BIOARCTIC AB (PUBL)
NASDAQ STOCKHOLM: BIOA B

Interim Report January-September 2019

Stockholm, October 24, 2019

Gunilla Osswald, PhD, CEO

Jan Mattsson, CFO

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BIOARCTIC

BioArctic – a unique Swedish biopharma company

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** generating **innovative projects**

Attractive and well-balanced project portfolio 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

Well-financed with BSEK >1 (MUSD >100) in cash, **positive financial results** during the last six years and **valuable collaboration agreements** totaling BSEK 9.3 (BUSD ~1) plus royalties

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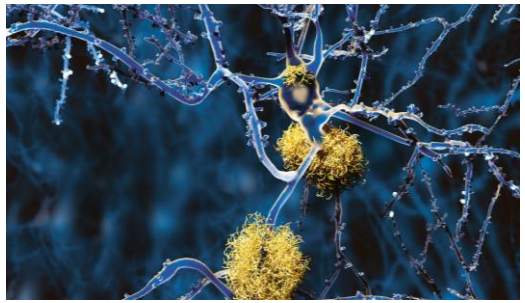
Significant progress in all areas 2019 year to date

ALZHEIMER'S DISEASE



BAN2401

- Phase 3 confirmatory study in early Alzheimer's disease started by Eisai (milestone received MEUR 15)
- Phase 2b open label extension study ongoing
- ACTC and Eisai prepare for secondary prevention study
- Data presented at AAIC July 2019

Discovery stage programs

- Progressed according to plan

PARKINSON'S DISEASE

ABBV-0805 (BAN0805)

- IND produced by BioArctic approved by FDA
- Phase 1 study started by AbbVie

Discovery stage projects

- Progressed according to plan in AbbVie collaboration

COMPLETE SPINAL CORD INJURY

SC0806

- Phase 1 safety evaluated and Phase 2 started

DIAGNOSTICS AND TECHNOLOGY

Blood Brain Barrier Technology Platform

- Vinnova grant of MSEK 10 received together with Uppsala University
- Internationally renowned scientist recruited

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Attractive and well-balanced project portfolio combines fully-financed partner projects and cutting-edge proprietary projects

	Product candidate	Indication	Partner	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Neurodegenerative Diseases	**BAN2401:** anti-Aβ antibody	Alzheimer's Disease	Eisai / Biogen[1]					
	BAN2401: anti-Aβ antibody	Down's Syndrome[2] Traumatic Brain Injury[2]	—					
	BAN2401 BACK-UP: anti-Aβ antibody	Alzheimer's Disease	Eisai					
	AD1801: Undisclosed information	Alzheimer's Disease	—					
	AD1502: Undisclosed information	Alzheimer's Disease	—					
	AD1503: Undisclosed information	Alzheimer's Disease	—					
	ABBV-0805[3]: anti-α-synuclein antibody	Parkinson's Disease	abbvie					
	PD1601: anti-α-synuclein antibody	Parkinson's Disease	abbvie					
	PD1602: anti-α-synuclein antibody	Parkinson's Disease	abbvie					
Diagnostics & Technology	**IMAGING AND BIOCHEMICAL BIOMARKERS:** Aβ	Alzheimer's Disease	—					
	IMAGING AND BIOCHEMICAL BIOMARKERS: α-synuclein	Parkinson's Disease	abbvie					
	BBB-TECHNOLOGY: blood-brain barrier	Multiple application areas	—					
Spine	**SC0806:** FGF1/medical device	Complete Spinal Cord Injury	—					

as of September 30, 2019

1) Eisai is BioArctic's partner for BAN2401 for treatment of Alzheimer's disease. Eisai partnered with Biogen for BAN2401 in 2014
2) Dementia and cognitive impairment associated with Down's syndrome and Traumatic Brain Injury
3) AbbVie in-licensed BAN0805 in late 2018 and will continue to develop BAN0805, now with the designation ABBV-0805

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Long-standing and extensive partnerships

Alzheimer's disease

Partner Track Record

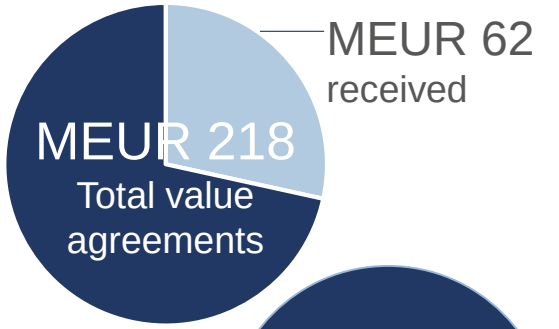
Eisai

Discovered and developed world's best-selling medicine for symptoms in Alzheimer's

