



# BioArctic AB

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# Company presentation

RedEye CNS Event, October 4, 2018



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# Helping Patients with Disorders in the Central Nervous System by Developing Innovative Treatments

## Alzheimer's Disease



Three key areas with high unmet medical needs – all lacking effective treatments today

Disease modifying treatment in Alzheimer's and Parkinson's Disease – areas with huge and growing markets due to aging populations

BAN2401 Phase 2b study in early AD in collaboration with Eisai – first late stage study demonstrating potential disease modifying effect on both cognition and biomarkers

## Parkinson's Disease



BAN0805 for PD in collaboration with AbbVie – preparing for clinical development and IND in the U.S.

Unique regenerative treatment for patients with Complete Spinal Cord Injuries in Phase 1/2

## Complete Spinal Cord Injury



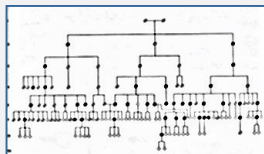
Attractive combination of fully financed partner projects and innovative pipeline with substantial market and out-licensing potential

Strong science based research and highly educated engaged teams with vast experience in drug development and great track record of high quality deliverables

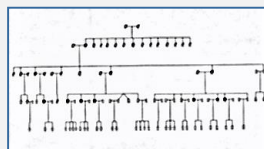
# Long History of Research Achievements Within Disorders of the Central Nervous System (CNS)

## Background to founding

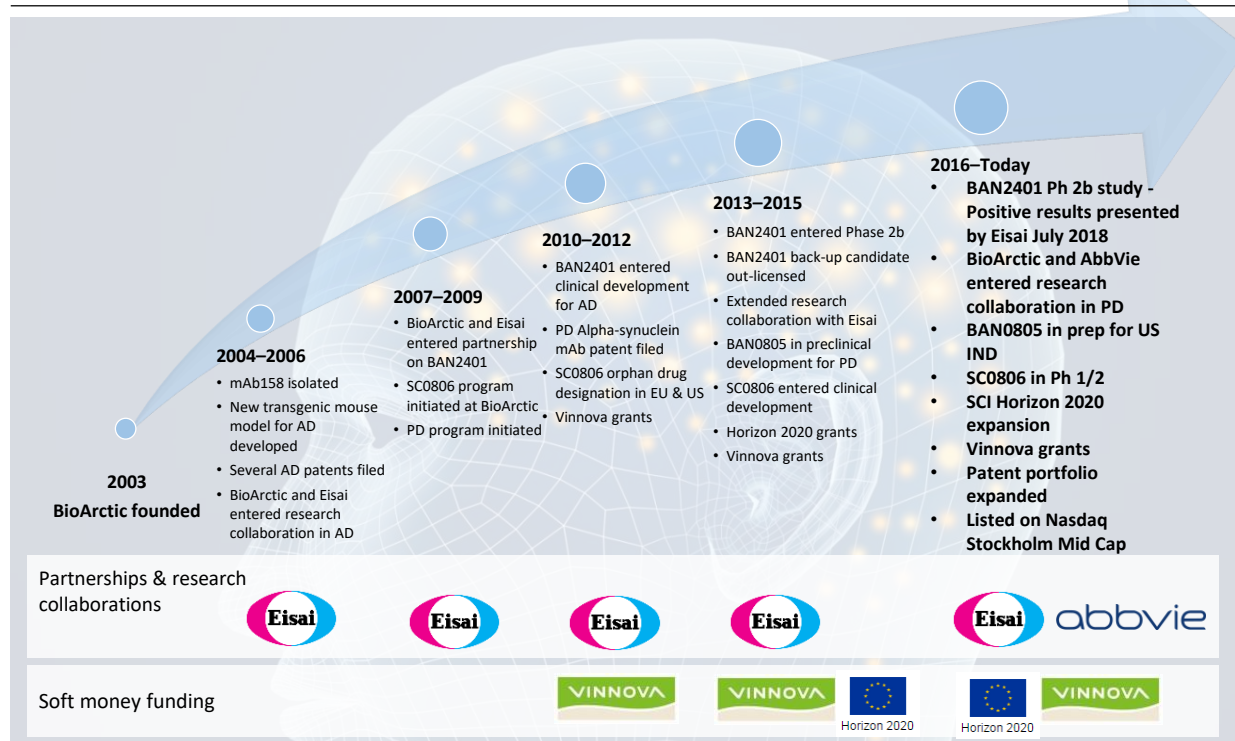
- ▲ Scientific discoveries by Professor Lars Lannfelt laid the foundation for BioArctic
- ▲ **The Swedish mutation** demonstrated for the first time in a clinical setting that amyloid-beta ( $A\beta$ ) peptide initiates the disease



