BIOARCTIC AB (PUBL)
NASDAQ STOCKHOLM: BIOA B

Company presentation

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BIOARCTIC

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Today's agenda

1. **BioArctic – a CNS disease frontrunner**
2. Lecanemab – towards a breakthrough in Alzheimer's disease
3. Rich clinical and pre-clinical pipeline
4. Concluding remarks
5. Appendix
    I. Additional clinical data
    II. IP
    III. Financial position

BioArctic – a unique Swedish biopharma company improving the lives of patients with central nervous system disorders

High unmet need for disease-modifying treatments for Alzheimer's and Parkinson's diseases creates **large commercial opportunity**

World-class research and development driven organization with basis in founder's breakthrough discoveries and fruitful collaborations with leading **academic researchers** and **pharma companies** generating and developing **innovative projects**

Attractive and well-balanced project pipeline with projects from discovery through Phase 3 and combination of both proprietary projects with substantial marketing and out-licensing potential and partnered projects generating income

Industry leading partners and **valuable collaboration agreements** totaling BSEK 8.9[1] (BUSD ~1) plus royalties

Note: 1) FX as per September 30, 2021

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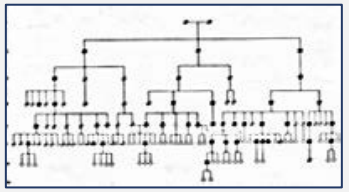
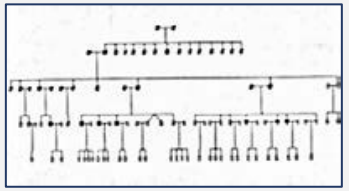
Long and successful track-record in R&D within central nervous system (CNS) disorders

Background to founding

- Scientific discoveries by Professor Lars Lannfelt laid the foundation for BioArctic
- **The Swedish mutation** demonstrated for the first time in a clinical setting that amyloid-beta (Aβ) peptide initiates the disease



- **The Arctic mutation** revealed that soluble aggregated forms of Aβ, oligomers and protofibrils, are toxic and likely driving the disease



Company history

2003 BioArctic founded

2004 – 2006
- mAb158 isolated
- New transgenic mouse model for AD developed
- Several AD patents filed
- BioArctic and Eisai entered research collaboration in AD

2007 – 2009
- BioArctic and Eisai entered partnership BAN2401
- SC0806 program initiated at BA
- PD program initiated

2010 – 2012
- BAN2401 entered clinical development for AD
- PD Alpha-synuclein mAb patent filed
- SC0806 orphan drug designation in EU & US

2013 –2015
- BAN2401 entered Phase 2b
- BAN2401 back-up candidate out-licensed
- Extended research collaboration with Eisai
- BAN0805 in pre-clinical development for PD
- SC0806 entered clinical development

2016 – 2018
- BAN2401 Ph2b Eisai
- BioArctic and AbbVie entered research collaboration in PD
- AbbVie exercised full license
- BAN0805 in prep for US IND
- SC0806 in Phase 1/2
- Listed on Nasdaq Stockholm Mid Cap with a market cap of BSEK 2.1

2019 – Today
- Lecanemab = BAN2401 Eisai Ph 3 Clarity AD, AHEAD 3-45
- Expanded research collaboration Eisai
- ABBV-0805 = BAN0805 AbbVie Phase 1 preparing for Phase 2 in PD
- SC0806 closed
- BBB technology and project portfolio expanded
- Current market cap: BSEK 11.2[1)]

	Total funding to date
Partnerships & research collaborations	66 MEUR
	130 MUSD
Soft money funding	>6.5 MEUR
	>15 MSEK

Successful collaborations with pharmaceutical industry validating high quality research and commercialization opportunity for BioArctic

Source: 1) FactSet (As of 12 November 2021)

Rich and well-balanced pipeline with fully-financed partnered projects and cutting-edge proprietary projects

	Project	Partner	Discovery	Pre-clinical	Phase 1	Phase 2	Phase 3
ALZHEIMER'S DISEASE	Lecanemab (BAN2401) *(Clarity AD)*	Eisai[1)]	Early Alzheimer's disease[3)]				
	Lecanemab (BAN2401) *(AHEAD 3-45)*	Eisai[1)]	Pre-clinical (asymptomatic) Alzheimer's disease[4)]				
	BAN2401 back-up	Eisai					
	AD1801						
	AD1502						
	AD1503						
	AD-BT2802						
	AD-BT2803						
	AD2603						
PARKINSON'S DISEASE	ABBV-0805[2)]	AbbVie					
	PD1601	AbbVie					
	PD1602	AbbVie					
OTHER CNS DISORDERS	Lecanemab (BAN2401)		Down's syndrome[5)] Traumatic brain injury[5)]				
	ND3014		ALS				
BLOOD-BRAIN BARRIER	Brain Transporter (BT) technology platform						
DIAGNOSTICS	Imaging and biochemical biomarkers – Alzheimer's disease						
	Imaging and biochemical biomarkers – Parkinson's disease	AbbVie					

1) Partnered with Eisai for lecanemab (BAN2401) for treatment of Alzheimer's disease. Eisai entered partnership with Biogen regarding lecanemab (BAN2401) in 2014
2) AbbVie in-licensed BAN0805 in late 2018 and develops the antibody with the designation ABBV-0805
3) Mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease
4) Normal cognitive function with intermediate or elevated levels of amyloid in the brain
5) Dementia and cognitive impairment associated with Down´s syndrome and with traumatic brain injury

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Long-standing and successful partnerships – de-risking clinical development and optimizing commercialization

	Alzheimer's disease	Parkinson's disease
Partner track record	Eisai Discovered and developed world's best-selling medicine for symptoms in Alzheimer's Industry-leading pipeline in dementia area Aricept donepezil HCl tablet Used to treat confusion (dementia) related to Alzheimer's disease	abbvie World's all-time best-selling medicine (BUSD 20) Duopa carbidopa/levodopa Approved product for symptoms associated with Parkinson's disease HUMIRA adalimumab 10 different indications in immunology
Collaboration and license	**MEUR 222** *Total value agreements* **MEUR 66** RECEIVED **Royalties High single digit %** **BioArctic retains rights to lecanemab in other indications and option to market in the Nordics**	**MUSD 755** *Total value agreements* **MUSD 130** RECEIVED **Royalties Tiered %** **AbbVie has global rights to alpha-synuclein portfolio for all indications**

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Recent highlights

Alzheimer's disease – Lecanemab

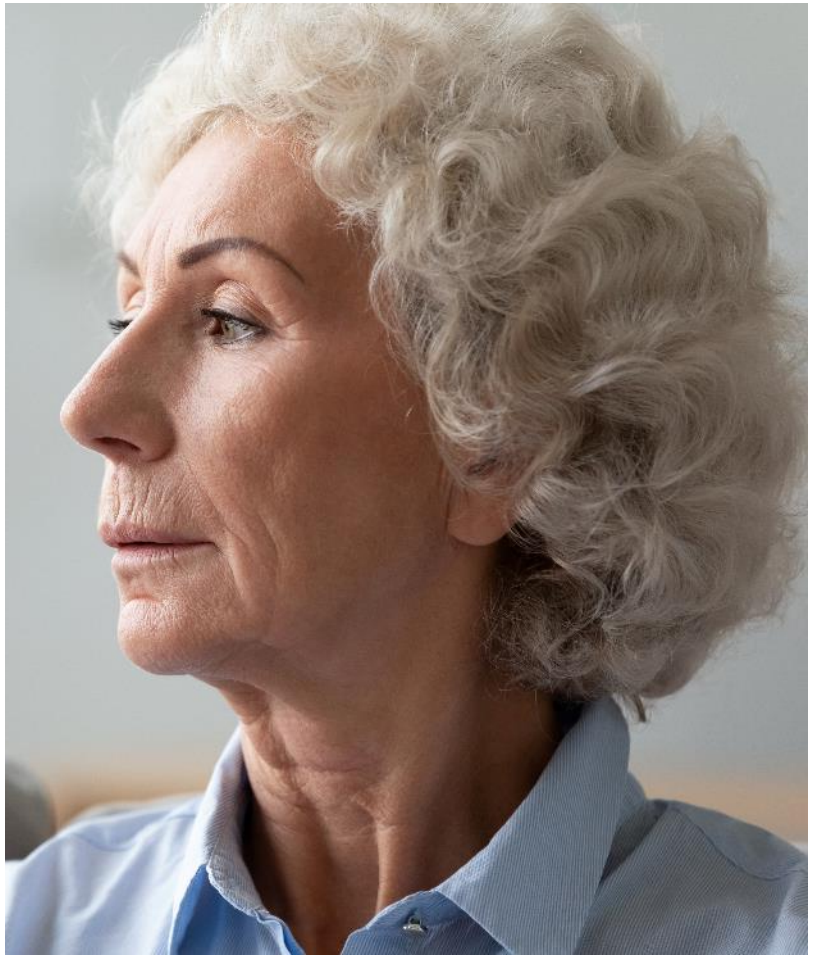
- Eisai has after agreement with FDA initiated a rolling BLA submission under the accelerated approval pathway which is expected to be completed during H1 2022
- Data presented at CTAD congress in November continue to further strengthen and differentiate lecanemab towards competitors
- Lecanemab selected for DIAN-TU clinical trial for dominantly inherited Alzheimer's disease

Parkinson's disease – ABBV-0805

- Encouraging pre-clinical data presented at the MDS congress in September and published in Neurobiology of Disease in November
- Phase 1 results presented by AbbVie at the MDS congress in September support Phase 2 development with dosing once a month

Other

- Build-up of commercial organization initiated
- Expanding into new indications and treatment target (TDP-43)



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Today's agenda

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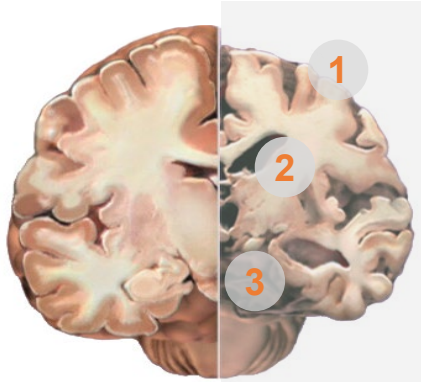
Alzheimer’s disease – high unmet medical need

Alzheimer’s Disease

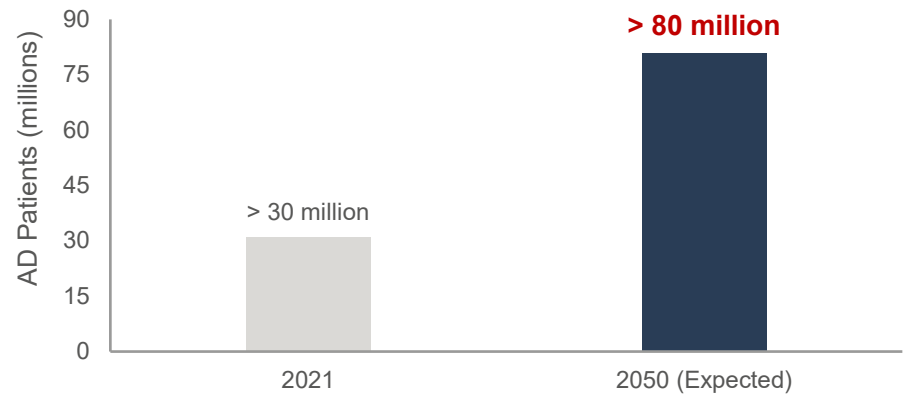
- Alzheimer’s disease (AD) is a devastating condition where neurons (nerve cells) in the brain die from exposure to toxic aggregates of a protein called amyloid beta (Aβ)
- The disease can commence up to 15 to 20 years before the patient shows clinical symptoms. The brain can shrink by almost 30 percent during the disease progression before the patient eventually dies
- AD leads to a progressive decline in memory and cognitive abilities, such as thinking, language, and learning capacity

Alzheimer’s progressively degenerates critical brain regions resulting in functional compromise

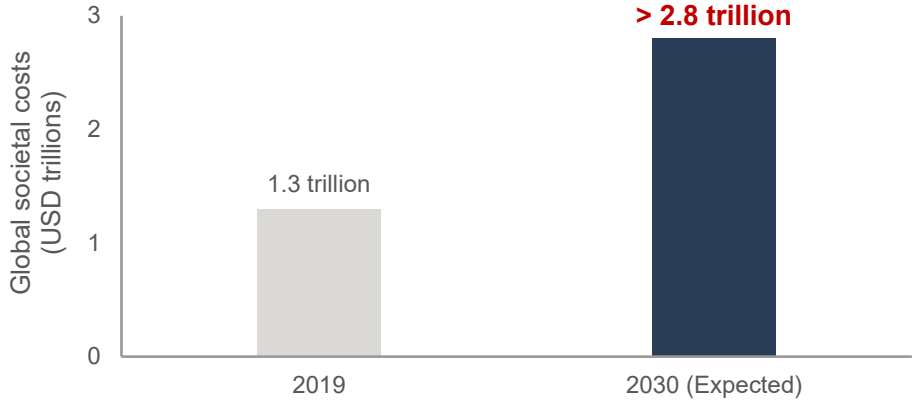


1. Cerebral cortex shrinks
   - Involved in memory, planning, thinking, language and more
2. Ventricles enlarged
   - Liquid-filled cavities. Indicate loss of surrounding regions
3. Hippocampus shrinks
   - Responsible for memory formation

High unmet medical need



High cost to society



Source: WHO

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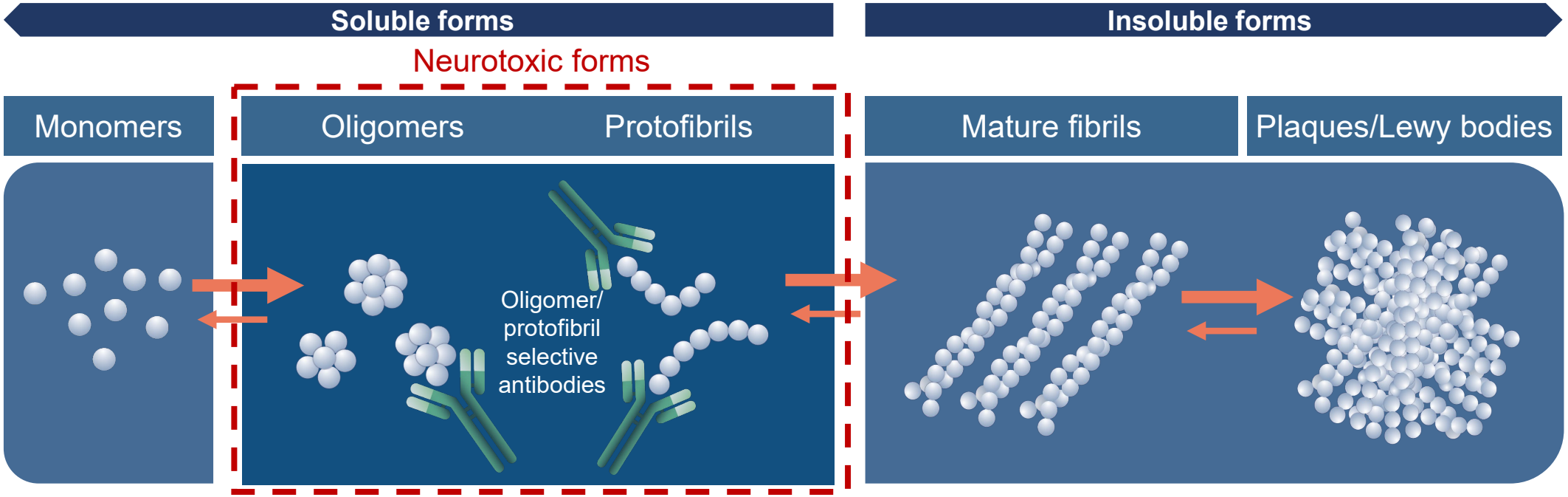
Neurotoxic forms of aggregated misfolded proteins – a promising target for disease modifying treatments in CNS disorders