Aricept donepezil HCl tablet

Industry-leading pipeline in dementia area

Collaboration and license



Royalties
High single digit %

- BioArctic retains rights to BAN2401 in other indications and option to market in the Nordics

Parkinson's disease

Partner Track Record

abbvie

World's all-time best-selling medicine (BUSD 20)

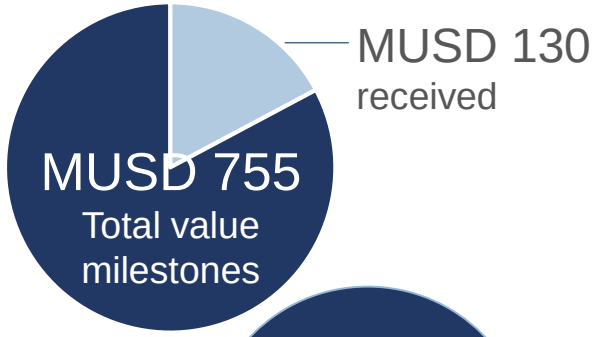
HUMIRA® adalimumab

10 different indications in immunology

Approved product for symptoms associated with Parkinson's disease

Duopa carbidopa/levodopa

Collaboration and license



Royalties
Tiered %

- AbbVie global rights to alpha-synuclein portfolio for all indications

Sources: Eisai, AbbVie and BioArctic corporate information

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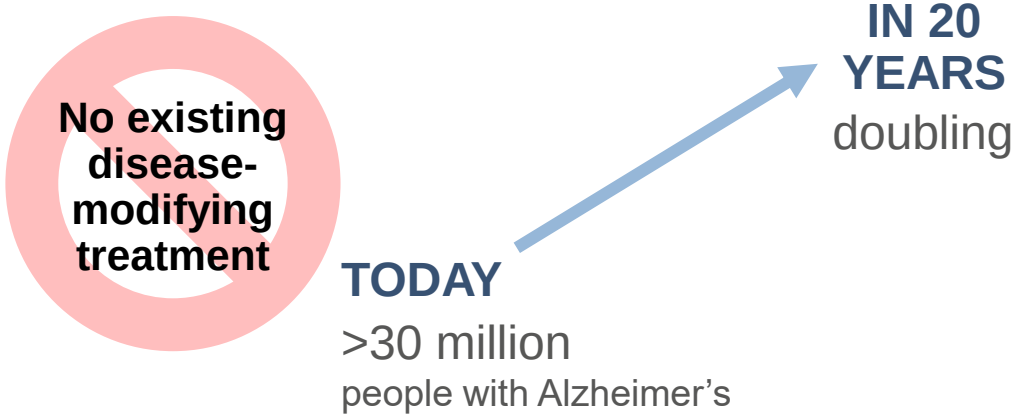
BAN2401: potential disease modifying antibody for Alzheimer's disease with positive Phase 2b results now in Phase 3

High unmet medical need



BAN2401 unique profile

Unique and targeted binding profile

- Highly selective for toxic forms of misfolded Abeta (oligomers/protofibrils)

Unique clinical fingerprint

- Rapid onset of clinical effect
- Consistent effects
- No titration required due to low frequency of ARIA–E

BAN2401 has positive Phase 2b results

- **Large trial:** 856 early Alzheimer's patients
- **Consistent effects** on clinical outcomes, imaging and neurodegenerative biomarkers
- **Effect increase over time**
- **Good safety profile**

Eisai announced three clinical trials underway

1. **Confirmatory Phase 3 study** ("Clarity AD") started
   - Primary endpoint final readout expected 2022
2. Phase 2b open label extension study ongoing
3. Secondary prevention study ("A45 Study") in planning to start 2020