- ▲ **The Arctic mutation** revealed that soluble aggregated forms of  $A\beta$ , oligomers and protofibrils, are toxic and likely driving the disease



## Company history



Source: Company data

**Successful collaborations with pharmaceutical industry validating potential value and commercialization potential for BioArctic**

# Long-standing and Extensive Partnerships

## Eisai collaboration and license agreements Alzheimer's Disease



### Description of agreements

- Two research collaborations – disease modifying therapies for AD – resulted in two licenses for A $\beta$  oligomer/protofibril antibodies: BAN2401 and BAN2401 Back-up
- Third research collaboration – new target as a disease modifying therapy for AD

### Milestone / royalty potential

- Total aggregated value of the research collaborations and license agreements is approx. EUR 218m in signing fee and milestones, plus high single digit royalties
- BioArctic has received approx. EUR 47m for the research collaborations, signing fees and milestones

## AbbVie collaboration agreement Parkinson's Disease



### Description of agreements

- Research collaboration – alpha-synuclein antibodies as disease modifying therapies for PD incl. BAN0805 to IND, follow-up compounds and diagnostic
- Option for AbbVie for a license to develop and commercialize the antibodies




### Milestone / royalty potential

- Total potential value of the agreement is up to USD 755m incl. an up-front fee, option exercise fee, and success-based milestones plus tiered royalties
- BioArctic has received an USD 80m up-front payment for the research collaboration

***Strategic collaborations with pharmaceutical industry validating potential value and commercialization potential for BioArctic with proven track record of delivering on research collaborations***

# Strategic Partnerships and Cutting-Edge Proprietary R&D

per June 30, 2018

	PRODUCT CANDIDATE	INDICATION	PARTNER	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
NEURODEGENERATIVE DISEASES	<b>BAN2401</b> anti-A $\beta$ antibody	Alzheimer's disease	 <sup>1)</sup>	[Progress bar from Discovery to Phase 2]				
	<b>BAN2401</b> anti-A $\beta$ antibody	Down's syndrome <sup>2)</sup> Traumatic Brain Injury	—	[Progress bar from Discovery to Preclinical]				
	<b>BAN2401 back-up</b> anti-A $\beta$ antibody	Alzheimer's disease		[Progress bar from Discovery to Preclinical]				
	<b>AE1501</b> undisclosed information	Alzheimer's disease		[Progress bar from Discovery to Preclinical]				
	<b>AD1502</b> undisclosed information	Alzheimer's disease	—	[Progress bar from Discovery to Preclinical]				
	<b>AD1503</b> undisclosed information	Alzheimer's disease	—	[Progress bar from Discovery to Preclinical]				
	<b>BAN0805</b> anti- $\alpha$ -synuclein antibody	Parkinson's disease	abbvie	[Progress bar from Discovery to Preclinical]				
	<b>PD1601</b> anti- $\alpha$ -synuclein antibody	Parkinson's disease	abbvie	[Progress bar from Discovery to Preclinical]				
	<b>PD1602</b> anti- $\alpha$ -synuclein antibody	Parkinson's disease	abbvie	[Progress bar from Discovery to Preclinical]				
DIAGNOSTICS & TECHNOLOGY	<b>Imaging and biochemical biomarkers</b> A $\beta$	Alzheimer's disease	—	[Progress bar from Discovery to Preclinical]				
	<b>Imaging and biochemical biomarkers</b> $\alpha$ -synuclein	Parkinson's disease	abbvie	[Progress bar from Discovery to Preclinical]				
	<b>BBB-technology</b> blood-brain barrier	Multiple application areas	—	[Progress bar from Discovery to Preclinical]				
SPINE	<b>SC0806</b> FGF1/medical device	Complete Spinal Cord Injury	—	[Progress bar from Discovery to Phase 1]				

<sup>1)</sup> Partner with Eisai on BAN2401 for treatment of AD. Since 2014, Eisai partnered with Biogen in AD

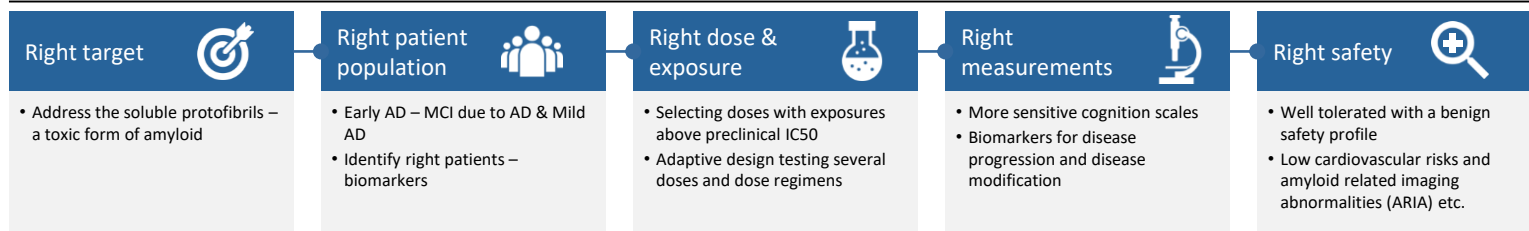
<sup>2)</sup> Dementia and cognitive impairment associated with Down's syndrome and Traumatic Brain Injury

Source: company data

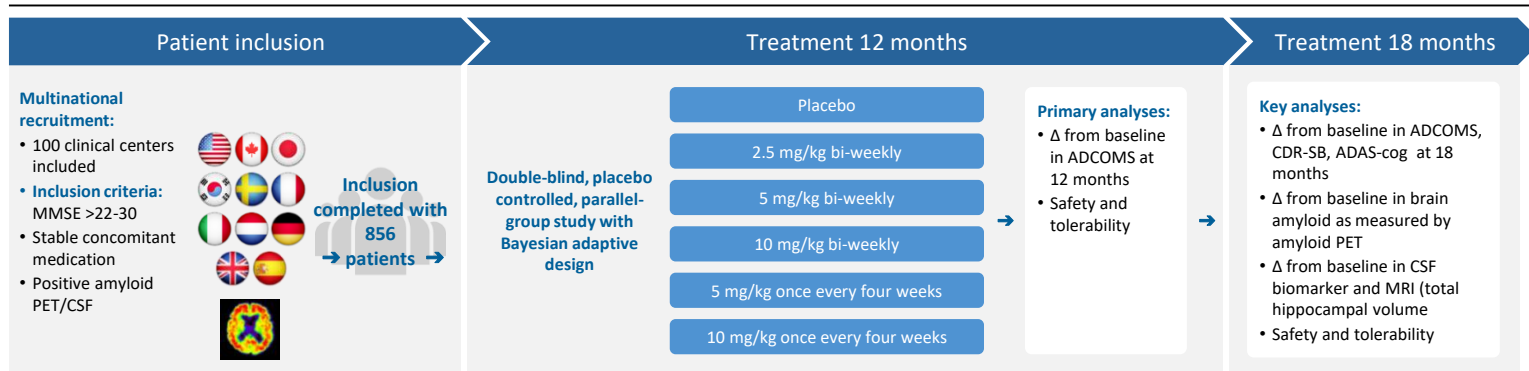
# BAN2401 – Learnings from Previous Clinical Trials in AD Incorporated in Phase 2b Study Design

## Positive 18 Month Results reported in July 2018

### Important parameters



### Phase 2b study design



**BAN2401 18 months treatment demonstrated an effect on both cognition and biomarkers with a good tolerability profile**

**Completion of study after 18 months treatment and 3 months follow-up - Q4 2018**

Source: Company information

Note: ADCOMS = Alzheimer's Disease Composite Score, an evaluation tool developed by Eisai

# BAN2401 Showed Effect on Clinical Parameters and Biomarkers with Good Tolerability in Early AD Patients - I

## Clinical effect:

- ADCOMS
- ADAS-Cog
- CDR-SB

- **ADCOMS**, cognition scale (the key efficacy parameter) showed statistically significant slower decline of 30% ( $p=0.034$ ) with 10 mg/kg twice a month (highest dose) at 18 months
- ADCOMS showed effect already at 6 months – as well as after 12 and 18 months treatment – with the highest dose
- **ADAS-Cog** (well-known cognition scale) showed statistically significant slower decline of 47% ( $p=0.017$ ) with 10 mg/kg twice a month at 18 months
- **CDR-SB** (cognition and function scale) showed slower decline of 26% ( $p>0.05$ ) with 10 mg/kg twice a month at 18 months

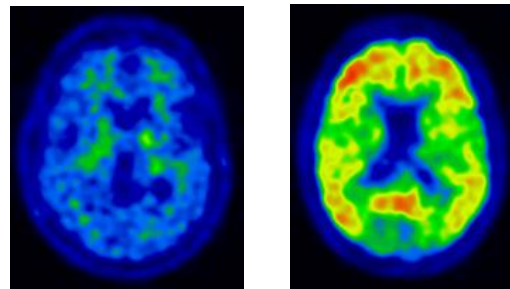


# BAN2401 Showed Effect on Clinical Parameters and Biomarkers with Good Tolerability in Early AD Patients - II

## Biomarkers:

- Amyloid PET
- CSF Aβ, t-tau

- **Amyloid PET:** BAN2401 reduced brain amyloid-beta dose-dependent and statistically significant, amyloid decreased ~70 units (from 74.5 at baseline to 5.5 at 18 months for the top dose) with Centiloid scale ( $p < 0.0001$ )
- Amyloid PET visual read showed dose-dependent and statistically significant improvements and 81% of the patients in the BAN2401 top dose converted from amyloid positive to amyloid negative
- **CSF:** Aβ increased dose-dependent and statistically significant and t-tau decreased for the two top doses
- Biomarkers support a disease modifying effect of BAN2401



*Brain images provided by PET-Centre, Uppsala University Hospital, Sweden, showing a normal brain (left) and an Alzheimer brain (right).  
The images are illustrative examples of PET scans and are not images from the BAN2401 Phase 2b study.*

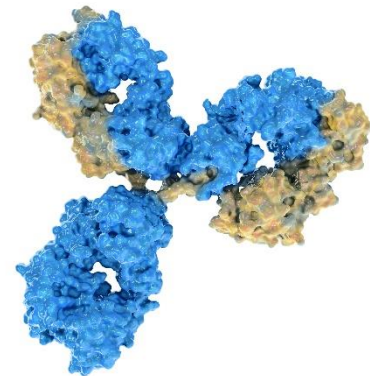
# BAN2401 Showed Effect on Clinical Parameters and Biomarkers with Good Tolerability in Early AD Patients - III

## Safety & tolerability

- BAN2401 was **well-tolerated** with infusion reactions and ARIA as the most common side effects (mostly mild to moderate)
- ARIA-E incidence:
  - <10% at any dose
  - <15% in APOE4 carriers at the highest dose
  - ~90% of ARIA-E cases were asymptomatic

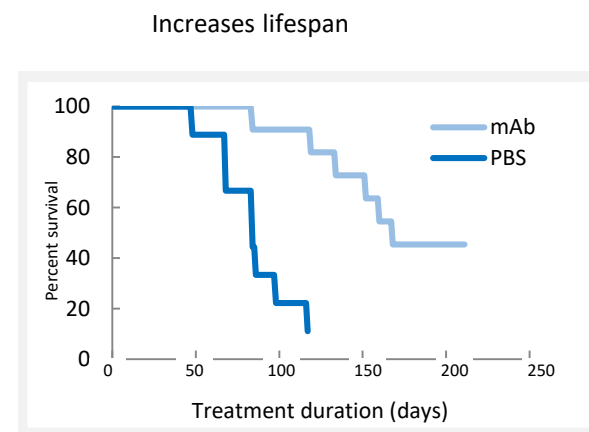
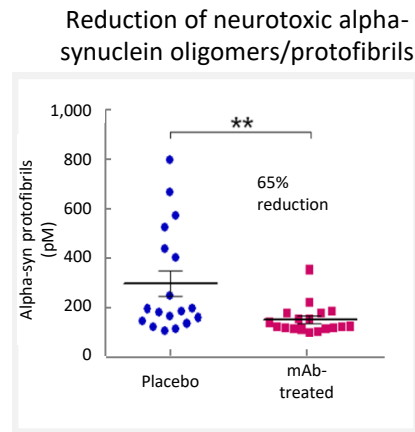
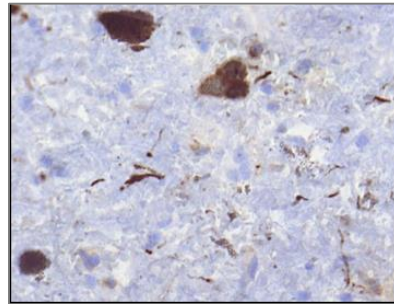
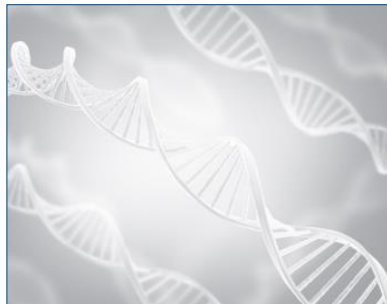
## BAN2401 – Next Steps

- Eisai is currently preparing for interactions with regulatory agencies regarding the future BAN2401 program
- Further analyses are on-going and will be presented by Eisai at CTAD (11th Clinical Trials on Alzheimer’s Disease) on Oct 24-27, 2018 in Barcelona, Spain
- The study will be completed in Q4 2018 and includes a further 3 months follow-up after completion of 18 months of treatment (at 21 months)



# BAN0805 – Groundbreaking Disease Modifying Drug in PD with Rationale for Selective Targeting of Alpha-synuclein Oligomers/Protofibrils

## Rationale for targeting alpha-synuclein



Alpha-synuclein mutations lead to PD or Dementia with Lewy Bodies and are associated with increased oligomer/protofibril formation

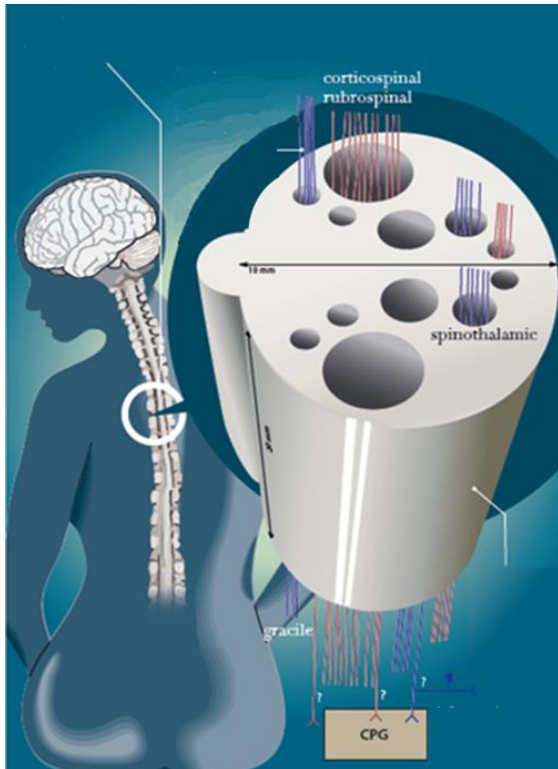
Alpha-synuclein deposition is a hallmark of PD pathophysiology and alpha-synuclein oligomers/protofibrils are elevated in PD

**Oligomer/protofibril selective antibody** reduces neurotoxic alpha-synuclein oligomer/protofibril levels, delays disease progression and increases life-span in a PD mice model

# SC0806 – Unique Regenerative Treatment of Complete SCI

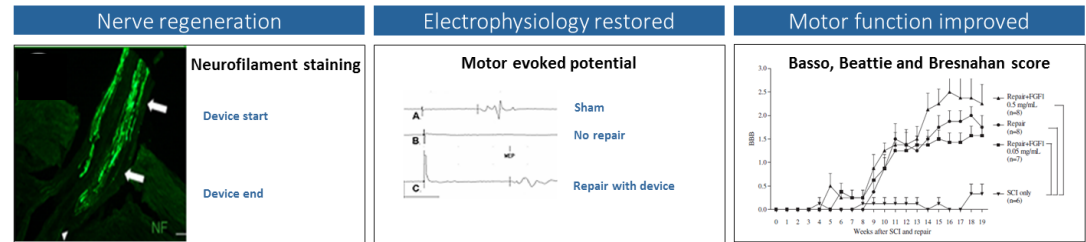
## SC0806 – Regenerative Treatment of Complete SCI

## Treatment Rationale



### SC0806 makes nerve regeneration possible

FGF1 activated by heparin	<ul style="list-style-type: none"> <li>Stimulation of central axon outgrowth</li> <li>Decreases gliosis</li> </ul>
Peripheral nerve autografts	<ul style="list-style-type: none"> <li>Optimal regeneration environment</li> </ul>
Biodegradable device	<ul style="list-style-type: none"> <li>Provides sustained release of FGF1</li> <li>Positioning of nerve grafts from white to gray matter</li> </ul>



### Preclinical Proof of Concept shown in rats

- Rat experiments demonstrate nerve regeneration, restored electrophysiology and motor function
- The motor evoked potential (MEP) has been restored in rats with resected spinal cords

Source: Nordblom et al. Restorative Neurology and Neuroscience 30 (2012) 91–102

# SC0806 – Unique Regenerative Treatment of Complete SCI

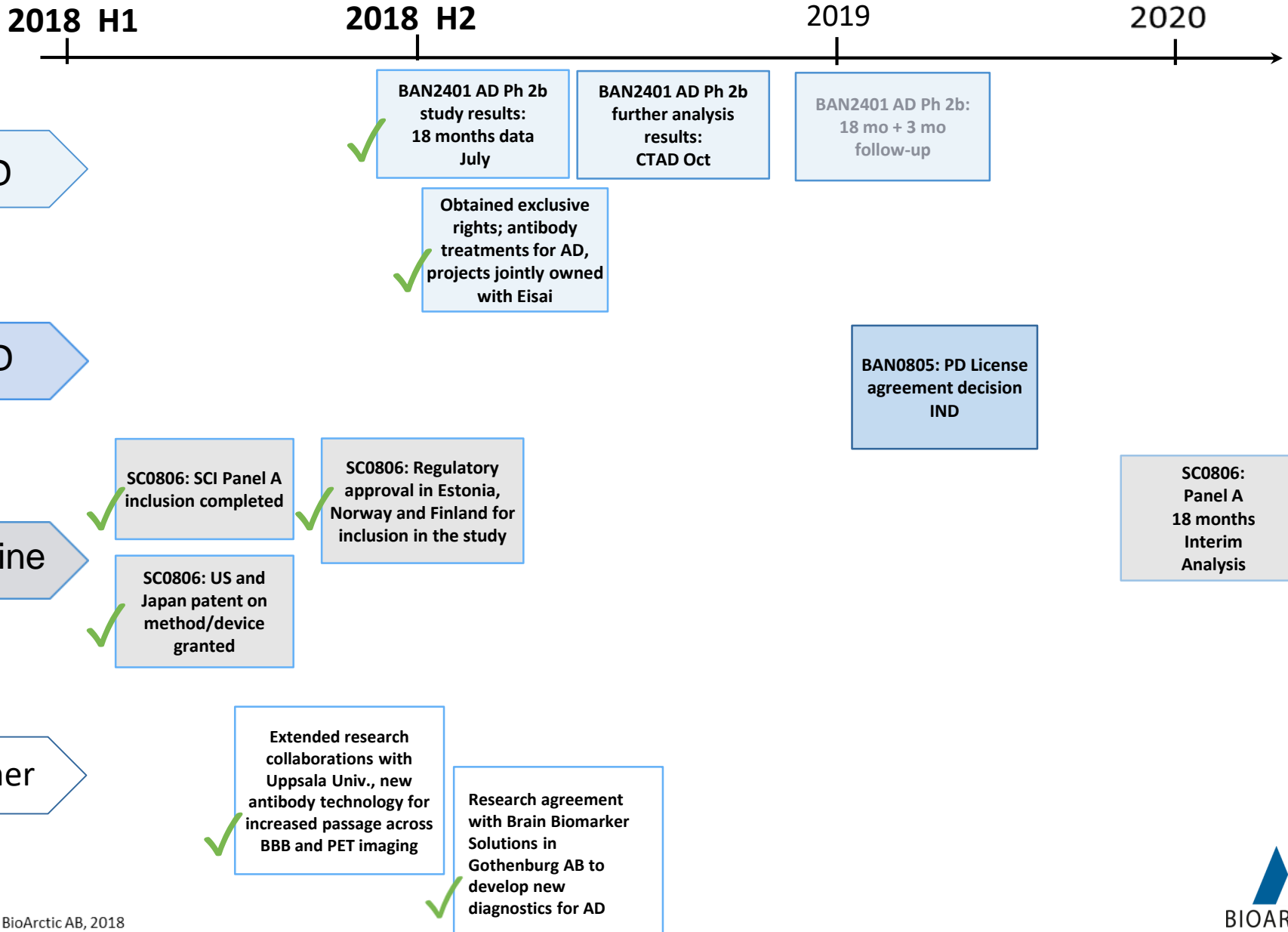
## The Lokomat™ used in the Rehabilitation



## Project Status

- Clinical Phase 1/2 trial ongoing with SC0806 in patients with Complete Spinal Cord Injury
  - Surgery in Sweden
  - Rehabilitation 18 months with Lokomat™ in Sweden, Estonia, Finland and Norway
  - Patients receiving SC0806 treatment are given the option of 12 months additional participation in an extension study
  - 9 patients included in Panel A (6 treated with SC0806 and 3 control patients)
  - Interim analysis planned Q4 2019/Q1 2020
- Orphan Drug designation in US and EU – granting 7 and 10 years exclusivity, respectively
- EU Horizon 2020 research and innovative program Grant Agreement No. 643853 of MEUR 6.4

# Recent & Anticipated News Flow



Gunilla Osswald, PhD, CEO



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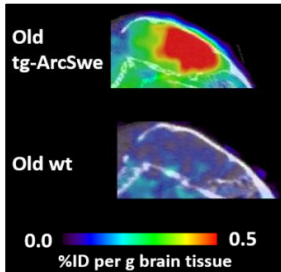
- ▶ **STO:BIOA B**  
BioArctic's B-share is listed on Nasdaq Stockholm Mid Cap
- ▶ **Next report**  
Q3 November 8, 2018
- ▶ **IR contact**  
Christina Astrén  
+46 8 695 69 30 [ir@bioarctic.se](mailto:ir@bioarctic.se)



# Several Novel Approaches to Improve Diagnostics and Treatment

## Imaging and biochemical biomarkers in AD

### A $\beta$ protofibril PET tracer



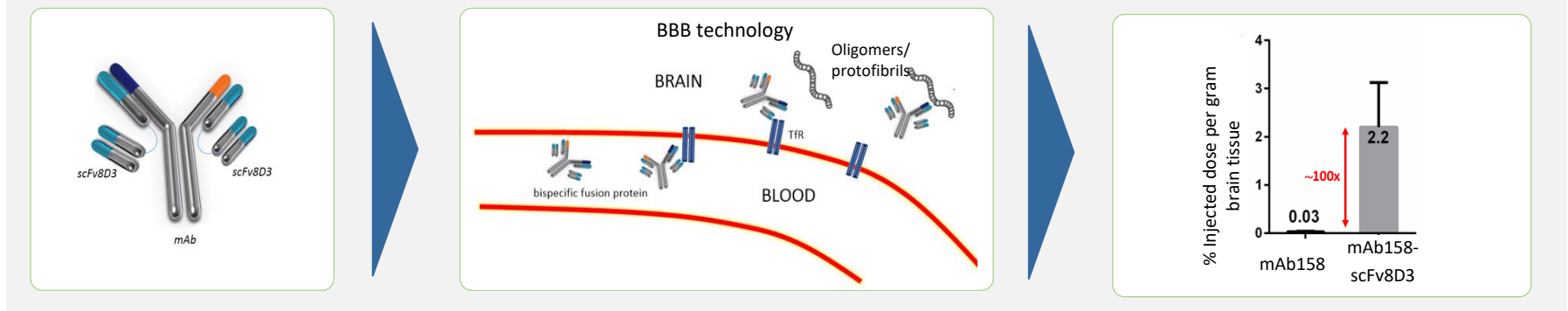
- PET with an antibody-based ligand
- Binding to A $\beta$  oligomers/protofibrils
- Has short half-life
- Improved BBB penetration

### A $\beta$ protofibril biochemical biomarker



- Sensitive biochemical method for A $\beta$  measurement in development is of great clinical importance

## Blood-brain barrier technology



Source: Sehlin et al 2016 Nature Communications. Hultqvist et al 2017, Theranostics.

**Substantially increased antibody brain uptake by BioArctic's brain shuttle technology**