Alzheimer's disease: misfolded amyloid beta results in amyloid plaques

Parkinson's disease: misfolded alpha-synuclein results in Lewy Bodies

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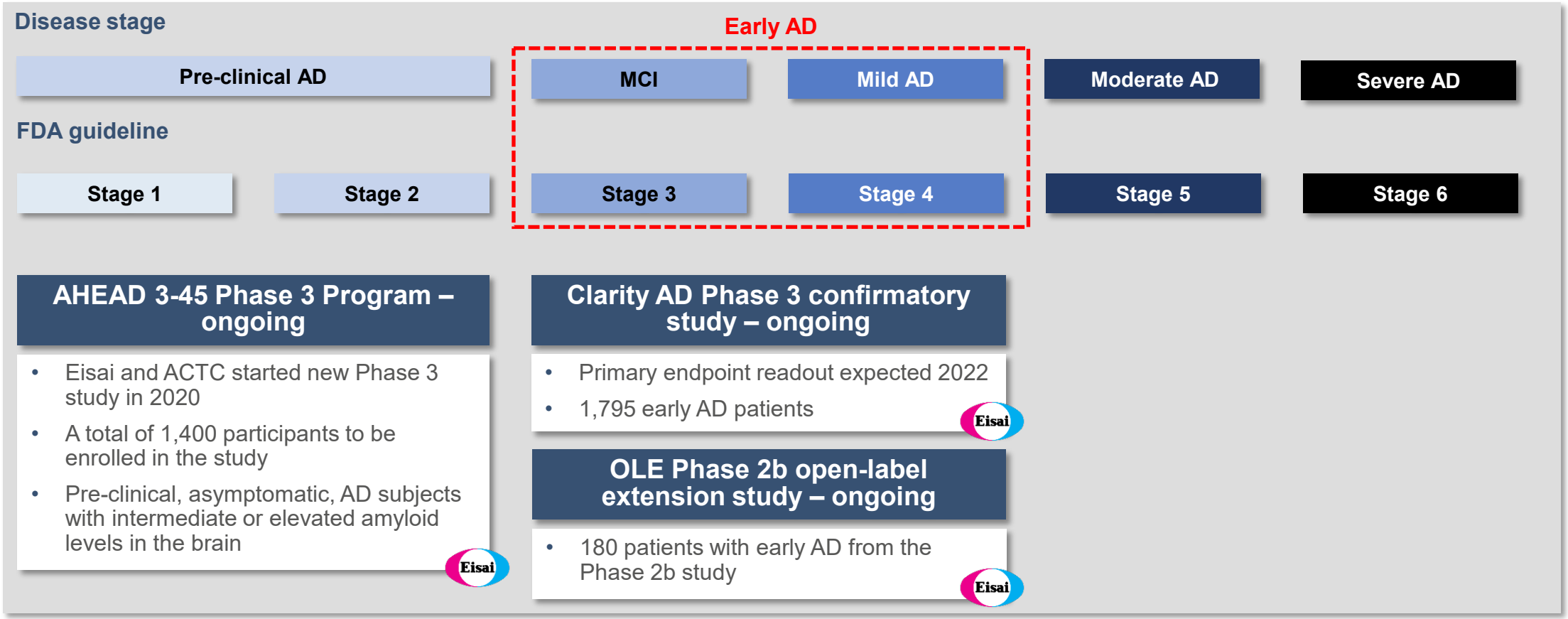
Lecanemab – broad late-stage clinical program



➢ *Selected for the DIAN-TU Tau NexGen study*

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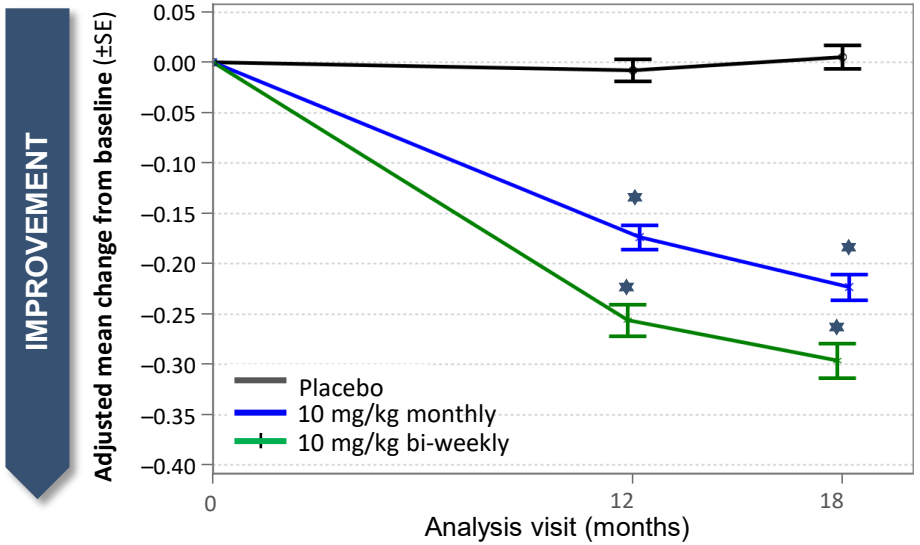
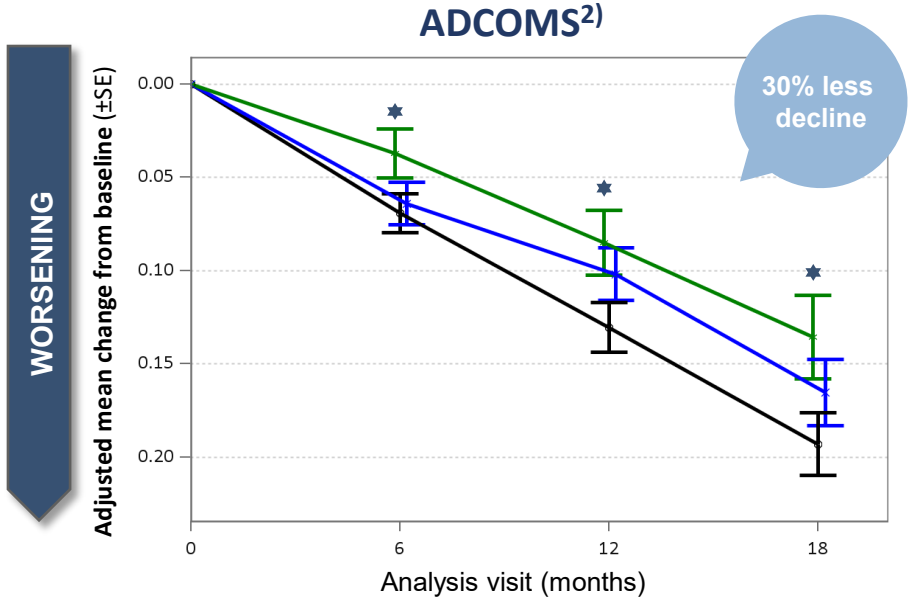
Lecanemab – potential disease modifying antibody with encouraging Phase 2b efficacy & safety profile

Amyloid PET[1)] SUVr



0.30 reduction in PET[1)] SUVr
>90% of patients negative amyloid PET[1)]

ADCOMS[2)]



Similar results for CDR-SB and ADAS-cog

Lecanemab has positive Phase 2b results

- **Large trial –** 856 early Alzheimer's patients
- **Consistent effects** on clinical outcomes, imaging and neurodegenerative biomarkers
- **Rapid onset** of clinical effect
- **Effect increases over time**
- **Good safety profile –** no titration required due to low frequency of ARIA–E (<10%)

✸ *Statistically significant*

Source: Presented at the Clinical Trials on Alzheimer's Disease Conference 2018; Barcelona, Spain. October 25, 2018, Alzheimer's Research & Therapy volume 13, Article number: 80 (2021). Note: 1) PET: positron emission tomography, 2) Alzheimer's disease composite score

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Clarity AD – pivotal Phase 3 study to confirm positive Phase 2b results

Important parameters

- Right target
- Right patient population
- Right dose & exposure
- Right measurements
- Right safety

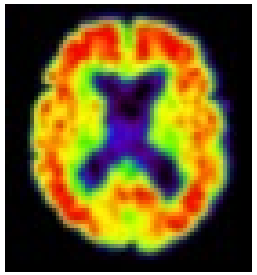
Phase 3 Study Design

Patient inclusion

Global recruitment:
- US, EU and Asia

Inclusion criteria:
- MCI due to AD or mild AD
- Positive amyloid PET/CSF

1,795
Early Alzheimer patients



Treatment 18 months

Randomized, double-blind, placebo controlled, parallel-group study

Lecanemab
10 mg/kg twice a month

Placebo

Primary analysis:
- Change from baseline in CDR-SB

Key analyses:
- Change from baseline in ADCOMS, ADAS-cog
- Change from baseline in brain amyloid PET SUVr
- Biomarkers: amyloid PET positive to negative conversion, tau PET, blood and CSF biomarkers incl. Aβ, p-tau, t-tau, neurogranin, Neurofilament light
- Safety and tolerability

Open-label extension (OLE)

Lecanemab
10 mg/kg twice
a month

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Eisai has initiated a rolling BLA submission in the US for accelerated approval of lecanemab in early Alzheimer's disease

- In June 2021, the FDA granted **Breakthrough Therapy designation** for lecanemab in Alzheimer's disease
- Eisai has after agreement with FDA initiated a **rolling submission** under the accelerated approval pathway, expected to be completed during H1 2022
- The BLA submission for lecanemab is primarily based on
  - the results from the Phase 2b study in 856 early AD patients with confirmed amyloid pathology,
  - the Open label extension study with 180 patients all receiving lecanemab 10mg/kg biweekly, and
  - blinded safety data from Clarity AD
- The Phase 3 Clarity AD study in 1795 early AD patients **can serve as the confirmatory study to verify the clinical benefit** of lecanemab

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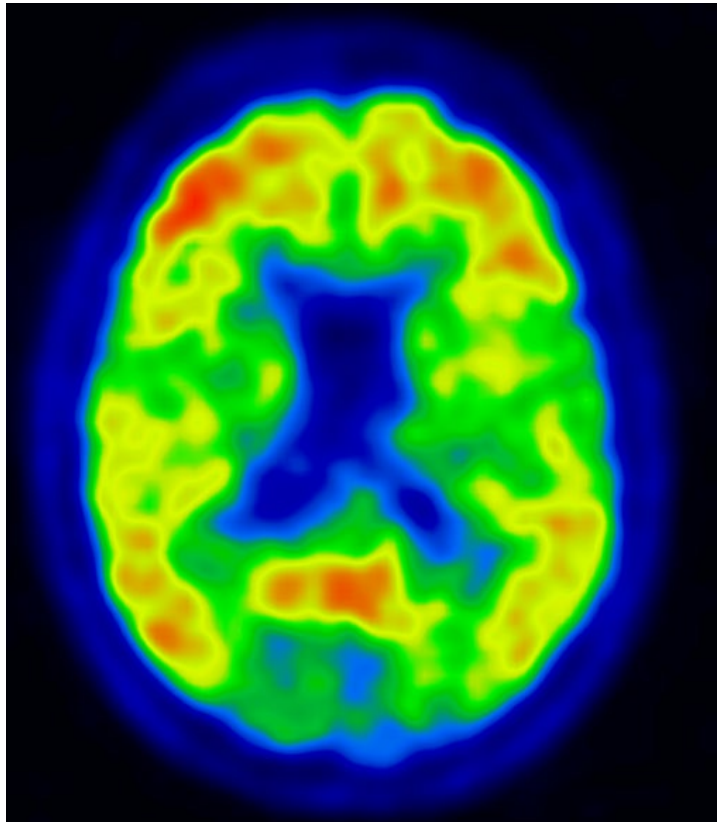
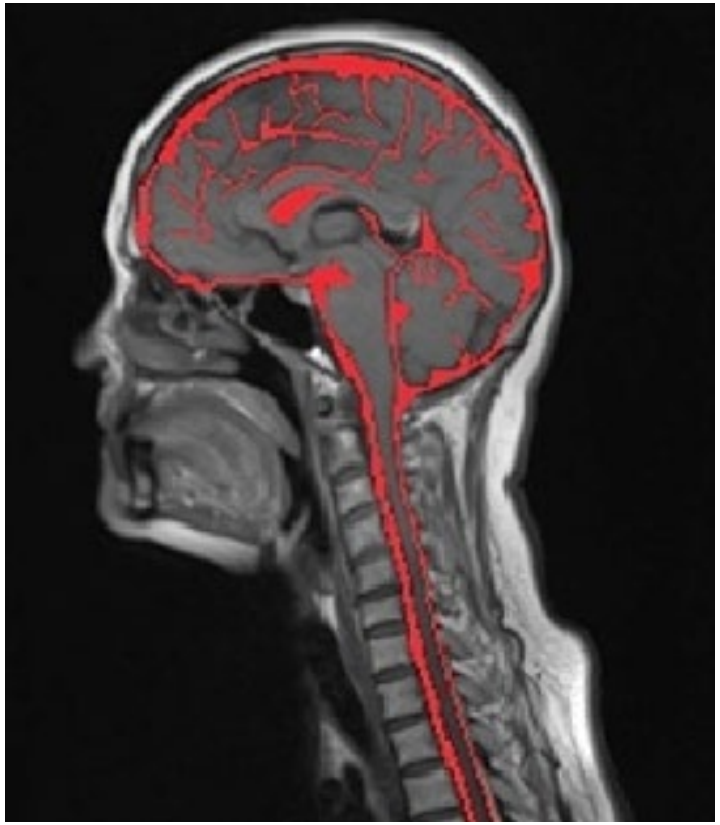
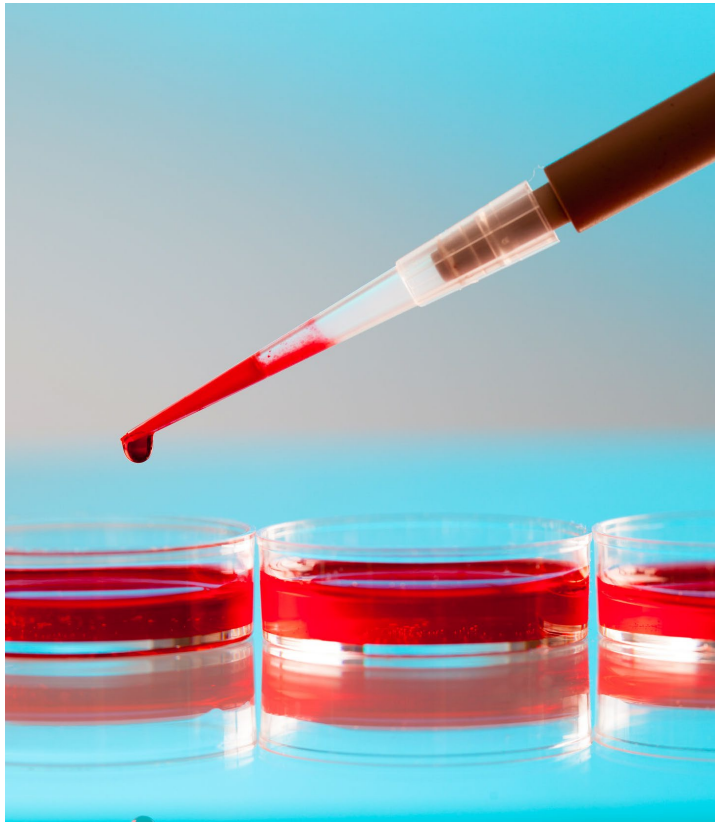
Our view on current developments in the Alzheimer's disease field

Significant progress within AD diagnostics and biomarkers

Amyloid PET	AD proteins in CSF	Blood biomarkers
		

Identify relevant patients, diagnostics, follow disease progression and monitor treatment effect

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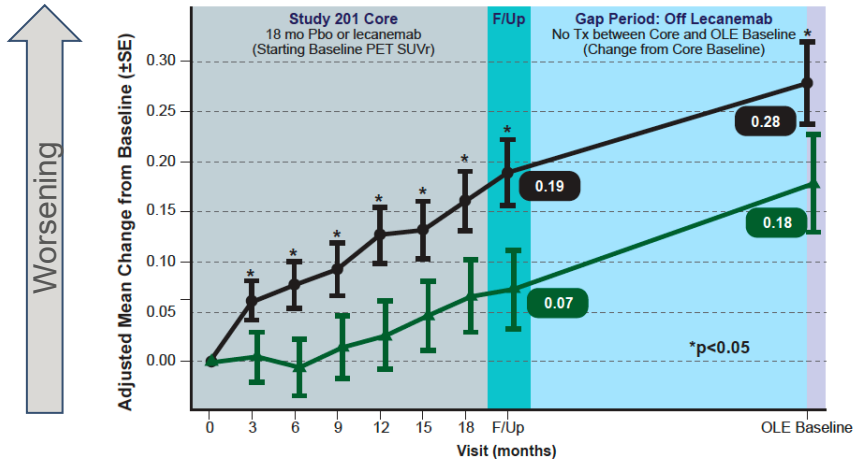
Latest data presented at CTAD continues to strengthen lecanemab (1/2)

ADCOMS



”We are in the beginning of a new era for Alzheimer’s disease, both with regards to new treatments and biomarkers” – US KOL at CTAD

Lecanemab has a unique binding profile vs competition

Lecanemab is an anti-amyloid protofibril antibody

Lecanemab is a strong binder to soluble toxic aggregated forms Aβ and highly selective for protofibrils vs monomers and fibrils

Early clinical effect

No titration needed – full dose from day one

Statistically significant difference observed already within 6 months in the Phase 2b study

Robust efficacy across end-points and analytical methods in the Phase 2b study

Clinical efficacy results are consistent across endpoints (ADCOMS, ADAS-cog, CDR-SB)

Consistent outcomes with 6 different statistical methods

Potential disease modifying effect

Clinical treatment difference maintained after discontinued dosing during the 24-month gap period, suggesting potential disease modifying effect

Source: Data presented at CTAD 2021 by BioArctic and Eisai

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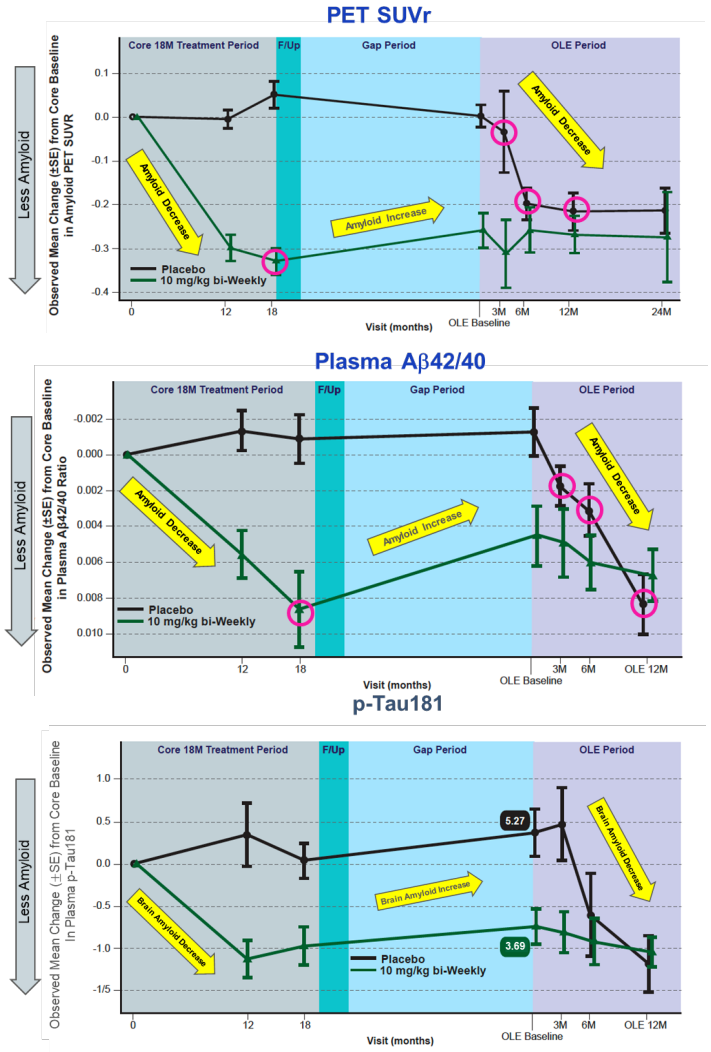
Latest data presented at CTAD continues to strengthen lecanemab (2/2)



Source: Data presented at CTAD 2021 by Eisai

Rapid and profound clearance of brain amyloid

Early reduction of amyloid observed already after 3 months

>80% were amyloid PET negative at 18 months in Phase 2b study

>80% newly treated were amyloid PET negative at 12 months in OLE study

Blood biomarker Aβ42/40 and p-tau 181 correlate with PET and cognition

Blood biomarkers Aβ42/40 and p-tau 181 correlate with amyloid PET SUVr and clinical cognition endpoints following treatment with lecanemab

Blood biomarkers may have potential to monitor treatment effects

Aβ42/40 in blood now used to screen subjects for the Phase 3 AHEAD 3-45 study in pre-symptomatic individuals

Well tolerated with continued low frequency of ARIA-E

<10% ARIA-E for top dose in Phase 2b and open label extension studies

<2% symptomatic ARIA-E for top dose in Phase 2b and open label extension studies

Lecanemab – favourable safety profile and encouraging efficacy data as key differentiators

	Lecanemab	Aducanumab	Gantenerumab	Donanemab
Companies	BioArctic/Eisai/Biogen	Neurimmune/Biogen/Eisai	Morphosys/Roche	Eli Lilly
Primary target	Aβ oligomers/protofibrils	Aβ fibrils	Aβ fibrils	pGlu3-Aβ
Epitope	N-terminus 2-8	N-terminus 3-7	N-term + mid 3-11, 18-27	Aβ p3
Strong reduction of brain amyloid measured by PET	✓	✓	✓	✓
Clinical effect signal on ADAS-cog, CDR-SB	✓	✓	TBD	✓
ARIA-E, brain edema	10%	35%	30%	27%
Need for titration	No	6 months	9 months	3 months

Opportunities for differentiation include; rapid clinical effect, better tolerability profile, no titration - full dose from day 1

Sources: M. Tolar Alzheimer's Research & Therapy 2020 ; Int J Mol Sci 2021; Aduhelm FDA label, Klein et al. Alzheimer's Research & Therapy (2019) 11:101, Swanson C et. al.Alzheimers Dement. 2018;14(Suppl):1668.

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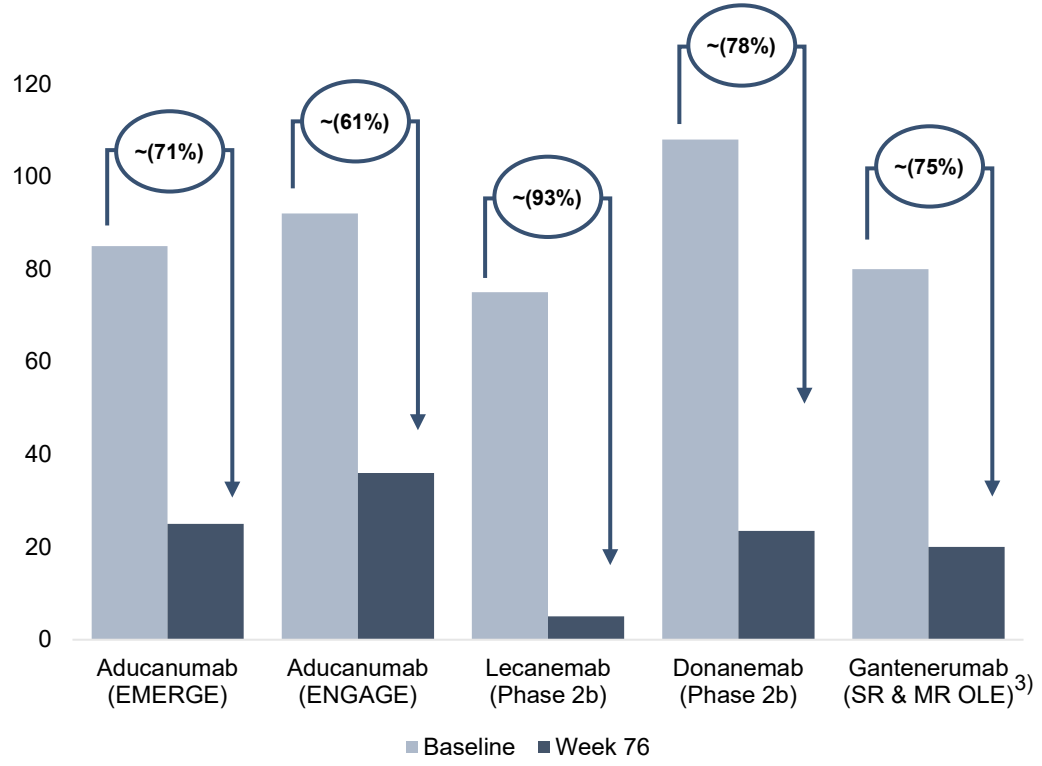
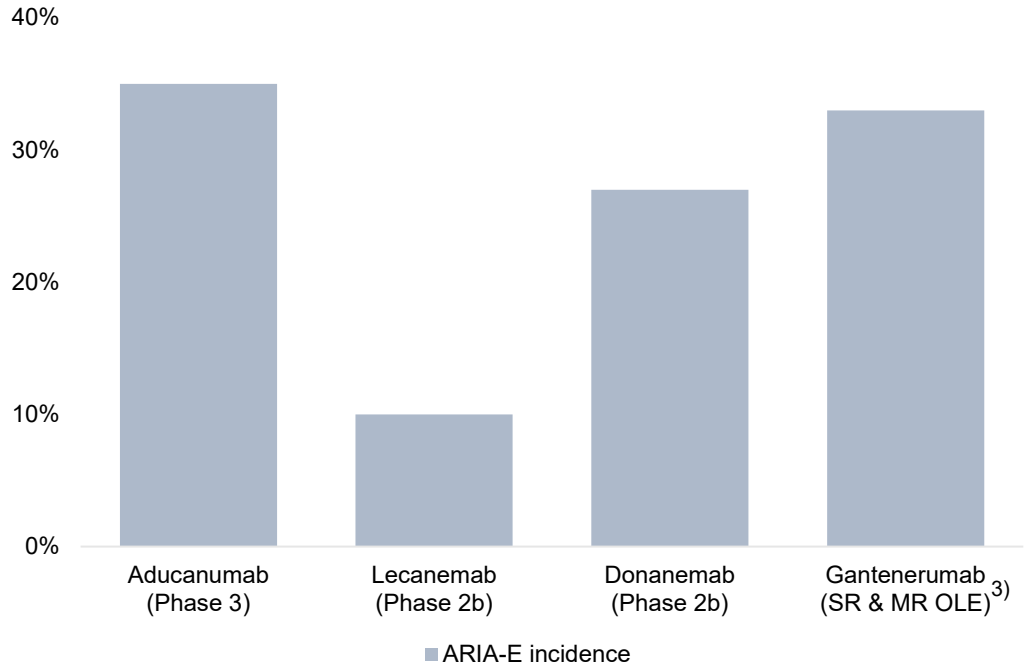
Lecanemab – strongest reduction of brain amyloid and lowest ARIA-E incidence among competitors

PET[1] amyloid, centiloids



ARIA-E[2] incidence



Note: 1) PET: positron emission tomography, 2) Amyloid related imaging abnormalities edema, 3) Week 104
Curtesy Carnegie research

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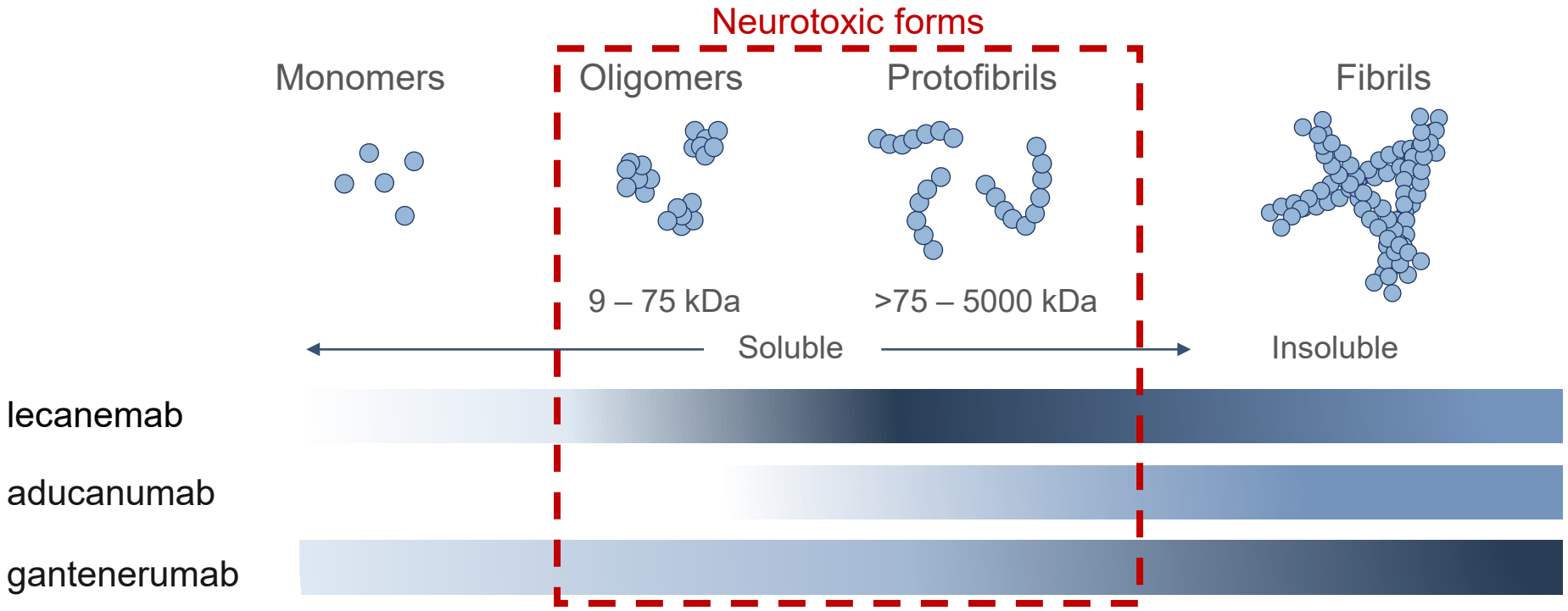
Lecanemab – unique selectivity towards toxic soluble species of Aβ

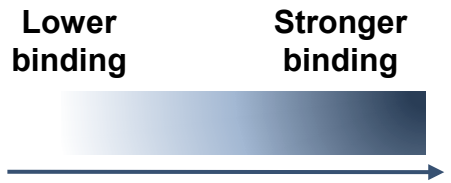


Lecanemab had the highest preference for soluble protofibrils/oligomers versus monomeric and fibrillar forms of Aβ

Aducanumab and gantenerumab had a preferences for the insoluble fibrils

Aducanumab showed a lower binding to all Aβ species

Gantenerumab had somewhat higher binding to monomers and prefers fibrils



Source: Presented at CTAD 2021. Note: Illustration is based on data from Biacore, inhibition ELISA and immunoprecipitation

BIOARCTIC

Anticipated news flow for late-stage anti-Aβ antibodies

Date	Project	Event
Q4 2021	Aduhelm	Biogen to receive CHMP opinion (and subsequently EC decision)
March 2022	AD/PD	International conference
H1 2022 (Jan & Apr)	Aduhelm (and other)	Medicare's nationwide coverage decision expected to be announced
H1 2022	Lecanemab	Eisai aims to complete rolling submission for accelerated approval
H1 2022	Donanemab	Eli Lilly aims to complete rolling submission for accelerated approval
August 2022	AAIC	International conference
September 2022	Lecanemab	Eisai expects top-line data from Clarity AD
H2 2022	Gantenerumab	Roche expected to report data from the two Phase 3 studies
November 2022	CTAD	International conference
H2 2022	Donanemab	Eli Lilly may report top-line data from Trailblazer-Alz 4 comparing donanemab with aducanumab
Mid-2023	Donanemab	Eli Lilly may report top-line data from Phase 3 Trailblazer-Alz 2

Opportunity to be first with full approval in US for lecanemab

BIOARCTIC

The next step on a transformational journey for BioArctic

Establish commercial organization in the Nordic countries, with stepwise and timely recruitment, including support functions and IT infrastructure

- Increase awareness about;
  - early Alzheimer's disease,
  - current and future diagnostics incl blood-based biomarkers,
  - the possibility of future paradigm-shifting disease modifying treatments
- Build and prepare pricing and market access strategies demonstrating the value of lecanemab
- Build a solid case for the positioning of lecanemab vs competition
- Prepare patient centric infrastructure to support launch based on the patient journey and digital education initiatives
- Prepare for Life Cycle Management (subcutaneous formulation, indication expansions)

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Lecanemab – potential to lead the paradigm shift in the treatment of Alzheimer's disease

Increased likelihood for lecanemab success

- → Positive and consistent Phase 2b results
- → Phase 2b OLE further strengthens the Phase 2b results
- → Phase 3 study "Clarity AD" designed to confirm the positive Phase 2b results

✓

Opportunity to be first with full approval in US

- → Accelerated approval pathway initiated - expected to be completed H1 2022
- → Submission for full approval pending topline Phase 3 data expected Sept 2022

✓

Opportunity to differentiate

- → Rapid and profound brain amyloid clearance
- → Early onset of clinical effect in slowing cognitive decline
- → Better tolerability profile than competition
- → Full dose from day one

✓

Further development programs

- → Subcutaneous injection
- → Expanded Alzheimer's disease populations:
  - → Selected for AHEAD in pre-symptomatic individuals
  - → Selected for DIAN-TU – dominantly inherited Alzheimer disease

✓

BIOARCTIC

Today's agenda

1. BioArctic – a CNS disease frontrunner
2. Lecanemab – towards a breakthrough in Alzheimer's disease
3. **Rich clinical and pre-clinical pipeline**
4. Concluding remarks
5. Appendix
    I. Additional clinical data
    II. IP
    III. Financial position

Significant progress and expansion of the pipeline

Parkinson's disease

ABBV-0805

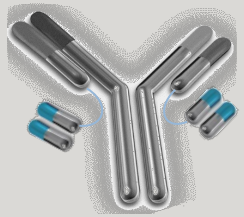
- Potential disease modifying antibody in Phase 1 preparing for Phase 2

Discovery stage projects

- Pre-clinical stage alpha-synuclein projects

abbvie

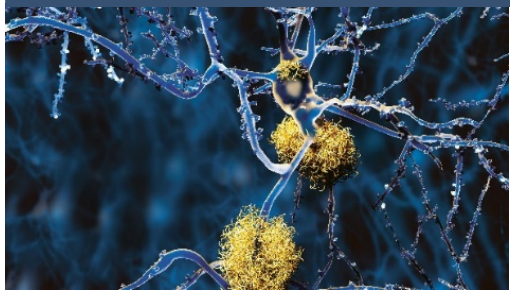
Blood-brain barrier



Brain Transporter (BT)

- Continued development of Brain Transporter (BT) technology platform
- 2nd generation under development

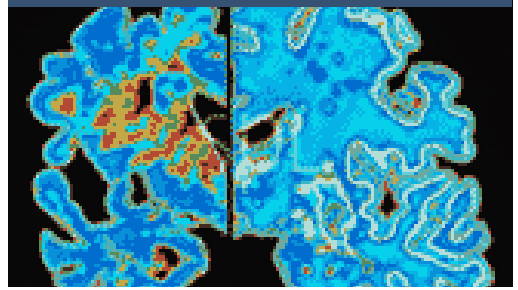
Alzheimer's disease



Discovery stage programs

- Expanded early-stage portfolio with two new AD+BT projects
- Six internal disease modifying antibody projects in Alzheimer's disease

Other CNS disorders



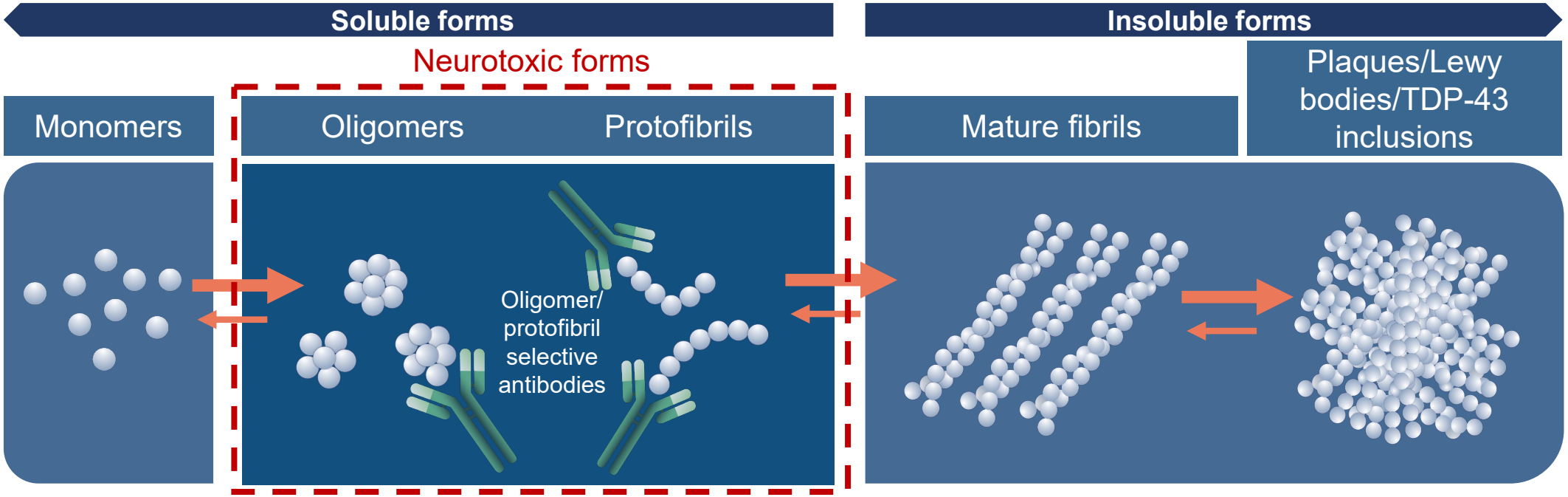
Neurodegeneration research

- Lecanemab in indications outside of Alzheimer's disease
- Research project in neurodegeneration ("ND") with potential in various CNS disorders, including orphan indications such as ALS[1)]

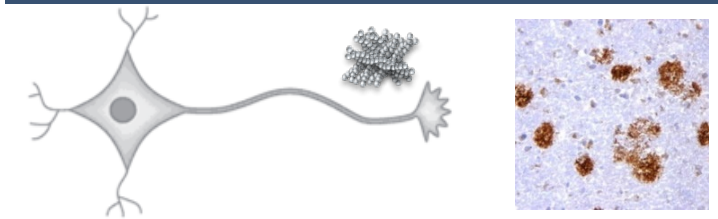
Note: 1) Amyotrophic lateral sclerosis

BIOARCTIC

Neurotoxic forms of aggregated misfolded proteins – a promising target for disease modifying treatments in CNS disorders

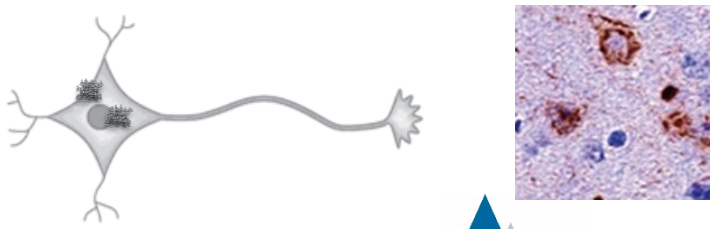


Alzheimer's disease: misfolded amyloid beta results in amyloid plaques



Parkinson's disease: misfolded alpha-synuclein results in Lewy Bodies

ALS: misfolded TDP-43 results in TDP-43 inclusions



BIOARCTIC

ABBV-0805 – potential disease modifying antibody in Parkinson's disease in preparation for Phase 2

ABBV-0805

High unmet medical need

No existing disease-modifying treatment

Younger patient group, still at working age

TODAY

>6 million[1]
people with Parkinson's

Unique profile

Unique and targeted binding profile

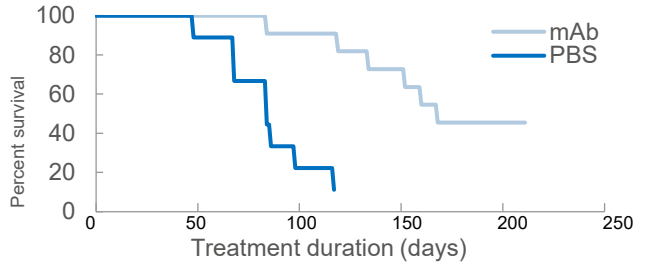
- Highly selective (>100.000) for pathological forms of misfolded alpha-synuclein (oligomers/protofibrils) vs physiological forms (monomers)

Built on genetic and pathology rationale

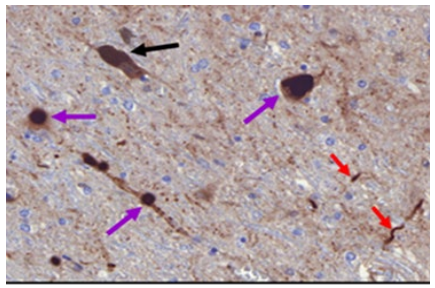
- Alpha-synuclein mutations lead to PD
- Alpha-synuclein oligomers/ protofibrils are elevated in PD

Pre-clinical proof of concept

- Reduction of neurotoxic alpha-synuclein oligomers/protofibrils
- Delays disease progression and increases lifespan



Human target binding of ABBV-0805 in PD brain



Black: neuromelanin ,Purple: Lewy bodies, Red:Lewy neurites

Phase 1 results presented at MDS congress in Sept 2021 support Phase 2 development with dosing once a month

Source: 1) Dorsey and Bloem, JAMA Neurology 2018;75:9-10
Data presented at the International Congress of Parkinson's disease and movement disorders® (MDS), held virtually September 17 to 22, 2021, and published in Neurobiology of Disease in November 2021.

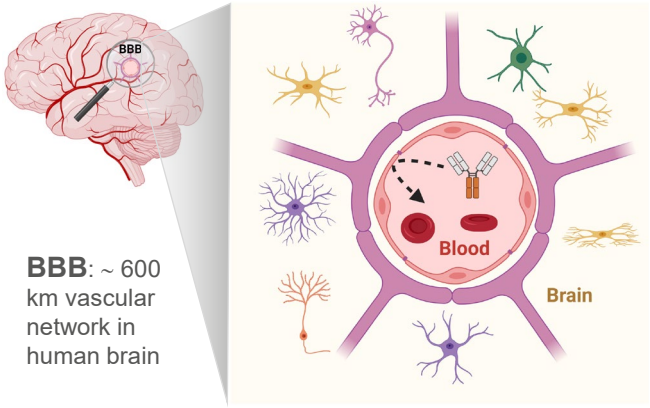
BIOARCTIC

Brain Delivery of Biotherapeutics

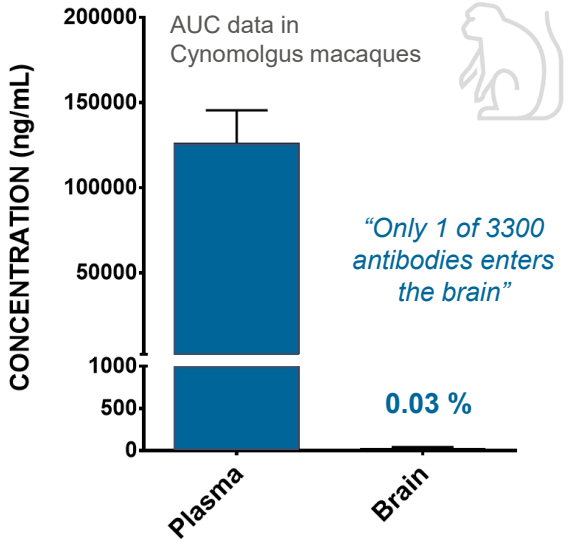
Solving the Blood-brain barrier (BBB) challenge with the Brain Transporter (BT) technology

BT

The BBB challenge

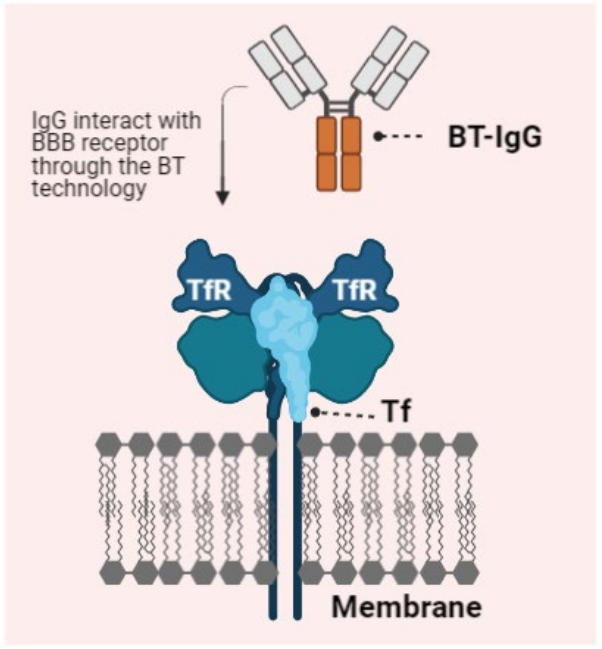


BBB: ~ 600 km vascular network in human brain

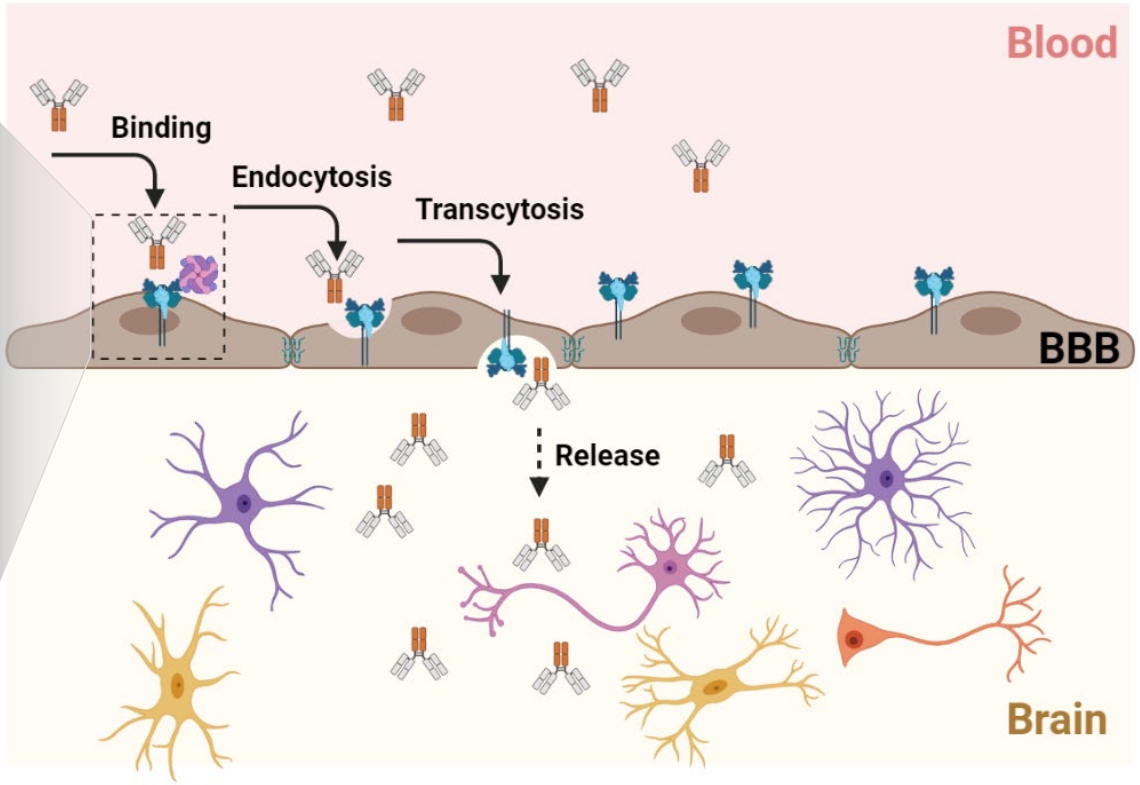


"Only 1 of 3300 antibodies enters the brain"

BioArctic's solution



Receptor-mediated transport across the BBB



- BT technology mediates binding of standard antibodies to the Transferrin Receptor (TfR)
- Cross the BBB into the brain compartment using active transport

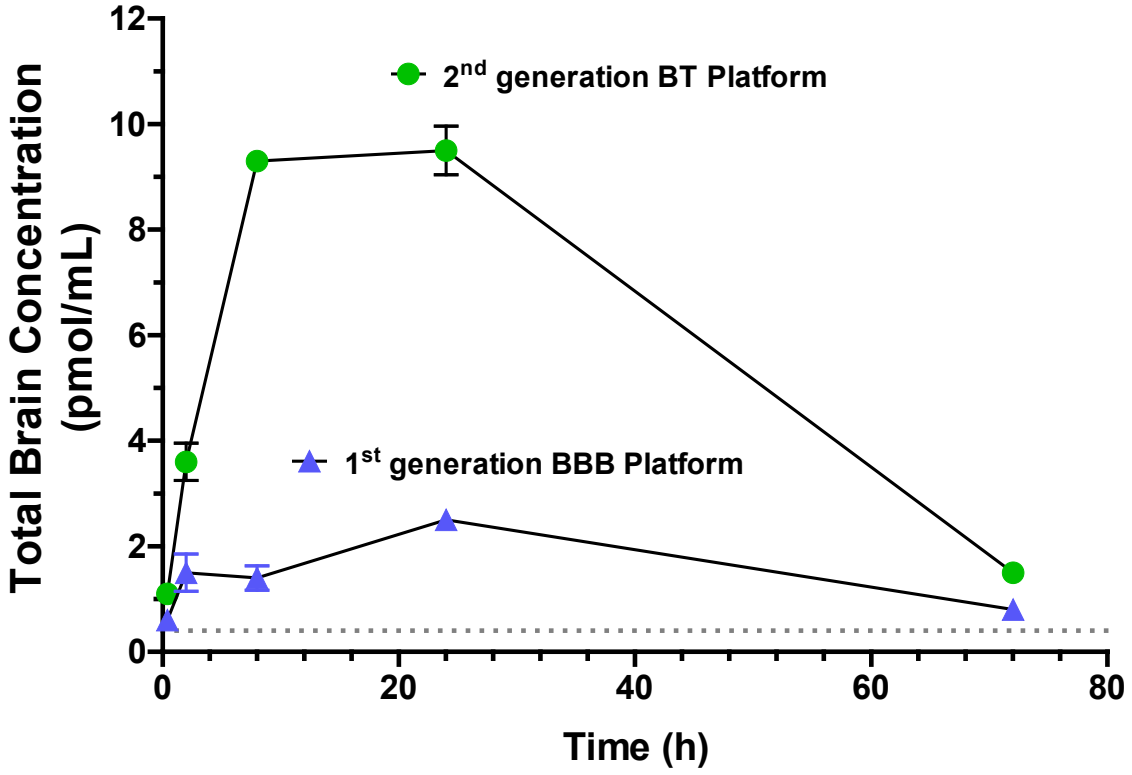
BIOARCTIC

BioArctic's Brain Transporter (BT) technology platform

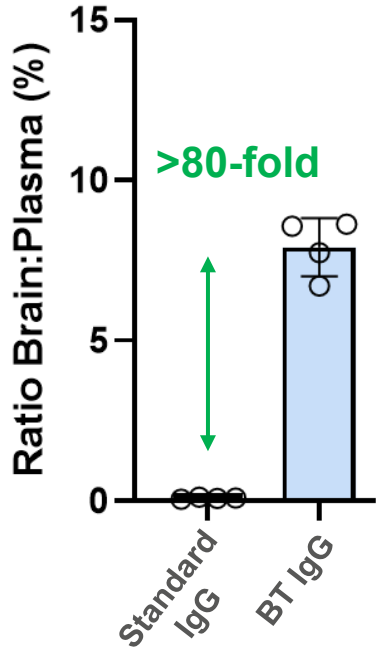
Further improved brain exposure based on second generation

BT

Second generation technology provides superior brain exposure in pre-clinical study



Boosting brain uptake of standard antibodies mediated by the BT technology



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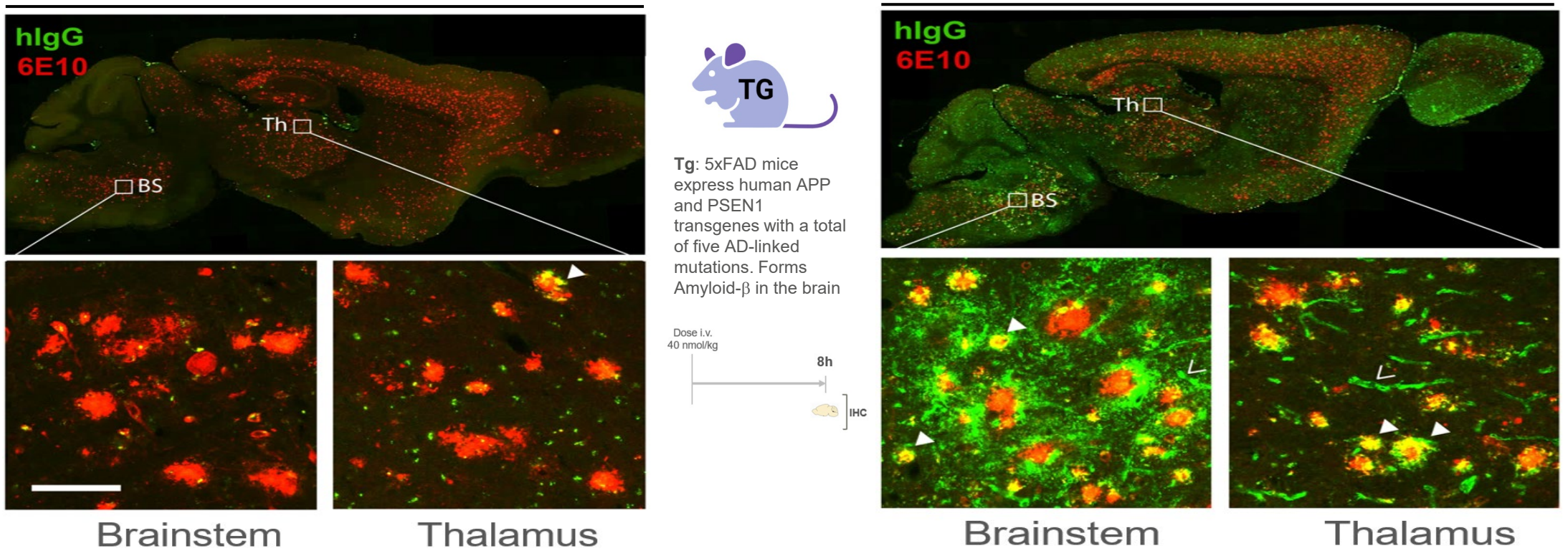
Improve potency for a clinically relevant antibody

Improve brain exposure, global distribution and target engagement

BT

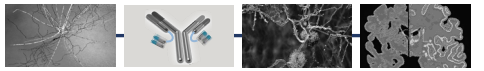
mAb158
(Pre-clinical version of Lecanemab)

BT-mAb158
(Pre-clinical version of Lecanemab coupled with BT technology)



Red: Amyloid-β plaque in the brain
Green: Antibody in the brain at the Amyloid-β target

BIOARCTIC



BT

Brain Transporter (BT) technology platform

Potential to revolutionize engineering brain delivery of biotherapeutics

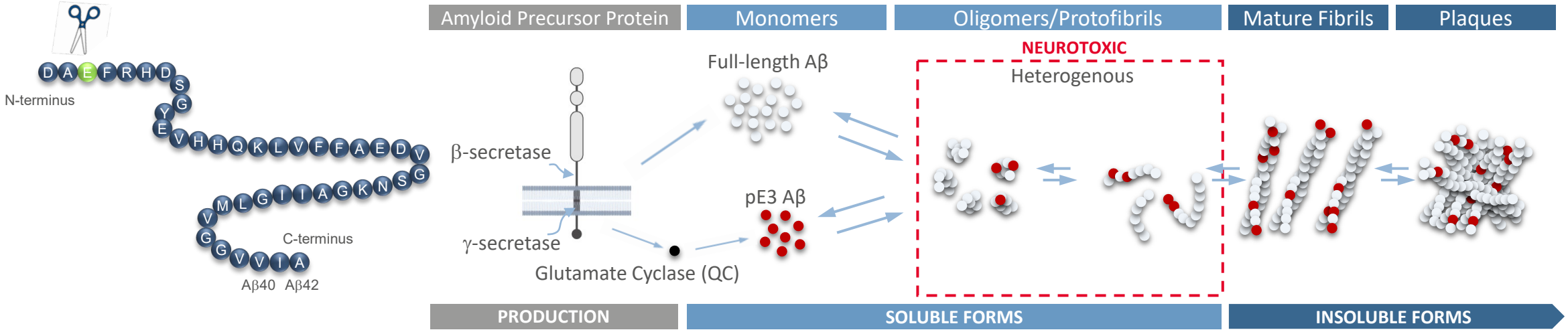
- Based on many years of experience in the Blood-brain barrier (BBB) field and brain delivery of biotherapeutics, BioArctic is developing a new Brain Transport (BT) technology with novel properties with the ambition to be best-in-class
- BT delivers efficacious concentrations and provides broad distribution of biotherapeutics to the brain via receptor mediated transport
- BioArctic´s BT technology platform has significant potential in the treatment of several different brain diseases – opportunity to use together with our own projects and for external projects with several non-exclusive license deals
- BT has progressed very well and has now been applied to two AD disease modification projects in BioArctic's portfolio AD-BT2802 and AD-BT2803

BIOARCTIC

Antibodies targeting N-terminal truncated pE3-Aβ
Disease modifying approach for Alzheimer's disease

AD1503

pE3-Aβ, truncated forms of Aβ prone to form toxic aggregates, leading to rapid protofibril formation, neuronal death and cognitive decline



BioArctic pE3-Aβ selective antibodies

- Antibodies selectively target a shorter (truncated) form of amyloid beta (pE3-Aβ)
- Complementary treatment to lecanemab
- Opportunity for differentiation vs other anti-amyloid antibodies including donanemab

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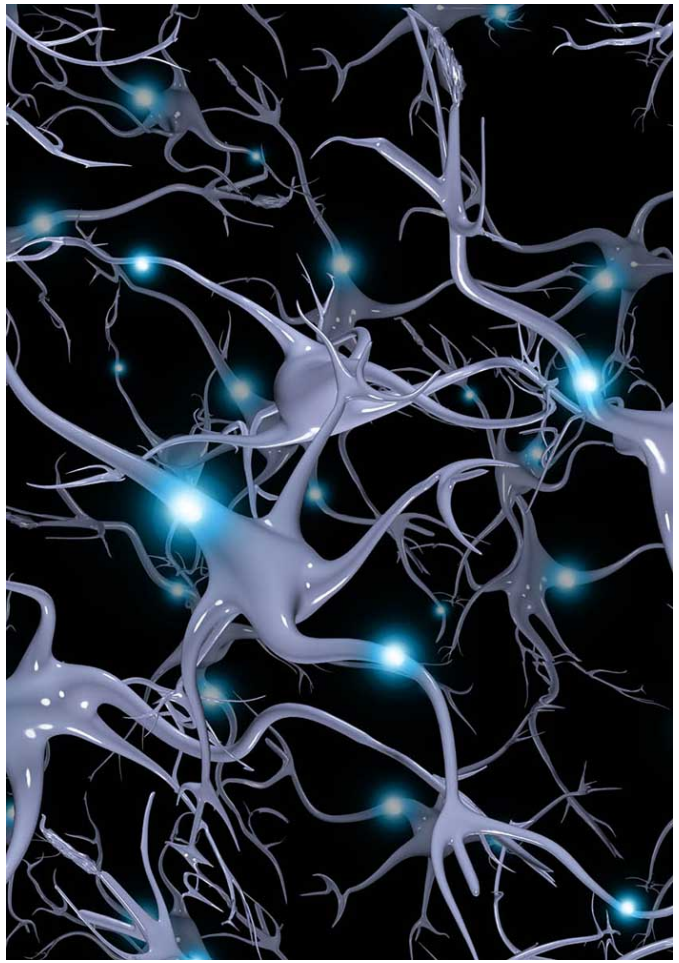
Amyotrophic lateral sclerosis (ALS) – a debilitating rare disease

- Progressive neurodegenerative disease characterized by motor neuron degeneration
- The main symptom being systemic muscular atrophy and progressive muscular weakness
- Annual incidence of ALS in Europe is 2–3 cases per 100.000/year with a 1:400 overall lifetime risk of developing the disease
  - Prevalence 3-5/100.000
  - Age of onset typically ~ 60 years
  - 5% of cases diagnosed before age 30
  - Approximately 5-10% of ALS cases are familial with the remaining 90-95% being sporadic
  - Familial ALS associated with earlier onset
- Two approved drugs that slow down disease progression: riluzole and edaravone, both with modest efficacy



TDP-43 – opportunity for ALS and other neurodegeneration ("ND") disorders

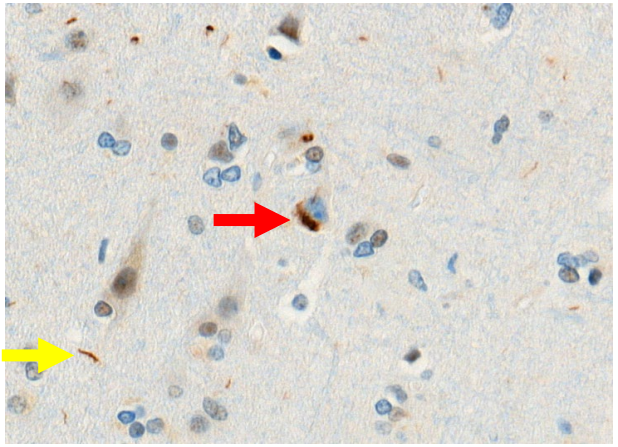
ND3014

TDP-43 – Transactive response DNA binding Protein 43 kDa

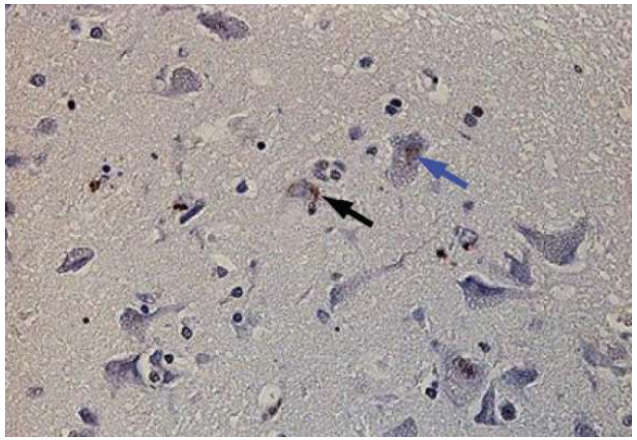
Several mutations in TARDBP (encoding TDP-43) are linked to familial ALS[1)] and FTD[2)]

Pathological aggregation of TDP-43 is found in multiple neurodegenerative diseases

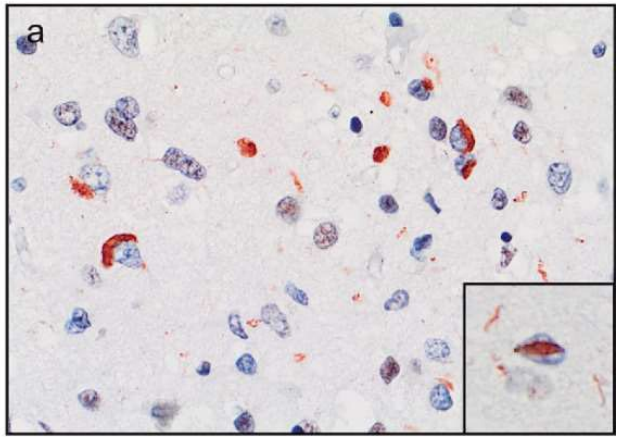
- 97% of **ALS[1)]** cases (orphan drug indication)
- 50% **AD[3)]** cases
- 45% **FTD[2)]** cases



TDP-43 pathology very common in **ALS[1)]**



Abnormal TDP-43 immunoreactivity is common in **AD[3)]**



Abnormal TDP-43 immunoreactivity is common in **FTD[2)]**

Source: Ling et. al. 2013
Note: 1) Amyotrophic lateral sclerosis, 2) Fronto temporal dementia, 3) Alzheimer's disease

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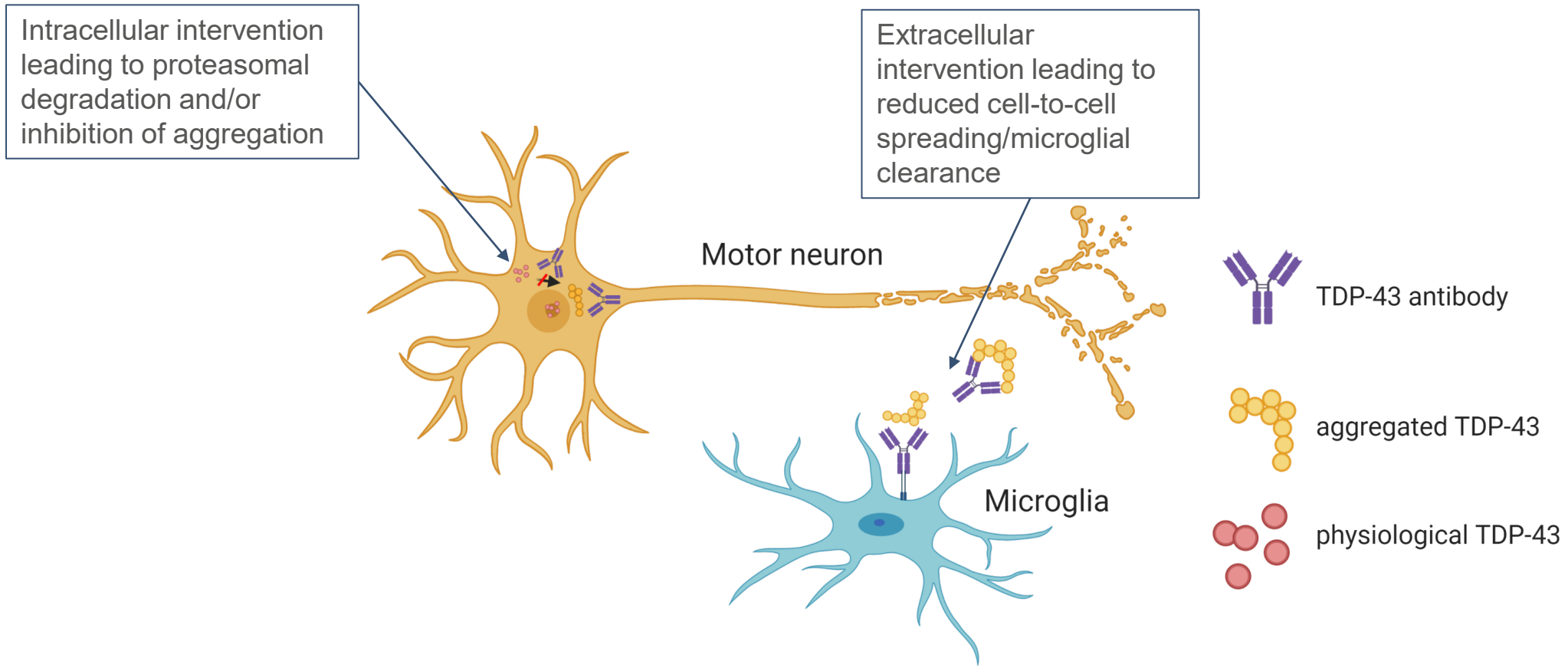
Antibodies targeting TDP-43

Disease modifying approach for multiple neurodegenerative diseases

ND3014

Objective: To generate antibodies targeting disease-associated aggregated forms of TDP-43 for the treatment of ALS and AD/FTD as secondary indications



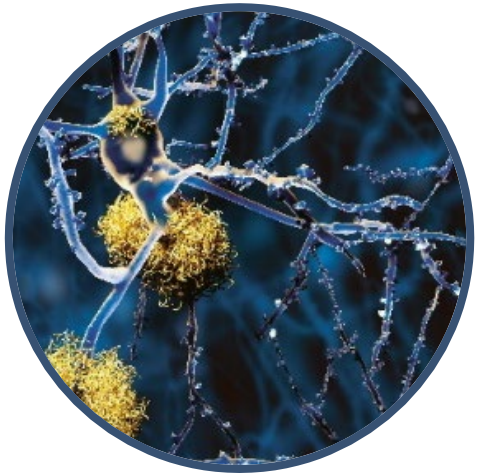
BIOARCTIC

Today's agenda

1. BioArctic – a CNS disease frontrunner
2. Lecanemab – towards a breakthrough in Alzheimer's disease
3. Rich clinical and pre-clinical pipeline
4. **Concluding remarks**
5. Appendix
    I. Additional clinical data
    II. IP
    III. Financial position

Upcoming news flow

Alzheimer's disease



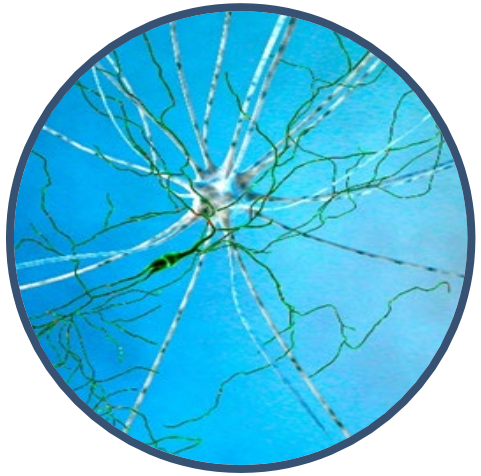
Lecanemab (Eisai)

- Rolling submission for accelerated approval in the US expected to be completed H1 2022
- Clarity AD topline data expected in September 2022
- Data to be disclosed at international congresses

Discovery stage programs

- Advancement of projects

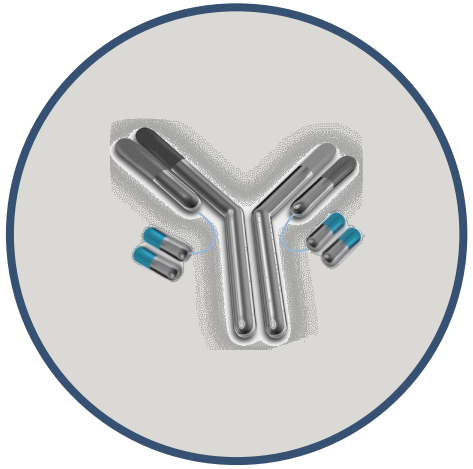
Parkinson's disease



ABBV-0805 (AbbVie)

- Start Phase 2
- Data presented at international congresses

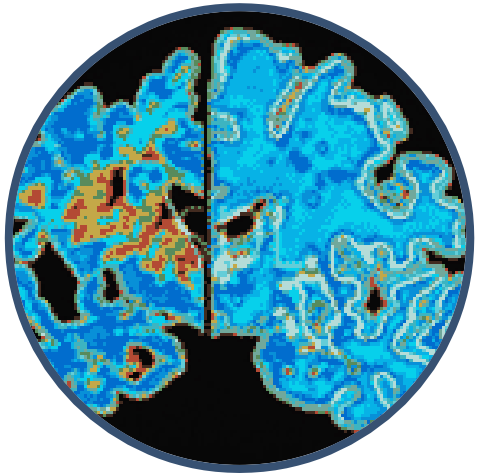
Blood-brain barrier



Brain Transporter (BT) technology platform

- Further development of the technology platform
- Data to be disclosed at international congresses

Other CNS disorders



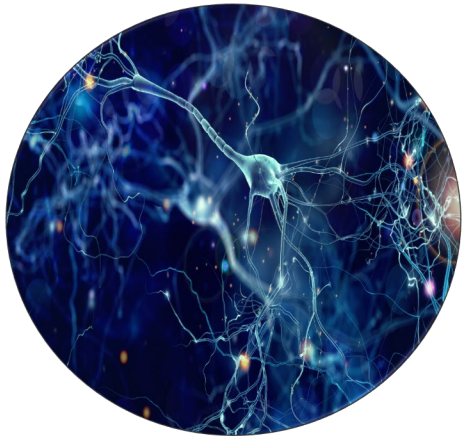
Neurodegeneration

- Data to be disclosed at international congresses

BIOARCTIC

BioArctic – with patients in Mind

Great science



Great projects

Great partners

Great people

BIOARCTIC

Today's agenda

1. BioArctic – a CNS disease frontrunner
2. Lecanemab – towards a breakthrough in Alzheimer's disease
3. Rich clinical and pre-clinical pipeline
4. Concluding remarks
5. **Appendix**
   - **I. Additional clinical data**
   - II. IP
   - III. Financial position

Experienced management, innovative scientists and collaborations with universities to bring forward the next groundbreaking therapy

EXPERIENCED R&D LEADERSHIP

Gunilla Osswald, PhD
CEO
Former VP AstraZeneca (portfolio, projects, clinical, marketing)
30+ years relevant experience

Tomas Odergren, MD, PhD
CMO
Senior positions in clinical development at AstraZeneca and H Lundbeck
20+ years relevant experience

Christer Möller, PhD
CSO
Extensive experience from small biotech (research & development)
20+ years relevant experience

Johanna Fälting, PhD
VP Head of Research
Former AstraZeneca R&D (discovery & drug projects)
20+ years relevant experience

Mikael Moge, PhD
VP CMC
Former AstraZeneca (Pharmaceutical Development) and Syntagon (Head Development & Pilot Plant)
20+ years relevant experience

Hans Basun, Professor, MD
Senior Dir Clin Dev
Geriatrician at Memory Clin, Uppsala former AstraZeneca (clinical development)
35 years relevant experience

Per-Ola Freskgård, PhD
Distinguished Scientist
Former Roche Head of Neurovascular Biology, AstraZeneca, Novo Nordisk
20+ years relevant experience

Lars Lannfelt, Professor, MD
Co-founder, SVP University Collaborations
Senior Professor, Uppsala University
Discovered the Swedish and Arctic mutations in Alzheimer's Disease
35+ years relevant experience

INNOVATIVE SCIENTISTS

COLLABORATION WITH UNIVERSITIES

UPPSALA UNIVERSITET
Karolinska Institutet
GÖTEBORGS UNIVERSITET
Stockholm University
KTH VETENSKAP OCH KONST
LINKÖPINGS UNIVERSITET

BIOARCTIC

Alzheimer’s disease

Lecanemab – Phase 2b study in early Alzheimer's disease – positive 18-month results reported by Eisai, further strengthened by OLE data

Important parameters

- Right target
- Right patient population
- Right dose & exposure
- Right measurements
- Right safety

Phase 2b Study Design

Patient inclusion

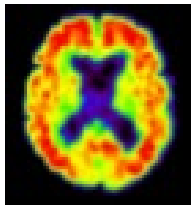
Multinational recruitment:

- 100 clinical centers

Inclusion criteria:

- MMSE >22-30
- Stable concomitant medication
- Positive amyloid PET/CSF

Inclusion completed with 856 patients



Lecanemab or placebo treatment 18 months

Double-blind, placebo controlled, parallel-group study with Bayesian adaptive randomization design

- Placebo
- 2.5 mg/kg twice a month
- 5 mg/kg once a month
- 5 mg/kg twice a month
- 10 mg/kg once a month
- 10 mg/kg twice a month

Primary analyses:

- Change from baseline in ADCOMS at 12 months
- Safety and tolerability

Key analyses:

- Change from baseline in ADCOMS, CDR-SB, ADAS-cog at 18 months
- Change from baseline in brain amyloid PET SUVr
- Biomarkers: amyloid PET positive to negative conversion, CSF biomarkers incl. Aβ, p-tau, t-tau, neurogranin, Neurofilament light

Gap period

2 years on average (9-59 months) with no treatment

Open label extension

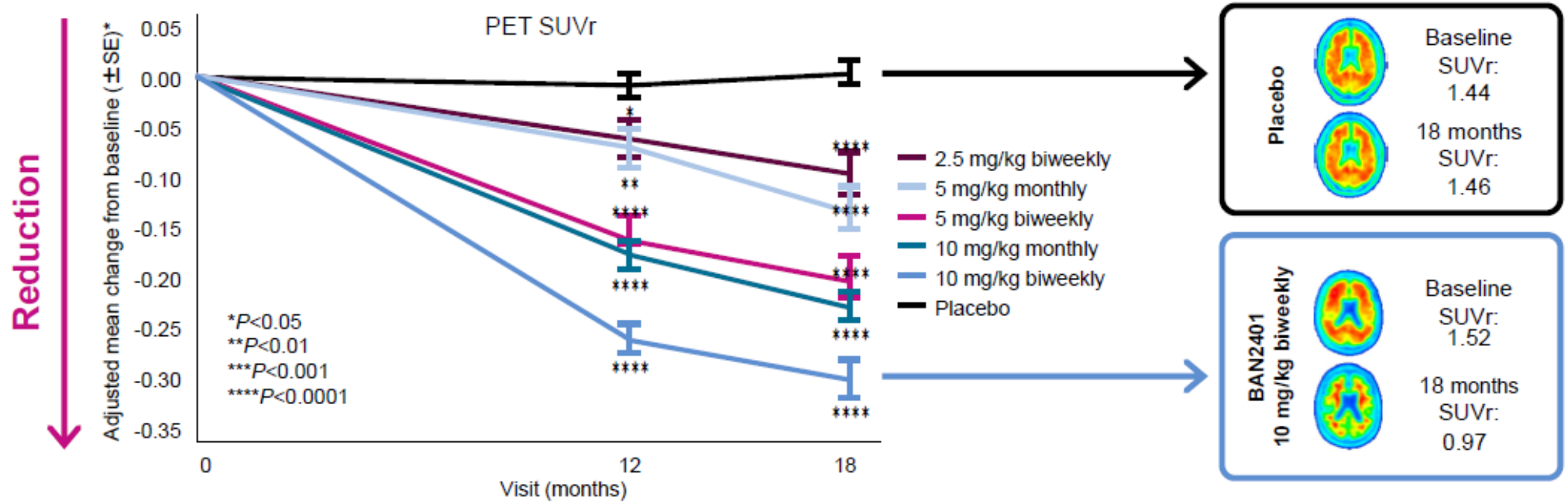
Lecanemab 10 mg/kg twice a month

BIOARCTIC

Profound clearance of brain amyloid with lecanemab in Phase 2b

Amyloid reductions measured by PET imaging assessments: PET SUVr, centiloid and visual read

PET SUVr



Level for being amyloid positive: > 1.15 (SUVr)

Amyloid reduction – PET centiloid scale

>90% reduction from base-line at highest dose
From 74.5 at base-line to 5.5 after 18 months

Amyloid conversion – PET SUVr/Visual read

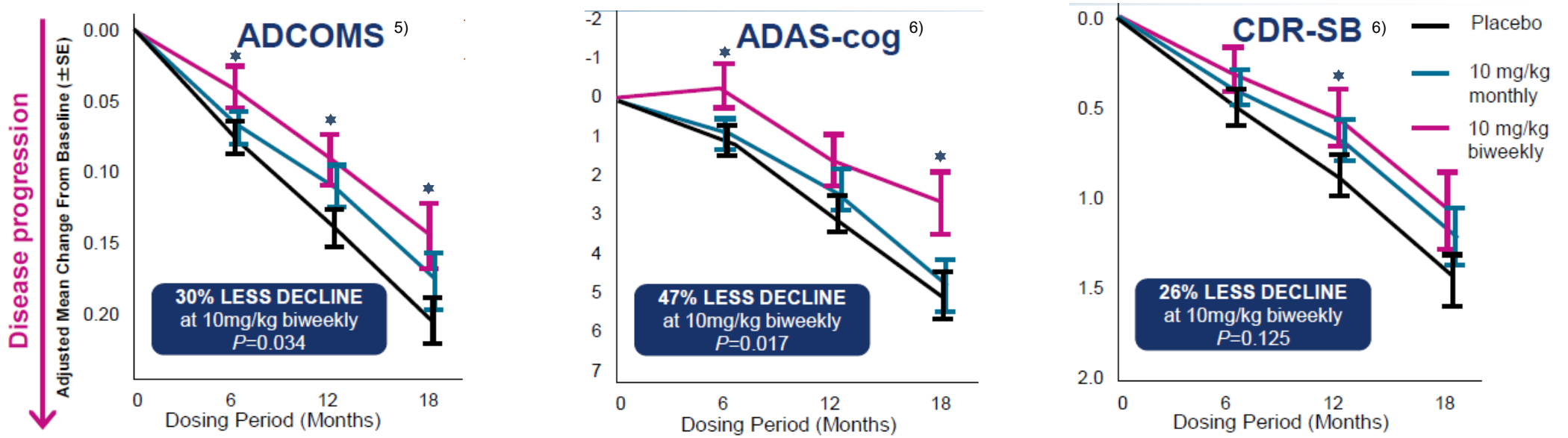
>90% of amyloid positive converted to negative at highest dose (PET SUVr)
>80% converted to negative at highest dose (PET visual read)

Source: Data presented at AAIC 2018 and AD/PD March 2019 by Eisai

BIOARCTIC

Lecanemab Showed Effect on Clinical Parameters in Phase 2b

ADCOMS cognition scale (the key efficacy parameter)	ADAS-Cog (well-established cognition scale)	CDR-SB (cognition and function scale)



- Showed effect already at 6 months – as well as after 12 and 18 months of treatment
- Slowing of disease progression observed across sub-groups[1)]
- Clinical effect increased over time

✸ *Statistically significant*

Source: Presented at CTAD October 2018 by Eisai. Note: 1) MCI due to AD – mild AD, ApoE4 carriers – non-carriers, with or without symptomatic treatment, 2) ADCOMS – Alzheimer's Disease Composite Score, 3) ADAS-Cog – Alzheimer's Disease Assessment Scale, cognitive subscale, 4) CDR-SB – Clinical Dementia Rating – sum of boxes, 5) Statistical significance across all dosing periods, 6) Statistical significance at 18 month dosing period, 7) Statistical significance at 12 month dosing period

BIOARCTIC

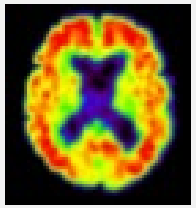
Lecanemab – Eisai and ACTC´s Phase 3 study “AHEAD 3-45” in pre-clinical asymptomatic Alzheimer´s disease

AHEAD 3-45 PHASE 3 STUDY DESIGN

Patient inclusion → Treatment 4 years → Read-outs

Pre-clinical stages of AD
Inclusion criteria:

- A45: no or limited cognitive decline, elevated amyloid in brain
- A3: cognitively normal, intermediate amyloid in brain



Amyloid PET
A45: elevated
A3: intermediate

No of subjects

- A45 up to 1,000
- A3 up to 400

Recruitment geographies:
US, Japan, Australia, EU

Randomized, double-blind, placebo controlled, parallel-group study

A45
- Lecanemab
- Placebo

A3
- Lecanemab
- Placebo

Primary endpoints:
A45: change from baseline; PACC5
A3: change from baseline; brain Aβ PET SUVr

Key endpoints:
Safety and tolerability

A45: change from baseline in cognitive function index
Change from baseline in brain Aβ and tau PET SUVr

A3: change from baseline in brain tau PET SUVr

BIOARCTIC

Regulatory pathway scenarios for lecanemab

US FDA – BLA[1)] application

1. Full approval for lecanemab
   - A. Standard BLA – all documentation
     OR
   - B. Rolling submission - stepwise
   1. Standard review (~10 mo)
      OR
   2. Priority review (~ 6 mo)
2. Accelerated approval with Clarity AD as post marketing requirement
   - A. Standard BLA – all documentation
     OR
   - **B. Rolling submission - stepwise**
   1. Standard review (~10 mo)
      OR
   2. Priority review (~ 6 mo)
3. Rejection and request of further data

EU EMA – MAA[2)] application

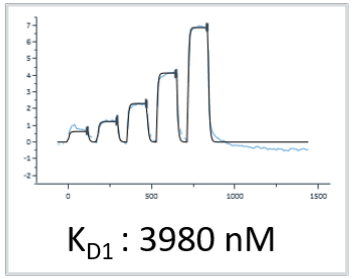
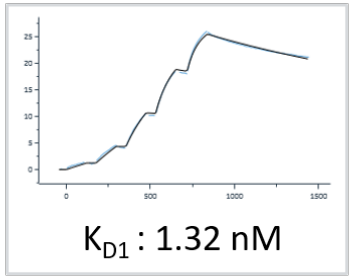
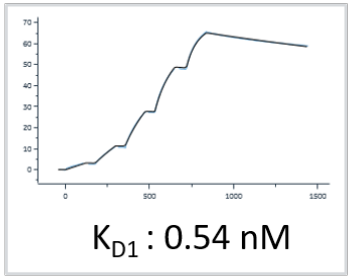
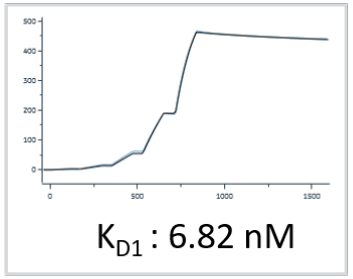
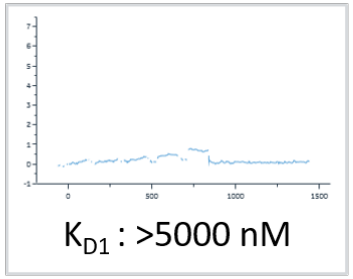
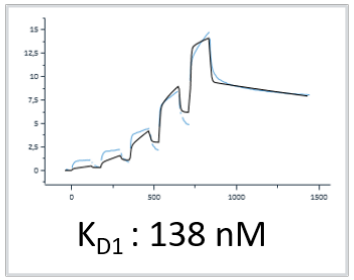
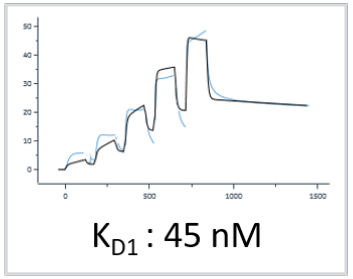
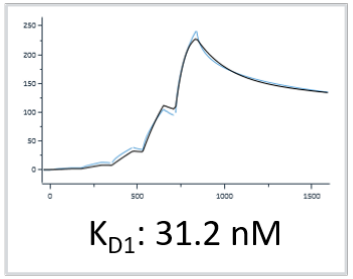
1. Full approval for lecanemab
   1. Standard review (11-15 mo)
      OR
   2. Accelerated assessment (8-10 mo)
2. Conditional approval with Clarity AD as post marketing requirement
   1. Standard review (11-15 mo)
      OR
   2. Accelerated assessment (8-10 mo)
3. Rejection and request of further data

Note: 1) Biologics license application, 2) Marketing authorisation application

BIOARCTIC

Lecanemab showed stronger binding than aducanumab to all Aβ species, especially to protofibrils

Surface Plasmon Resonance confirmed data from inhibition ELISA

	Monomers	Small protofibrils	Large protofibrils	Fibrils
Lecamemab	 K_{D1} : 3980 nM	 K_{D1} : 1.32 nM	 K_{D1} : 0.54 nM	 K_{D1} : 6.82 nM
aducanumab	 K_{D1} : >5000 nM	 K_{D1} : 138 nM	 K_{D1} : 45 nM	 K_{D1}: 31.2 nM
Fold difference:	**-**	**105**	**83**	**4.4**

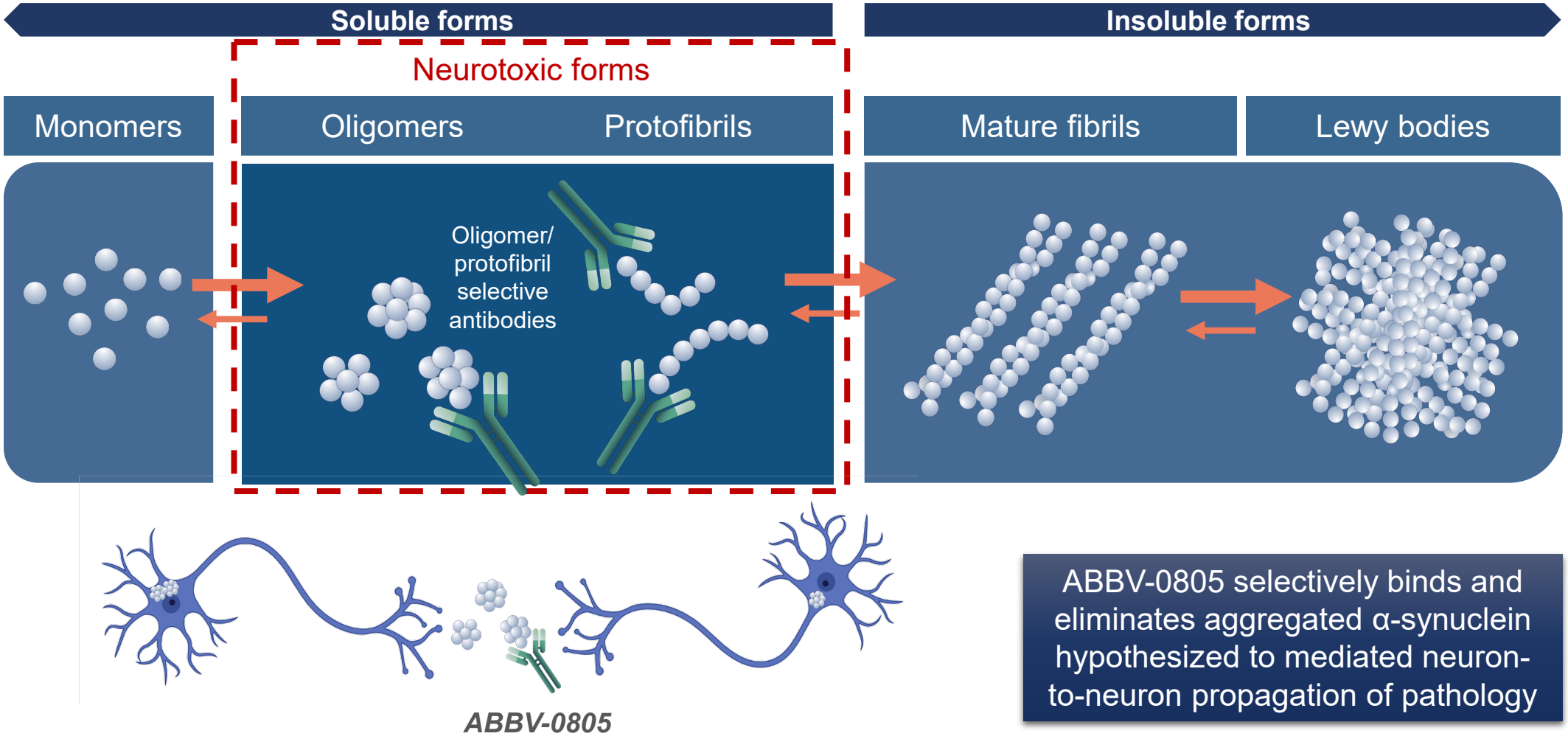
In SPR, the monomer affinities were determined by injecting monomers over captured antibodies. For protofibrils and fibrils, the antibodies were injected over immobilized Aβ species.

Presented by Lars Lannfelt at CTAD, December 7, 2019

BIOARCTIC

Parkinson’s disease

ABBV-0805: An α-synuclein antibody targeting aggregated misfolded α-synuclein targeted to reduce Neuron-to-neuron propagation of pathology



ABBV-0805 selectively binds and eliminates aggregated α-synuclein hypothesized to mediated neuron-to-neuron propagation of pathology

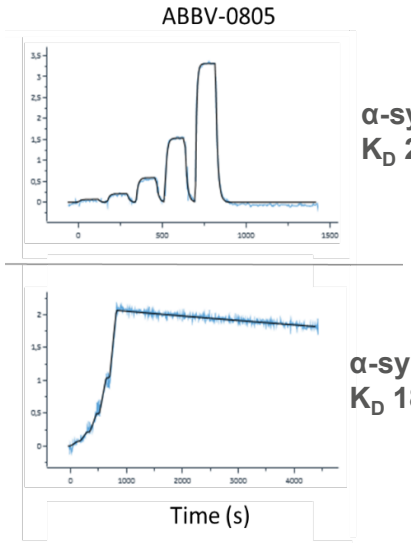
Source: Data presented at the International Congress of Parkinson's disease and movement disorders® (MDS), held virtually September 17 to 22, 2021

BIOARCTIC

ABBV-0805 selectively binds and eliminates aggregated α-synuclein leading to a delay in disease progression and increased lifespan in mice

UNIQUE SELECTIVITY PROFILE

Highly selective for toxic α-syn oligomers/protofibrils and very low affinity for monomers



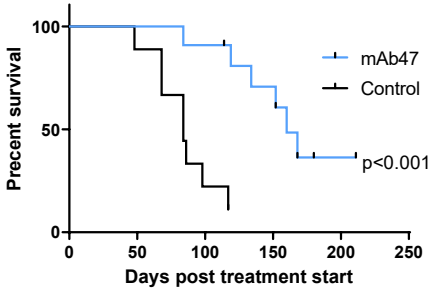
α-syn oligomers/PF
K_D 2200 nM

α-syn monomers
K_D 18 pM

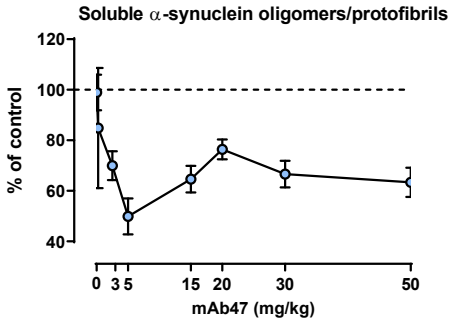
>100.000 x selectivity

PRE-CLINICAL PROOF OF CONCEPT

Delays disease progression and increases lifespan

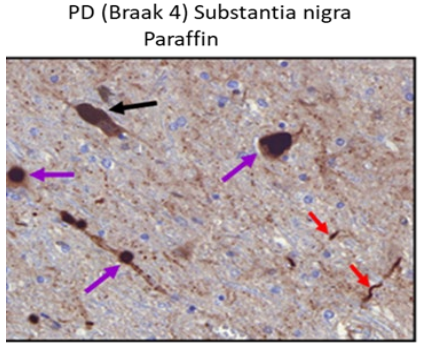


Reduction of toxic α-syn oligomers/protofibrils in brain



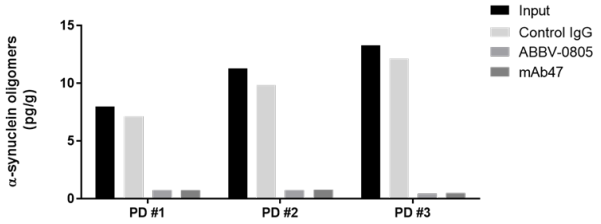
HUMAN TARGET BINDING

Human target binding of ABBV-0805 in Parkinson disease brain



Black: neuromelanin ,Purple: Lewy bodies, Red:Lewy neurites

ABBV-0805 immunodepletion of aggregated α-syn in Parkinson disease



Note: 1) Data presented at the International Congress of Parkinson's disease and movement disorders® (MDS), held virtually September 17 to 22, 2021

BIOARCTIC

ABBV-0805: potential disease modifying antibody for Parkinson's disease – in Phase 1 preparing for Phase 2

- ABBV-0805 selectively targets soluble toxic α-synuclein oligomers/protofibrils with a picomolar affinity and low affinity for monomers
- In α-synuclein transgenic mice, the murine version of ABBV-0805, mAb47, displayed dose-dependent reduction of both soluble and insoluble α-synuclein aggregates in brain, prevents α-synuclein spreading and prolonged lifespan
- Binding of ABBV-0805 to pathological α-synuclein was demonstrated in brains of Parkinson's disease patients both by IHC and immunodepletion
- Based on the strong pre-clinical findings, ABBV-0805 has been progressed into clinical development as a potential disease-modifying treatment for Parkinson's disease
- Overall, the human exposure and safety data being gathered in Phase I FIH-SAD study supports Phase II development of ABBV-0805 (T1/2: 30 days supporting Q28 days dosing)

  Ref: MDS 2021 poster 403 & 404 H Kalluri et al AbbVie Inc.

Source: Data presented at the International Congress of Parkinson's disease and movement disorders® (MDS), held virtually September 17 to 22, 2021

BIOARCTIC

AbbVie and BioArctic collaboration

Drug Discovery Today

ELSEVIER

feature

How partnership should work to bring innovative medicines to patients

Janice M. Twombly[1], jan@rhythmofbusiness.com, Johanna Fälting[2], Marco Giorgetti[3], Anna C. Maroney[3] and Gunilla Osswald[2]

Scientists increasingly find themselves working in bilateral drug development alliances. Alliances are conceptually simple, but operationally challenging, resulting in the value-eroding misalignment and delays that alliances often experience. This case study of an exemplary collaboration between a small biotech and a global biopharmaceutical company is based on 15 interviews and a lessons-learned workshop conducted with the principal alliance team members. We outline five repeatable practices identified as contributing to their success that other alliance teams can follow.

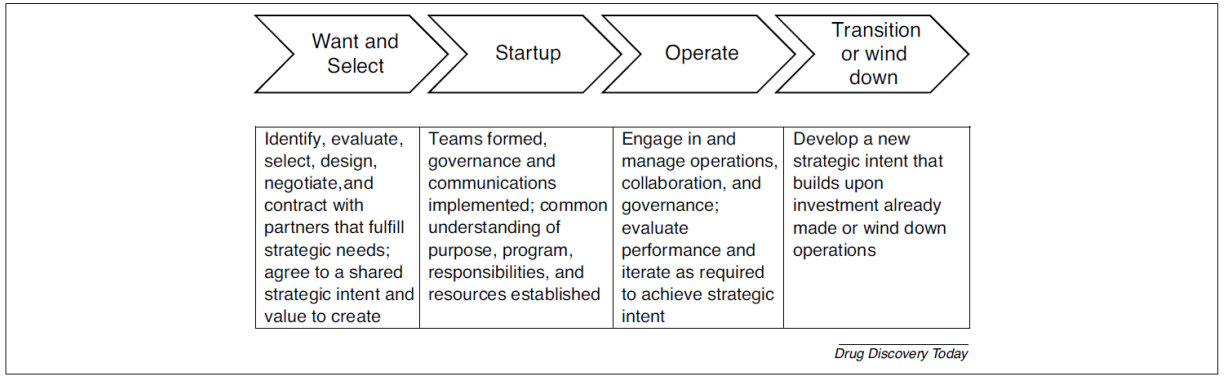
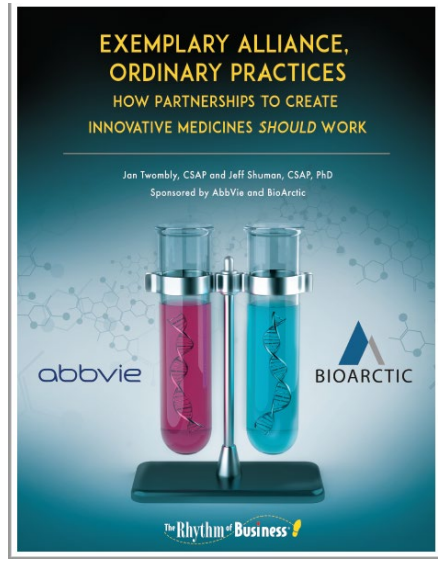


FIGURE 1

Simplified alliance lifecycle describing the focus of activities in each phase.



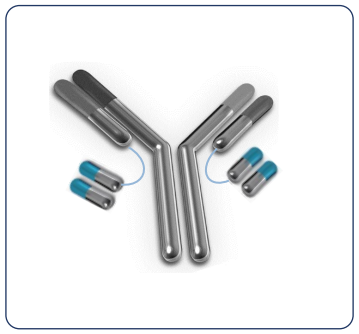
Five practices to drive successful outcomes in early-stage research alliances

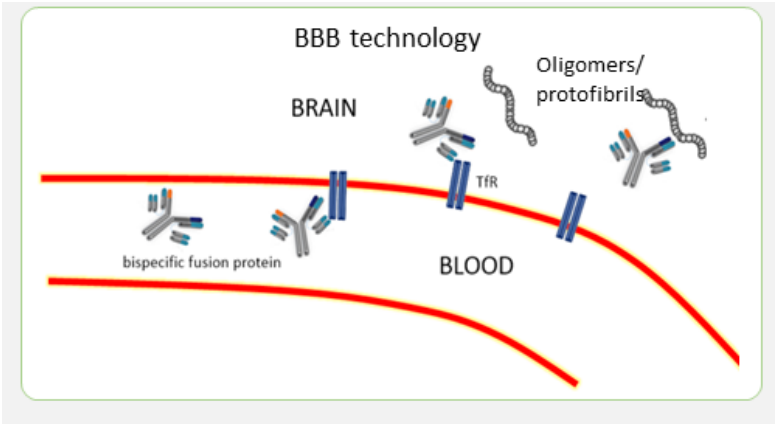
(1) Align on a strategic value assumption
(2) Plan to execute
(3) Start it right
(4) Meet regularly and often
(5) Transparent decision-making

BIOARCTIC

Blood-brain barrier

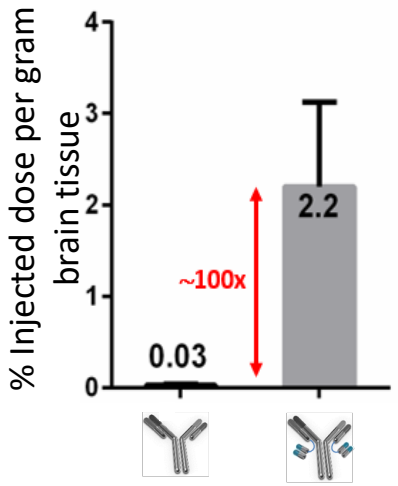
Blood-brain barrier transporter technology platform potential across multiple diseases with promising pre-clinical results



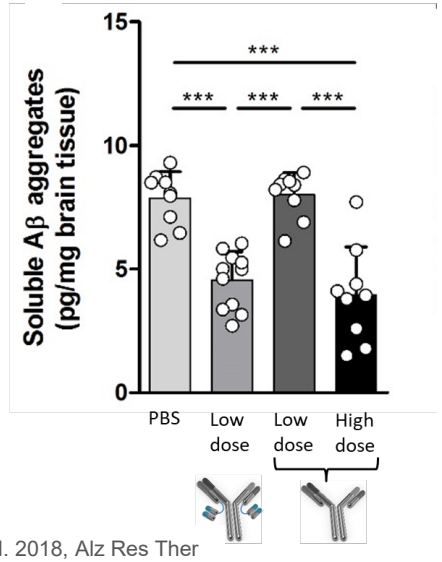


- Development of multi-specific antibodies with a transporter to facilitate passage across the Blood-brain barrier
- Collaboration with Uppsala University with a grant from Sweden's Innovation Agency, Vinnova
- Further investment in our Brain Transporter technology incl. recruitment of Distinguished Scientist Peo Freskgård and other senior scientists
- Second generation Brain Transporter platform under development

Substantially increased antibody brain uptake by BioArctic's Brain Transporter technology



Hultqvist et al 2017, Theranostics.



Syvänen et al. 2018, Alz Res Ther

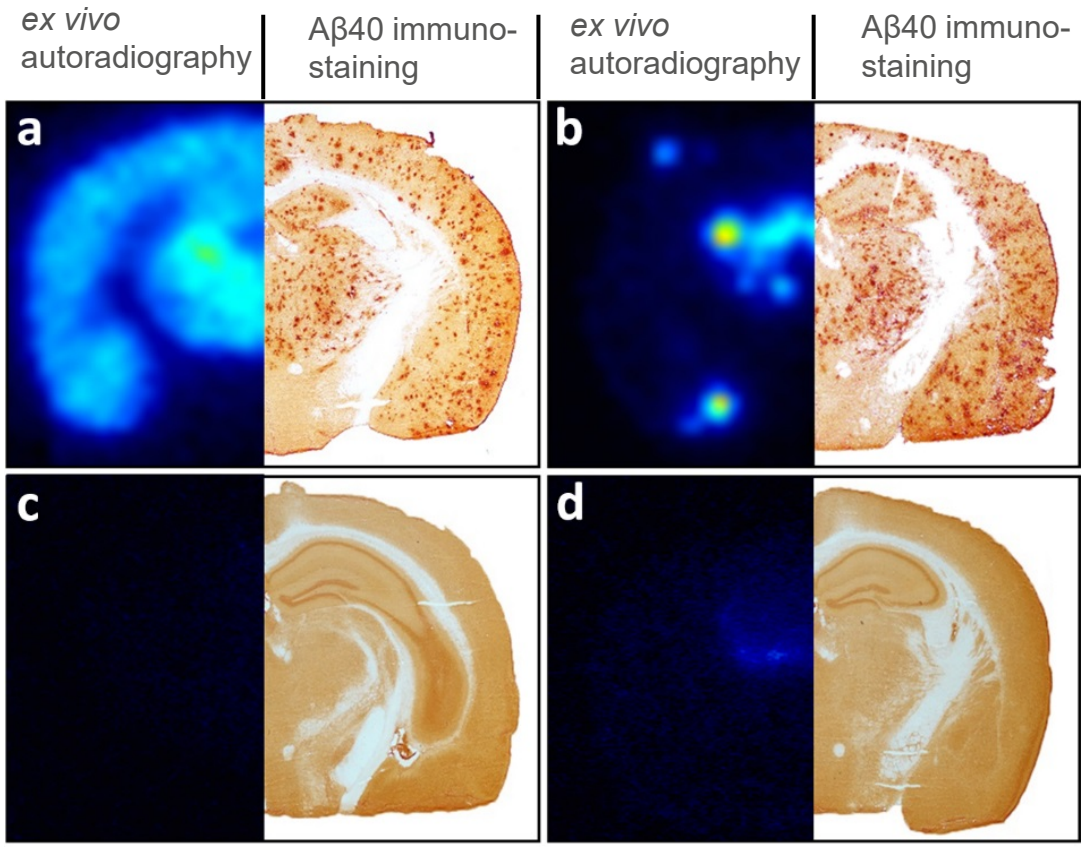
BIOARCTIC

Crossing the BBB enables direct and global access to brain targets

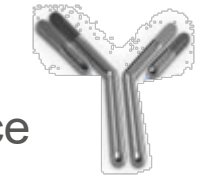
Target engagement promotes retention within the brain as shown by BioArctic's First-generation BBB technology

RmAb
158-scFv8D3
tg-ArcSwe mice

wt mice
no signal



RmAb158
tg-ArcSwe mice



wt mice
no signal

Conclusion

- First-generation BBB technology promote increased and global brain distribution of mAb158

Source: Syvänen et al Alz Res Ther 2018

BIOARCTIC

Today's agenda

1. BioArctic – a CNS disease frontrunner
2. Lecanemab – towards a breakthrough in Alzheimer's disease
3. Rich clinical and pre-clinical pipeline
4. Concluding remarks
5. **Appendix**
   - I. Additional clinical data
   - **II. IP**
   - III. Financial position

Strong IP Position in BioArctic's Business Areas

- More than 230 granted patents and 40 pending patent applications within 14 patent families
- Solid patent position for Alzheimer's Disease including BAN2401, with patent coverage until 2032, taking Patent Term Extension into account where available. Regulatory biologics data and market exclusivity 12 years in US and 10-11 years in Europe
- Solid patent position for Parkinson's Disease including ABBV-0805, with patent coverage at least until 2036, taking Patent Term Extension into account where available. Regulatory biologics data and market exclusivity 12 years in US and 10-11 years in Europe
- BioArctic holds a generally broad geographical patent coverage, including major markets (US, Canada, Australia, Europe, Japan and China)
- BioArctic's strategic partners also have active patent strategies with worldwide coverage

Note: As per 30 September 2021

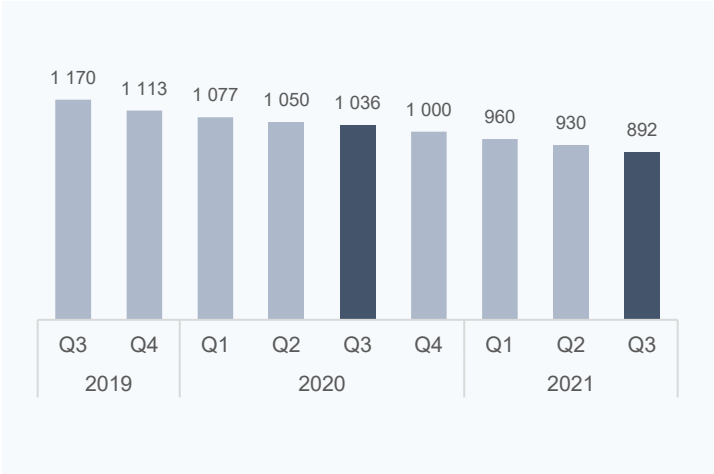
BIOARCTIC

Today's agenda

1. BioArctic – a CNS disease frontrunner
2. Lecanemab – towards a breakthrough in Alzheimer's disease
3. Rich clinical and pre-clinical pipeline
4. Concluding remarks
5. **Appendix**
   - I. Additional clinical data
   - II. IP
   - **III. Financial position**

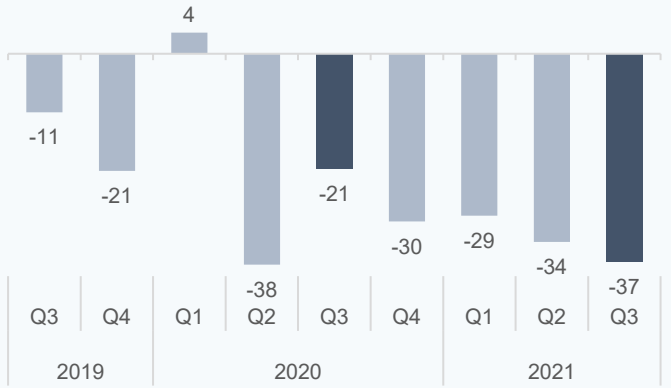
BioArctic has a strong financial profile

Cash Balance (MSEK)



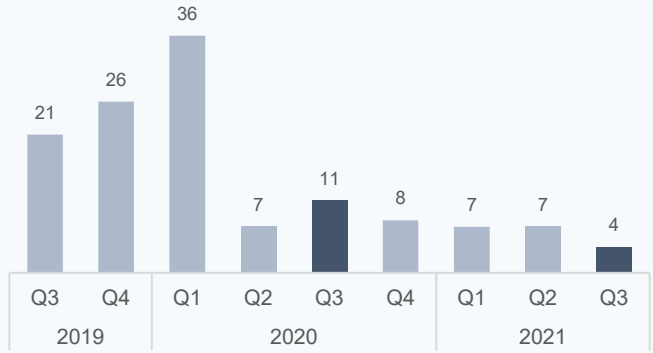
- Close to MSEK 900 (100 MUSD) in cash

Operating Profit/Loss (MSEK)



- Expected 2021 operating costs 160-190 MSEK

Net Revenues (MSEK)



- Significant funding from partner research collaborations and license agreements, as well as grants
- Total potential collaboration deal value[1)] of ~BSEK 8.9 (~1 BUSD)[1)] of which ~BSEK 1.8 (~0.2 BUSD)[1)] received
- Additional future royalty potential
- Milestone payments one-time nature explain fluctuations in financial results

Note: As of September 30, 2021

BIOARCTIC

Overview of shareholders and share price

Overview of ownership

Shareholder	# shares	Capital (%)	Votes (%)
Lars Lannfelt	31,268,050	35.5%	50.1%
Pär Gellerfors	20,846,299	23.7%	33.4%
Fjärde AP-fonden	4,300,000	4.9%	2.0%
Tredje AP-fonden	2,916,568	3.3%	1.3%
Unionen	2,391,835	2.7%	1.1%
Swedbank Robur Fonder	2,061,877	2.3%	0.9%
Gladiator	1,715,748	1.9%	0.8%
Investment AB Öresund	1,330,000	1.5%	0.6%
Wellington Management	1,266,319	1.4%	0.6%
Handelsbanken Fonder	1,236,703	1.4%	0.6%
Top 10 shareholders	**69,333,399**	**78.7%**	**91.4%**
Others	18,726,586	21.3%	8.6%
Total	**88,059,985**	**100%**	**100%**

Source: FactSet (As of 12 November 2021)

Share price development since IPO