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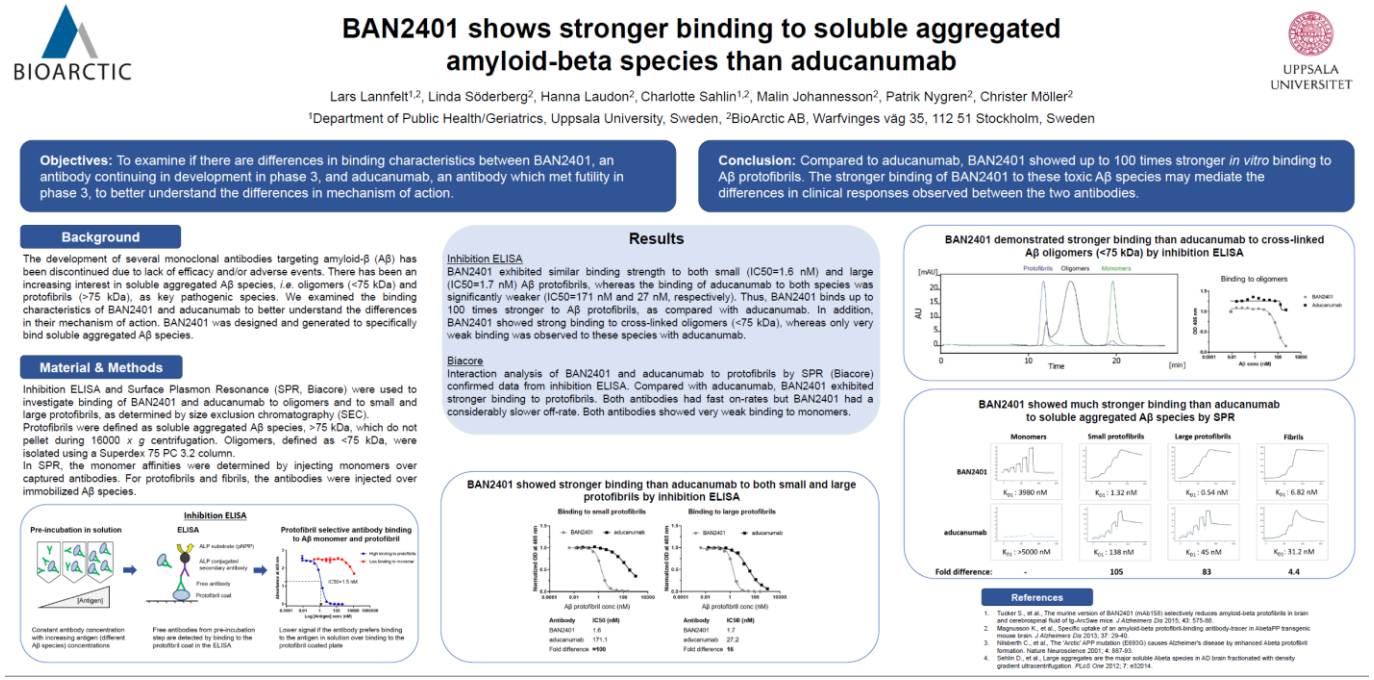
BAN2401 distinctive binding profile compared with aducanumab

BAN2401 specifically designed and generated to bind to toxic soluble aggregated forms of amyloid-beta

- Selectivity for protofibrils
  - More than 1000-fold selectivity versus monomers
  - About 10-fold selectivity versus fibrils
- BAN2401 binding profile distinctive from aducanumab
  - BAN2401 preferential binding to protofibrils and oligomers versus aducanumab preferential binding to fibrils
  - BAN2401 up to 100-fold stronger binding to protofibrils and oligomers versus aducanumab



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BAN2401 shows stronger binding to soluble aggregated amyloid-beta species than aducanumab

UPPSALA UNIVERSITET

Lars Lannfelt[1,2], Linda Söderberg[2], Hanna Laudon[2], Charlotte Sahlin[1,2], Malin Johannesson[2], Patrik Nygren[2], Christer Möller[2]

[1]Department of Public Health/Geriatrics, Uppsala University, Sweden, [2]BioArctic AB, Warfvinges väg 35, 112 51 Stockholm, Sweden

Objectives: To examine if there are differences in binding characteristics between BAN2401, an antibody continuing in development in phase 3, and aducanumab, an antibody which met futility in phase 3, to better understand the differences in mechanism of action.

Conclusion: Compared to aducanumab, BAN2401 showed up to 100 times stronger *in vitro* binding to Aβ protofibrils. The stronger binding of BAN2401 to these toxic Aβ species may mediate the differences in clinical responses observed between the two antibodies.

Background

The development of several monoclonal antibodies targeting amyloid-β (Aβ) has been discontinued due to lack of efficacy and/or adverse events. There has been an increasing interest in soluble aggregated Aβ species, *i.e.* oligomers (<75 kDa) and protofibrils (>75 kDa), as key pathogenic species. We examined the binding characteristics of BAN2401 and aducanumab to better understand the differences in their mechanism of action. BAN2401 was designed and generated to specifically bind soluble aggregated Aβ species.

Material & Methods

Inhibition ELISA and Surface Plasmon Resonance (SPR, