical Criteria*</b></p>  <ul style="list-style-type: none"> <li>Patient has been diagnosed with mild cognitive impairment (MCI) due to AD or mild dementia due to AD</li> <li>Patient has completed beta-amyloid testing</li> </ul>	
<p><b>General Rationale</b></p>  <ul style="list-style-type: none"> <li>Allows patients to leverage the benefits of their plan design</li> <li>Provides consistent support across the Biogen portfolio</li> <li>Helps distinguish patients with acute financial need</li> </ul>	



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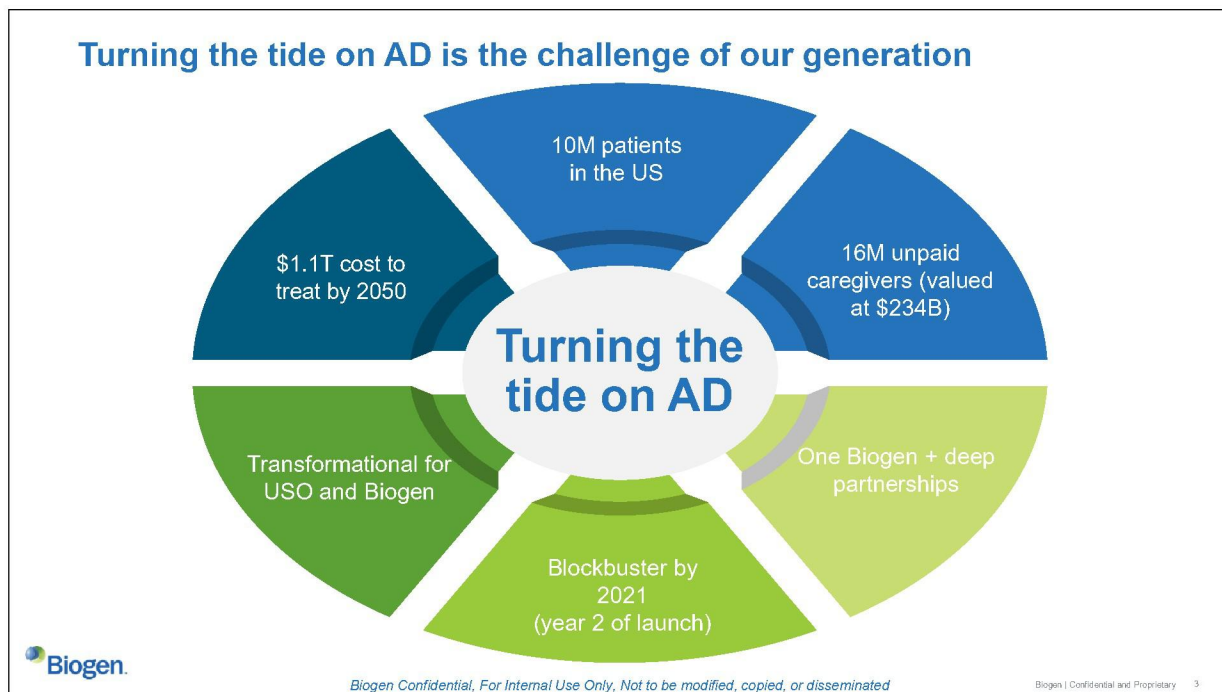


Field email and print piece talking about health equity  
What is the cross-functional pull through



## **Aducanumab US Launch Vision and Priorities**

**Board of Directors Meeting**  
Dec 4, 2019





## Aducanumab LRP and AD Portfolio Overview



Pre-read for OLC discussion on June 15, 2020

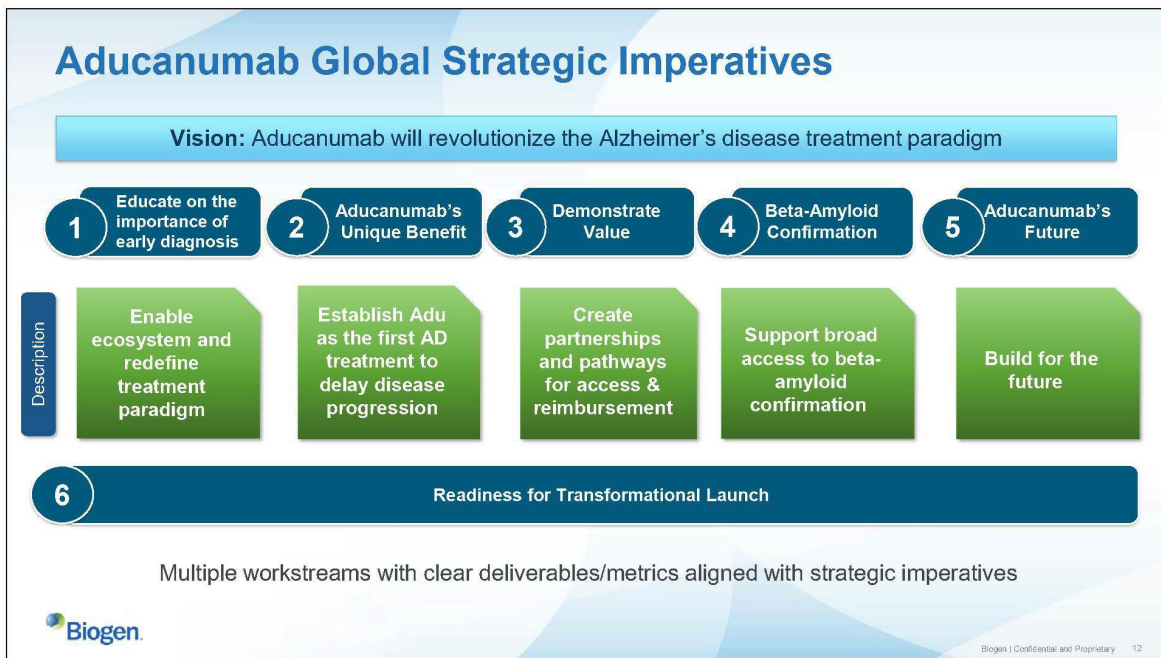
## Executive Summary

- Biogen will bring novel therapeutic solutions and redefine research, development, diagnosis, and care for people affected by Alzheimer's Disease (AD)
- Key R&D investments focus on building clinical and preclinical capabilities including improved diagnostics and biomarkers, innovative approach to clinical trials and greater understanding of disease pathology
- Launch of Aducanumab will establish DMTs as the standard of care, will revolutionize the AD treatment paradigm and set the stage for long term success of Biogen's AD portfolio (incl BAN2401, tau assets, future novel modalities)
- AD Franchise revenue potential projected at \$12.3 B in 2024 and \$53 B by 2035 with aducanumab peak sales of \$23 B\*
- To secure a transformational launch of Aducanumab and maximize its long term impact to patients and our business we need to invest in:
  - Education on early disease detection and diagnosis
  - Demonstration of aducanumab's unique benefit and value
  - Access to diagnostic solutions for amyloid beta confirmation
  - Best in class commercial capabilities including digital and flawlessly implementing GTM in collaboration with Eisai
  - Strong LCM program to anticipate competition and strengthen long term value proposition



\* Total collaboration revenue, Based on initial regional submissions. Will be reassessed 2H 2020; Not PTRS adjusted

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Pre-read & presentation

## White Paper on Positioning/Promoting Aducanumab for the Clinical Trial Population

### Current Assumptions:

- Aducanumab will receive a labeled indication far broader than the population in which it was studied: *for the treatment of Alzheimer's patients across the entire spectrum of the disease, from MCI to severe AD*
- Product labeling will not require confirmation of amyloid beta pathology, nor will it specify a recommended duration of therapy (which will be left to physician discretion)

### Rationale for the Positioning & Promotion of Aducanumab to be consistent with Clinical Trials:

- Ensures 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. Positioning or promoting aducanumab outside of this well-defined population would not be in the best interest of patients, as it would be exposing them to risk without any known benefit. Put another way, limiting the positioning and promotion of aducanumab to the clinical trial population **optimizes the risk-benefit calculation for patients**.
- **Increases the likelihood of positive outcomes**, which is not only in the best interest of patients, it's in the **best interest of Biogen**, in what will become a **more competitive AD market over time**. Real-world outcomes will play a big role in shaping physician, patient, and payer perception of the value of aducanumab. It's in Biogen's best interest for these outcomes to be as positive as possible in advance of the expected launch of Roche's DMT for AD in 2023. Put another way, promoting aducanumab for patients in which the value of the drug is unknown risks diminishing its product profile in advance of a competitive launch.
- Because of its mechanism of action, **a patient must have confirmed amyloid beta pathology for aducanumab to work**. It's therefore in the best interest of all involved (patients, providers, payers, and Biogen) to **confirm amyloid beta via PET Scan or CSF prior to initiating therapy with aducanumab**. As such, Biogen must partner with government agencies, diagnostic companies, and neurology treatment centers to facilitate access and reimbursement for diagnostics used to confirm amyloid beta pathology. Confirming amyloid beta pathology prior to initiating therapy with aducanumab increases the likelihood that the patient will benefit from therapy, which is in the best interest of all involved, including Biogen.
- Positioning & promoting aducanumab for only those patients with a **clinical diagnosis of either MCI or mild AD** is also in the best interest of all involved (patients, providers, payers, and Biogen). It helps ensure that aducanumab will be used only in patients where there is a known clinical benefit, while increasing the likelihood of positive outcomes. Conversely, positioning or

promoting aducanumab for patients with moderate-to-severe AD introduces risk to the patient without known clinical benefit, and **risks diminishing its product profile in advance of a competitive launch.**

- Aducanumab should only be prescribed by **specialists and treatment centers** who are **prepared/equipped to manage the first disease-modifying therapy for AD** (capacity and resources to confirm diagnosis before initiating therapy, ability to administer the infusion, access to multi-disciplinary teams for patient management and ongoing monitoring requirements (e.g., radiologists to monitor for ARIA-E, etc.)). Positioning and promoting aducanumab in a non-prioritized way would increase the likelihood that **patients get treated at sites not ready to manage a DMT, which could compromise patient outcomes.**
  - That said, Biogen will need to **encourage and facilitate the early identification and referral** of appropriate patients in **non-specialist settings** (where physicians are not financially incentivized to do work-ups and referrals) to ensure that **patients are started on therapy while they still have early-stage AD**, where they're **most likely to derive a clinical benefit.**
- Biogen will reinforce this desired positioning by working with **CMS** to educate them on the clinical profile of aducanumab and the importance of prioritizing patients where there is known clinical benefit, with the **goal of obtaining a coverage determination consistent with the clinical trial population.**
- Biogen will also reinforce this desired positioning by working with **Treatment Guideline committee members** to educate them on the clinical profile of aducanumab and the importance of prioritizing patients where there is known clinical benefit and the greatest likelihood of responding to therapy. The goal would be for the Treatment Guidelines to be **updated and issued around the time of product approval**, with guidance on patient prioritization. This would provide a **critical and credible tool to help payers and providers prioritize those patients most likely to benefit from aducanumab therapy.** In its absence, payers will have far less leverage to enforce proper patient selection.
- Biogen should **welcome reasonable payer efforts to prioritize patient access** to those where there is a known clinical benefit and the likelihood of a positive response. Signaling acceptance of this up-front would go a long way toward building trust with payers that Biogen is committed to positioning and promoting the product for the clinical trial population. It will also **shape the lens with which they view the price of aducanumab.**
- Positioning and promoting aducanumab for patients with **moderate-to-severe AD** would likely be giving **false hope** to patients **desperate** for anything that might slow the progression of the disease



**Rationale for NOT promoting aducanumab in a manner consistent with a broad label:**

- The potential to **overwhelm the healthcare system** with **patient volume**, and **impede or delay access** to those **patients who could truly benefit from aducanumab**
- The potential for **sub-optimal outcomes** in **patients with moderate-to-severe AD**, exposing them to risk without any known clinical benefit
- Risk of **diminishing** the perception of the **clinical benefit and value of aducanumab** in **advance of competitive launches**
- **Provider, patient, and caregiver frustration/anger over payer-imposed restrictions to access** resulting from the lack of prioritization (e.g., onerous prior authorizations, periodic recertifications required to stay on therapy, etc.)
- The potential for **reputational damage to aducanumab and Biogen** as result of **sub-optimal patient outcomes** and **restrictions to access and reimbursement** (for drug and diagnostics) driven by a lack of patient prioritization
- The likelihood that stakeholders will **attribute access restrictions and delays** to the **price of the product**, as opposed to the magnitude of patient volume, and **place pressure on Biogen to act**
- The potential for **criticism from clinicians and advocates** for providing **false hope** to **patients with moderate-to-severe AD**
- The **inefficient use of scarce resources and healthcare dollars**

# Aducanumab US Pricing: Strategic Considerations

## Presentation to the Board of Directors

November 13, 2020



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## Teams continue to engage actively with key stakeholders to solidify value story & pricing



### Key Engagement Focus Areas Across Stakeholders

- Value Story feedback and endorsement
- Economic modeling approach support and validation
- Payer stakeholder environment shaping
- Pricing environment preparation
- Optimizing HTA and payer evidence strategy
- CMS coverage for drug and diagnostics
- ICER Preparation
- Advisory Committee Assistance
- Education on ADLs
- Education on the Importance of Early Diagnosis



## Core Launch Price Framing Approach

### Three Additional Messages

#### *Preliminary Illustrative Language*

Based on our understanding of the science so far, **we are assuming Aducanumab is not a lifelong treatment for all patients**; it clears plaque in ~3 years resulting in improvements in cognition, function, and behavior. We will continue to learn as we evaluate it in the real world. Based on this we are launching Aducanumab with an annual list price of \$55k\*/year, which is less than half the annual cost of many monoclonal antibodies launched in oncology, and accurately reflects the value of aducanumab, the first disease-modifying treatment in AD.

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:

Based on this we are launching aducanumab and announcing its price with the following commitments:

1. **Price increases:** No price increase for the first 4 years
2. **Budget impact:** Aducanumab is a targeted treatment requiring Amyloid Beta positivity. Our intention is to promote it focusing on the patient population in our clinical study program. Should there be a significant increase in patient volume beyond this targeted patient population, or should it appear that most patients require treatment beyond 5 years, we commit to revisiting the price in good faith in order to ensure system sustainability
3. **International Price comparisons:** We intend to launch Aducanumab at a similar price in the US vs. other countries with similar GDP per capita.



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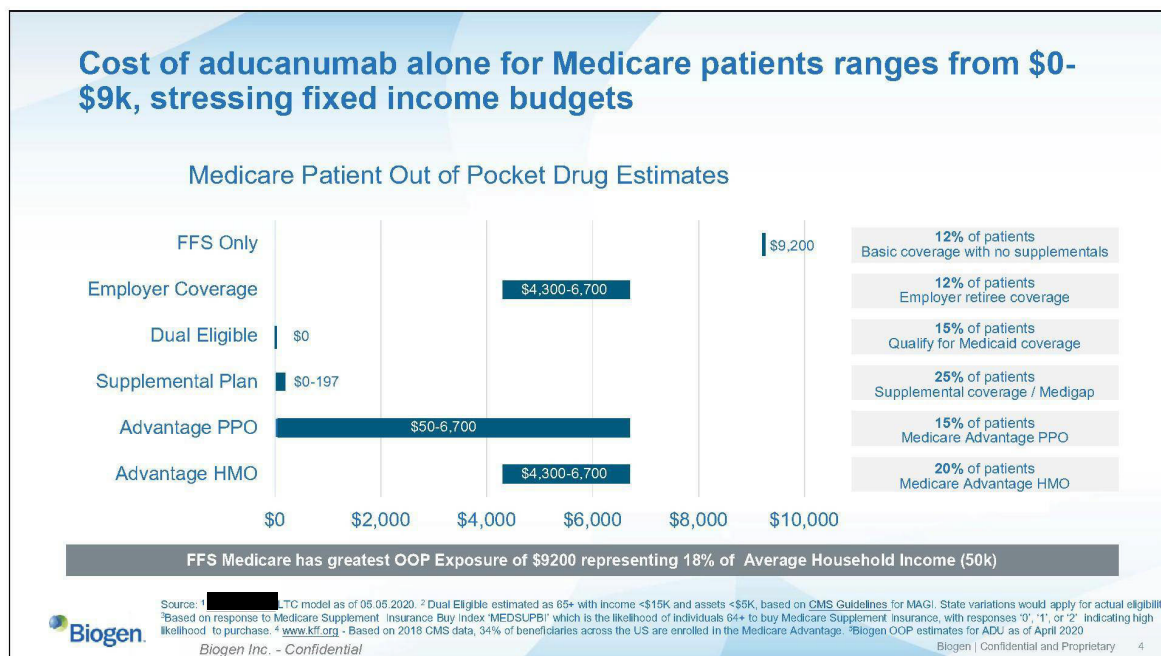
Biogen stands ready to work with policy makers and payers (public and private) to ensure appropriate patients receive diagnosis, treatment and care in a way that minimizes patient out-of-pocket and in accordance with existing legislation.



## Aducanumab Patient Affordability



May 2020

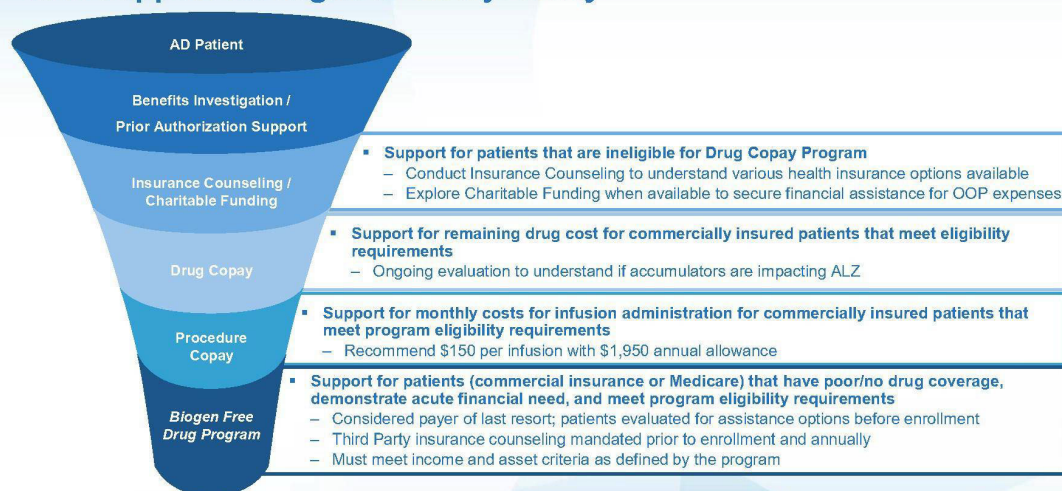


When you look at average household income, potential OOP can be up to 20% of income



When you look at average household income, potential OOP can be up to 20% of income

## Biogen's patient access strategy will provide appropriate patients with support throughout their journey



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# Aducanumab Pricing and Pricing Communications Considerations

*CONFIDENTIAL DRAFT*

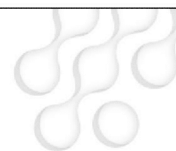
September 2020



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## Disclaimers



- Any prices discussed in this deck are illustrative and for discussion purposes only
- Material is highly confidential and for internal use only
- Do Not Forward or Share Beyond Original Recipients

**This material is confidential for internal discussions only**



## A range of potential launch prices remain under evaluation

Annualized US WAC (Illustrative Annual List Price per Patient\*)



We will continue to evaluate a range of potential US launch prices; final **US price determination will occur at US launch**

\*Price listing will be **tied to vial SKUs**; actual **realized annual price will vary by patient** based on dose received (variable due to titration schedule, weight-based dosing, and treatment stoppage due to ARIA or other factors)



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## Pricing considerations

Utilization	Limited impact on utilization management relative to price leads to a largely <b>flat volume curve unless public scrutiny reduces volume*</b>
Budget Impact Perception and Reality	<div> <div>@\$20K: <b>\$28B</b></div> <div>@\$40K: <b>\$56B</b></div> <div>@\$60K: <b>\$84B</b></div> </div> Illustrative <u>theoretical</u> maximum budget impact if 1.4M patients treated in US
Payer and Other Stakeholder Pushback	Pushback likely at all prices; though payer research suggests <b>increasing scrutiny above ~\$30-\$40K*</b>
Cost-Effectiveness Modeling	Leveraging cost-effectiveness model / traditional value frameworks is <b>most feasible at prices &lt;\$30K</b> ; higher prices require defense of scenarios involving stopping rules, etc.
Ex-US Access vs. Price Differential Trade-Off	Maintaining narrow US/Ex-US price differential risks delaying Ex-US access and may result in decisions not to launch in select markets; <b>degree of risk increases as US price increases</b>
Patient Affordability	Patient out of pocket expense throughout their AD journey is <b>highly dependent on insurance coverage and patient weight</b>
Competition	Anticipating actions for what <b>competitive options</b> may be available




# Aducanumab


## Patient Affordability and Policy Options

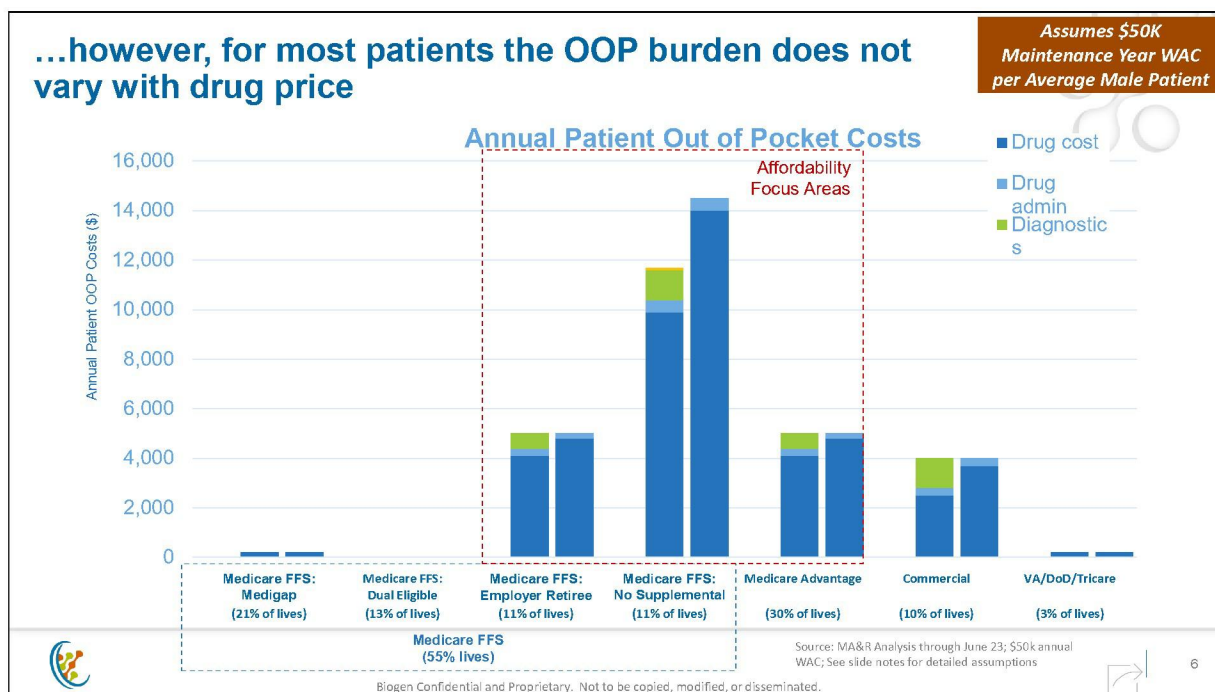
US MA&R      PPGA

April 2021



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Range of OOP in reality behind each of these bars – more art than science given this population is not well characterized. Best estimate is that most acute need is for patients with FFS only, but some Advantage (HMO range is \$4,300-\$6,700, PPO range is \$50-\$6,700) and Employer Retiree coverage (\$4,300-\$6,700), so we're focused on the outliers in Employer Retiree Coverage, Medicare Advantage, and FFS only

Team Assumptions as of June 17, 2020:

#### Medicare FFS Assumptions:

- \$50K annual WAC (annual assumed to mean a single maintenance year)

Medicare FFS reimbursement for drug = WAC + 3% for first 2Qs and ASP + 6% in 3Q and after (with ASP approximated to = WAC for illustration here, assuming limited contracting)

Patient contribution (coinsurance) = 20% of payment rate, with no supplemental insurance

Patient weight = 75kg, which is ~clinical trial mean male weight in US/EU

First 12 months includes 6 titration doses (2 x 1mg/kg, 2 x 3mg/kg, 2 x 6mg/kg) + 7 maintenance doses (10mg/kg)

Maintenance year includes 13 maintenance doses (all 10 mg/kg)

Assumes vial utilization (i.e. number of each of 170mg vials and 300mg vials) is optimized per dose administration in order to minimize wastage for a 75kg patient

Site of care is hospital outpatient department (HOPD) (Note – there will be slightly different cost-sharing amounts in physician office setting/freestanding infusion center settings)

Assumes 2 HCP visits for the initial cognitive assessment. Assumes 2 PCP visits and 1 specialist visit (3 total pre-Dx).

#### Med Advantage Assumptions:

- \$50K annual WAC (annual assumed to mean a single maintenance year)

Payment rate on drug assumed to be ASP + 12% (ASP is approximated to = WAC for illustration here, assuming limited contracting)

Patient contribution (coinsurance) = 30% of payment rate

Non-drug payment rates are based off of Medicare FFS (based on policy research - <https://www.cbo.gov/system/files/115th-congress-2017-2018/presentation/52819-presentation.pdf>)

Patient weight = 75kg, which is ~clinical trial mean male weight in US/EU

First 12 months includes 6 titration doses (2 x 1mg/kg, 2 x 3mg/kg, 2 x 6mg/kg) + 7 maintenance doses (10mg/kg)

Maintenance year includes 13 maintenance doses (all 10 mg/kg)

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Assumes 2 HCP visits for the initial cognitive assessment. Assumes 2 PCP visits and 1 specialist visit (3 total pre-Dx).



When you look at average household income, potential OOP can be up to 20% of income



## Recent "Hail Mary" Proposal was Tailored to Address Medicare FFS Population without Supplemental

### Biogen Approach



#### Policy Proposal

Allow Biogen to provide cost-sharing assistance to Medicare FFS patients without supplemental (gap) insurance who cannot afford their drug-related cost-sharing requirements, with appropriate guardrails

**And**

Emphasize Social Responsibility Model: Manage budget impact with commitment to no price increases for period of time.



- There is a strong public health need and desire to address
- Favorable OIG advisory opinions allow foundations to independently cover the patient portion.



- Three past request to CMS/CMMI have been denied: not "yet" (Can't quantify savings, only one product, timing).
- Recent CMS outreach 3/3 and 4/7
- Would require OIG (Anti-kickback) opinion, regulatory relief
- New CMS Administrator not confirmed until May 15th



#### Policy Pathway

##### Regulatory Pathway

- CMMI Pathway
- CMS Regulatory Relief: Anti-Kickback, Best Price ,
- Potential Timing
- Probability of Success

##### Legislative Pathway

- Potential Vehicle
- Potential Timing
- Political Reality
- Probability of Success



*\*\* Will need to involve legal internal (Biogen) and external counsel*

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## Aducanumab PDC Team Meeting

### Wednesday, July 29, 2020 – meeting minutes

Topic	Topic Owner	Objective	Purpose	Reference Materials
Opening Check-in	████	<ul style="list-style-type: none"> <li>Update from the weekly EC meeting - see email summary from █████</li> </ul>	<input checked="" type="checkbox"/> Inform <input checked="" type="checkbox"/> Align <input type="checkbox"/> Decision	See email from July 28
Indication statement label scenario discussion	Team	<ul style="list-style-type: none"> <li>Review input received from various stakeholder workshops, ad boards, etc.</li> <li>Team discussion on the questions and next steps</li> </ul> <b>Additional attendees:</b> █████ █████	<input checked="" type="checkbox"/> Inform <input checked="" type="checkbox"/> Align <input type="checkbox"/> Decision	Label Scenario Feedback and Discussion Questions

#### Topic 1 – Opening Check-in (████)

##### Summary:

- Two topics discussed at this week's EC weekly meeting – see email summary from █████ on July 28
- Team reviewed scenarios for the indication statement for the EU filing
- EC supports the recommendation of filing with the broad label consistent with the Core Data Sheet (CDS) and global position – important to be consistent globally and then prepare for mitigation plans on what happens if we get the broad indication statement and there are or are not payer restrictions as well as scenarios if we do not get the broad indication statement
- Compassionate Use (CU) / Early Access Program (EAP) update:
  - Biogen has not had a chance to discuss with regulators the possibility of implementing an EAP
  - At this time, Biogen team is preparing for a few scenarios at risk in case any of them need to be executed: (1) no EAP or patient access program, (2) single patient compassionate use, or (3) EAP program
  - Biogen team will continue to monitor the number of requests for this type of program – following the Day 60 / BLA acceptance, and depending on demand, Biogen will engage the FDA with a discussion to get their guidance on how best to approach
  - Preparing for the scenarios will allow Biogen to be ready to on the various options as needed, based on guidance from the FDA
  - Internal meeting planned for Friday to brainstorm some of the details around the scenarios; topic to be scheduled for discussion at the EAP Governance Committee
  - PDC will need to be involved in communications and supply planning

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- And the team is continuing assessments for EAP programs outside the U.S., with initial focus on the ECP region
- **Post-meeting note** – update planned for the PDC team meeting on August 5 on this topic

**PDC Actions:**

- 

**PRIVILEGED**

PDC Decisions: none

Communication Cascade: none

**Topic 2 – Indication Statement Label Scenario Discussion (Team)**

Summary:

Highlights from the functional workshops / ad boards / etc.:

- See **Label Scenario Feedback and Discussion Questions** presentation for further details
- Update from U.S. Medical Ad Board on Label Scenarios – [REDACTED]
  - 6 U.S. KME's evaluated two scenarios: (1) broad label (indication statement for the treatment of AD without amyloid-beta confirmation) and (2) narrow label aligned to EMERGE and ENGAGE with patients with MCI due to AD / Mild AD and amyloid-beta confirmation required
  - Important to note that these advisors are either familiar with E/E or other Ph III trials
  - Group 1 "broad label group" – general feedback:
    - Did not find much upside to this scenario; felt that this created a burden for the healthcare centers
    - General surprise that this scenario was being considered
    - Feels that the appropriate population to treat are patients that are aligned with the trial patient population
    - Still consider the amyloid-beta confirmation to be informative even if not required; but if it is an out-of-pocket expense for the patient, may not ask the patient to take on that burden
    - Trying to understand what this means for preclinical patients
    - Curious to know who was driving this scenario and why it was being considered
    - Felt that there was an opportunity for KME's / investigators to help with education – opportunity identified to develop a KME paper on the appropriate patient to treat in order to help guide other HCPs
    - Highlighted that there is minimal investment occurring at sites now to prepare for a product to be on the market – appears that HCPs are waiting for approval

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- before investing in changes to their sites to accommodate patients; need to ensure that Biogen is communicating appropriately about healthcare system capacity and readiness
    - Ideally, need to get internal alignment and endorsement to communicate to a small set of KME's that this could be an actual scenario
  - Group 2 "narrow label group" – general feedback:
    - This group also wondered why Biogen was assessing a broad label
    - Insights shared were consistent with feedback provided previously
    - Need to ensure that the community understands what patients would be appropriate based on MCI due to AD / Mild AD and what the terminology means
    - Discussed the possibility of a third party assisting with pre-screening (between a PCP and memory clinic) and that it would offer a lot of value, but would like more details on how that would work
    - Generally, feel like they are comfortable with this scenario and the concern is more that the general population understands who is appropriate for aducanumab
- Update from the Global Advocacy Steering Committee Meetings – [REDACTED]:
  - 6 U.S. advocacy groups and 3 ex-U.S. advocacy groups who Biogen has been engaging with since 2018
  - Surprised at the mention of a broad label scenario – many of these groups have heard that we want to move to the left and treat people earlier so surprised that the label could be to a broader group
  - Shared pros / cons with the broad label scenario:
    - Benefit – easier to communicate and educate about; potentially more inclusive and offers the possibility to help underserved populations
    - Challenges – capacity, stigma associated with AD diagnosis may reduce urgency, feedback from patients who don't see benefit
  - Important to communicate to the community that this is not a cure – ensure that people understand that even if they are progressing, they may still be benefiting
  - Saw an opportunity to focus on patients who have the right pathology with an amyloid-beta confirmation
  - Generally, focused on education and lack of awareness in the PCP community; need to educate PCP's and ensure that a broad label does not reduce the sense of urgency to treat early; felt that they could help with overall community education
  - PDC Team discussed that while PAG's 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
- Payer Advisors Discussions – [REDACTED]
  - The broader the label the higher the probability for payers to minimize access (e.g., not cover the diagnostic tests because they are not in the label and/or create other hurdles to minimize utilization)
  - Important to consider what happens if "all comers" are put on aducanumab initially

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- Value story perspective discussing scenarios and models and will rely on real-world evidence to help validate; if all comers get all the drug, real-world evidence will be diluted and may not show the impact from the scenarios modeled
  - Discontinuation rates could increase for patients who don't see benefits
- Feedback from U.S. MA&R – [REDACTED]:
  - Commercial payers may seek to limit to a patient population that they believe is valid and can leverage the label in its a totality (not just the indication statement; clinical study data will be included in section 5 of the label)
  - CMS – typically cover to label or indication; however, recent examples where they have limited access and typically do not provide coverage in the device or diagnostic space
  - In a scenario where we launch with a broad indication, likely to be a strong request from various parties for CMS to provide clearer guidance; that is typically a 12-18 month process to get to a national coverage determination (likely narrower than what the indication statement would lead us to)
  - Have seen in other disease areas that if there can be reluctance to purchase a product if a healthcare facility does not know if they will be reimbursed
  - If Biogen does not provide something to anchor the payers to, they will establish their own anchors
  - Anticipate getting additional feedback at the U.S. Payer Ad Board on August 10
- Vis Aid research – [REDACTED]:
  - A lot of education required and that has not changed
- EU label scenario discussion – [REDACTED]:
  - Important consideration is when other products (e.g., gantenerumab, BAN2401) are approved and the likelihood that they would have a broad indication statement
  - If a company starts with a narrow indication statement it becomes challenging to expand later if you don't have data
  - Team is preparing for a few different scenarios:
    - Potential broad label scenario, even though the probability of that scenario is low based on discussions to date with the EMA
      - Risk / mitigation plans being evaluated and developed for this scenario if payers limit and/or do not limit access upfront
    - Potential narrow label scenario and how much Biogen wants to try to negotiate with the EMA on this point
  - In any scenario, thorough real-world evidence data generation plan is important
  - PDC team will discuss at an upcoming meeting scenario planning for conditional approval and requirement of a study – different potential study designs depending on broad vs. narrow indication statement
- General team discussion:
  - At this point there is NO plan to push back on broad label indication internally or with the regulators; EU submission also planned with broad indication statement

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- PDC Team and the U.S. are NOT departing from what was agreed to with the EC previously in May – broad indication statement scenario is base case and our go-to-market strategy will still target getting patients on therapy that are consistent with the clinical trial population (MCI due to AD / mild AD dementia)
- U.S. and global teams are not changing from the agreed upon strategy and will continue to execute activities / tactics already aligned to that strategy; however, there is a need to ensure that we are appropriately prepared at launch to communicate on the broad indication (anticipate surprise, explain context and focus on MCI due to AD/mild AD)
- Necessary to have a discussion with the EC to reconfirm and ensure alignment with the base case and strategy for targeting the MCI due to AD / mild AD dementia patients
  - Critical to validate with the EC and document that we are all aligned and still targeting the early stages of AD and patients with early AD are best served by aducanumab
- From a payer perspective, Biogen needs to provide some guidance of who should be covered – if Biogen does not provide guidance, they will make their own determination for who is best to be covered
  - Critical that there is rationale for this recommendation and that we have a plan for how we will get more data to expand the patient population they are covering in the future
  - Important that this message gets reinforced / echoed in all communication channels and via corporate communications
- Once we validate, we need to ensure that we are using consistent nomenclature regarding the target patient population
- Discussed the possibility that the indication statement scenarios could be discussed as part of the Ad Comm and KMEs express in the Ad Comm the same views regarding the broad label as we heard in the recent advisory board
  - Important to be prepared for this possibility and various scenarios and feedback expected – small group will be connecting with [REDACTED] in late August to understand how the core deck and story is evolving to ensure everyone is aligned to the messages
- Goal is to ensure that we are ready for a patient population that is appropriate for aducanumab and the community understands what a broad indication statement means practically
- Specific action items identified during the meeting:
  - Following the Payer Advisory Board, need to align on when we will approach the payers with guidance
    - Confidential discussions occurring with payers regarding the broad indication statement scenario
    - Need to expand to a larger payer group to ensure that they understand the broad indication statement scenario
    - US M&AR requested specific confirmation of alignment on strategy to focus payer reimbursement on MCI due to AD / mild AD dementia

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- Get alignment and endorsement to bring some KME's (maybe iTF members) and some PAGs unblinded to this scenario – goal would be to engage them in possibilities, recommendations and ideas for how to prepare and ensure understanding with a broad indication statement following approval
- Establish corporate messaging aligned to this strategy and ensure that we are ready to communicate the broad indication statement scenario on Day 1 post approval
  - Prior to that, Biogen should take every opportunity to educate on the appropriate patients to treat and who should be prioritized when communications regarding aducanumab
  - Need to be clear on what a broad indication statement means, how it 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
- As the team continues to roll out the launch strategy globally, there will be the opportunity to continue to reinforce the strategy regarding the appropriate patient to treat. US and global team to continue to highlight to EC risks of broad indication at the launch / immediate post launch period.

#### PDC Actions:

- 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, 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.
  - Details of communication plan / implementation to be managed by the communications team.
- Team members to identify additional action items needed (besides those outlined above) to help ensure readiness for the broad indication statement scenario. Communicate any action items to [REDACTED] by Friday, August 7 with plan to present to EC.
- PRIVILEGED
- [REDACTED] will coordinate with [REDACTED] to get an update at a PDC meeting after August 10 from the Payer Advisory Board so the team can continue the discussion about any specific actions needed for the U.S. and the broad indication statement scenario.

PDC Decisions: none

Communication Cascade: none

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**Topic 3 (ad hoc) – AOB [REDACTED]**

**Summary:**

- May not be an EC weekly meeting on August 3 as many folks are out of the office
- Team members should continue to raise topics to [REDACTED] that they feel are appropriate for that forum

**PDC Actions: none**

**PDC Decisions: none**

**Communication Cascade: none**

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# Label Scenario Considerations

**Confidential: Aducanumab PDC Feedback**

March 4, 2020



## Context & Assumptions

- Draft CDS indication statement “MCI due to AD and Mild AD Dementia”
- Aducanumab Phase III trials had A $\beta$  amyloid enrichment (confirmation via beta amyloid PET scan) - this data will be included in clinical trials section (section 5) of the label
- In addition to section 5, draft CDS (Dec 2018) includes:
  - Section 2.2 (Dosage & Method of Administration) A $\beta$  language: “Prior to initiating treatment, the presence of amyloid beta pathology should be confirmed”
  - This is driven by team assessment versus regulatory guidance
  - Earliest potential feedback from regulatory about indication statement and label discussions, inclusive of A $\beta$  language would be at Pre-BLA meeting late April 2020 (if deemed appropriate)
- Principles of what would typically drive our position to recommend a diagnostic component in the label, this is based on:
  - Efficacy is dependent on appropriate diagnosis
  - Safety profile of the product to include a diagnostic to ensure only the right patients receive treatment



# Label Scenario Analysis

- Preliminary discussions with the FDA have signaled that there is a high chance the Agency will suggest a “broad label” indication, such as “treatment of AD”
- PDC team also preparing for the possibility that A $\beta$  confirmation may only be required in section 5 of the label (lower POS)
- Based on those assumptions, PDC team analyzed the following scenarios outlined on subsequent slides:
  1. Scenario 1: “MCI due to AD and Mild AD Dementia” in the label and A $\beta$  confirmation in sections 2.2 and 5
    - a) Note: This scenario is the current assumption in global draft CDS and base case TPP
  2. Scenario 2: “MCI due to AD and Mild AD Dementia” in the label and A $\beta$  information in section 5 only
  3. Scenario 3: Broad label and A $\beta$  confirmation in sections 2.2 and 5
  4. Scenario 4: Broad label and A $\beta$  information in section 5 only



## Executive Summary & Recommendation

Scenario 1: "MCI due to AD and Mild AD Dementia" in the label and A $\beta$  confirmation in sections 2.2 and 5



Most aligned to the current thinking of the Global Labeling Team, TPP and go-to-market (GTM) strategy and preparation in the U.S.

Scenario 2: "MCI due to AD and Mild AD Dementia" in the label and A $\beta$  information in section 5 only



Not having an A $\beta$  confirmation recommendation in the label creates risk for supply and current GTM strategy and assumptions as well as potential confusion for HCPs and patients

Scenario 3: Broad label and A $\beta$  confirmation in sections 2.2 and 5



While initial response might be excitement across the AD community, a broad label will add infrastructural pressure and create risk to current GTM strategy and assumptions as well as potential confusion for HCPs and patients

Scenario 4: Broad label and A $\beta$  information in section 5 only



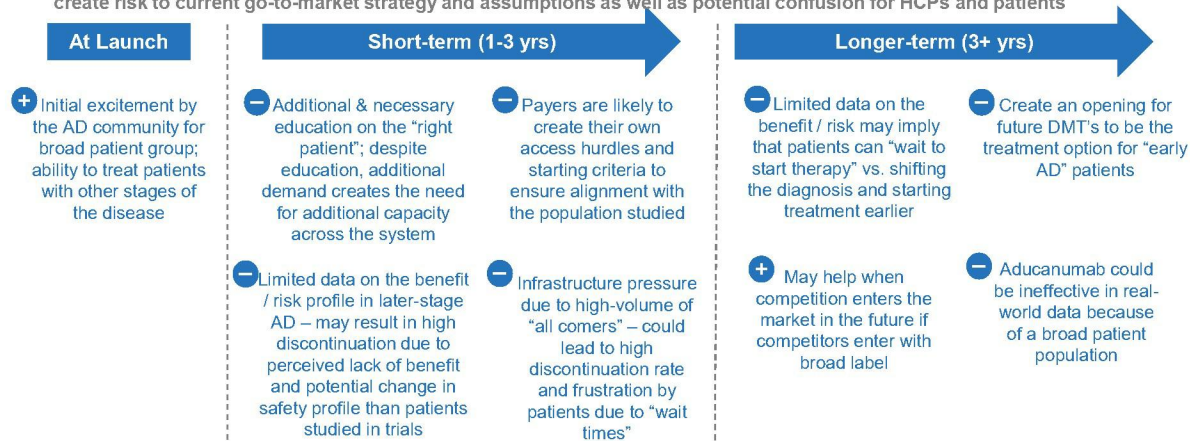
While initial response might be excitement across the AD community, this scenario will add infrastructural pressure and create risk to current GTM strategy and assumptions as well as potential confusion for HCPs and patients

Independent of the indication in the label, PDC believes that Biogen should continue to focus on identifying the appropriate patients for aducanumab. Given the high chance that the Agency will suggest a broad label, Biogen needs to be prepared for those scenario by investing more in educational initiatives to ensure that prescribers can identify the appropriate patients and preparing for potentially higher demand in the near-term.



## Scenario 3: Broad Label w/ A $\beta$ Confirmation Recommendation\* - PRIVILEGED & CONFIDENTIAL

While initial response might be excitement across the AD community, a broad label will add infrastructural pressure and create risk to current go-to-market strategy and assumptions as well as potential confusion for HCPs and patients



"Negative experience" with the efficacy of aducanumab and unknown safety profile in broad AD patient population could impact long-term uptake and: **PRIVILEGED**



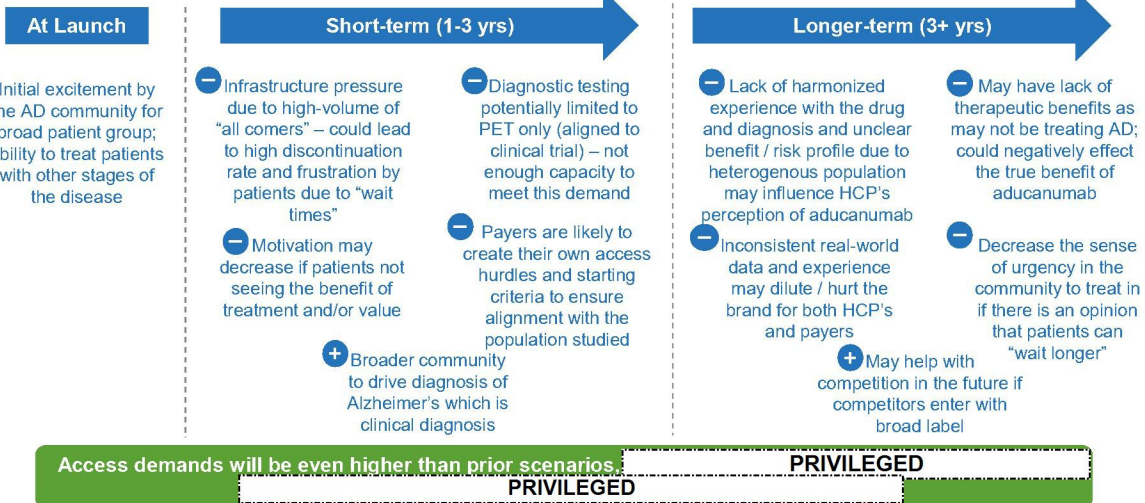
Biogen

\*Amyloid-beta confirmation in section 2.2 of CDS (Dosage and Method of Administration) and section 5 (Clinical Trials)

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## Scenario 4: Broad Label w/out A $\beta$ Confirmation Recommendation\* - PRIVILEGED & CONFIDENTIAL


While initial response might be excitement across the AD community, this scenario will add infrastructural pressure and create risk to current go-to-market strategy and assumptions as well as potential confusion for HCPs and patients



\*Amyloid-beta confirmation in section 5 (Clinical Trials) only

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## &lt;Medical&gt;

	Broad Alzheimer's Disease Label		MCI / mild dementia due to AD	
	Short-term**	Long-term***	Short-term**	Long-term***
With amyloid-beta confirmation in section 2.2* of CDS (Dosage and Method of Administration) and section 5 (Clinical Trials)	<ul style="list-style-type: none"> <li>HCPs might first focus on BM-diagnosis for more severe patients (already identified)</li> <li>BM-based diagnosis will impose dramatic changes in the management of later stages of disease and challenge HCPs' beliefs</li> <li>Limited data to assess what adu B/R profile is in later stages</li> <li>HCPs "first experience" with adu on the population that might benefit the least</li> <li>No strong driver for HCPs to move the diagnosis to the left</li> <li>Infrastructure challenges</li> <li>Disconnect between clinical behaviors and payer restriction leading to frustrations</li> <li>Unclear MoD/MoA narrative</li> </ul>	<ul style="list-style-type: none"> <li>(-) High discontinuation rate based on potential smaller benefits in changing the course of the disease in more advanced patients</li> <li>(-) Potential consequences on safety profile if drug used in a broader, clinically more impaired population</li> <li>(-) Delay in initiating earlier stage patient</li> <li>Potential "niche approach" for new entry such as gantenerumab (ix of choice for earlier stages)</li> </ul>	<ul style="list-style-type: none"> <li>Need efforts to explain appropriate population</li> <li>Efforts needed to establish BM-based diagnosis</li> <li>Limited data to assess B/R in later stages of disease</li> <li>Potential stopping criteria for continuers</li> </ul>	<ul style="list-style-type: none"> <li>(-) RW experience based on controlled population (certainty of underlying pathophysiology and level of impact)</li> <li>(-) Growing body of evidence in continuers might not enable label expansion</li> </ul>
With amyloid beta confirmation in section 5 (Clinical Trials) of CDS only, not in section 2.2* of CDS 	<ul style="list-style-type: none"> <li>High volume of all comers treated with AD resulting into infrastructural pressure</li> <li>Challenges to explain the need of BM-based confirmation if not part of the mandatory test</li> <li>Delay in inclusion of BM-confirmation in clinical guidelines (risk for BM-confirmation to be seen as part of tx cost instead of disease-cost)</li> <li>High rate of tx discontinuation due to inappropriate patients treated with aducanumab</li> <li>Lack of HCP focus on earlier symptoms, key area remaining the more advanced patients</li> <li>Unclear MoD/MoA narrative</li> </ul>	<ul style="list-style-type: none"> <li>(-) Lack of harmonized experience with drug and diagnosis</li> <li>(-) Unclear B/R profile due to heterogeneous treated population</li> <li>(-) Non concrete driver to have broad access to BMs</li> <li>(-) Differences in HCPs focus on early vs late diagnosis, potentially based on tiering of centers leading to unequal access to diagnosis and treatment</li> <li>(-) all comers experience with Adu might influence HCPs perception of B/R</li> <li>(-) lack of consistent RW data and experience on aducanumab also due to the all comers treated population</li> </ul>	<ul style="list-style-type: none"> <li>Challenges to explain appropriate population in case of non BM-based diagnosis</li> <li>No driver to establish broad access to Biomarkers, HCPs' reluctance to include BM in diagnosis</li> <li>Delay in inclusion of BM-confirmation in clinical guidelines (risk for BM-confirmation to be seen as part of tx cost instead of disease-cost)</li> <li>High rate of tx discontinuation due to inappropriate patients treated with aducanumab</li> <li>Unclear MoD/MoA narrative</li> </ul>	<ul style="list-style-type: none"> <li>(-) Lack of harmonized experience with drug and diagnosis</li> <li>(-) Unclear B/R profile due to heterogeneous treated population</li> <li>(-) Non concrete driver to have broad access to BMs</li> <li>(-) Differences in HCPs focus on early vs late diagnosis, potentially based on tiering of centers leading to unequal access to diagnosis and treatment</li> <li>(-) all comers experience with Adu might influence HCPs perception of B/R</li> <li>(-) lack of consistent RW data and experience on aducanumab also due to the all comers treated population</li> </ul>

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## **Broad Label Indication “for treatment of AD”; versus “for treatment of MCI due to AD & Mild AD”**

### Upside

- Broad label, would mean patients at other stages of disease could be treated. Most likely later stage of disease (e.g. including moderate and severe).

### Downside

- Broad label usage, may have less therapeutic benefits in population that has not been studied

### Key Questions

- A $\beta$  confirmation may still be required
- Do we lose some early MCI due to AD?
- Do we gain more from later?

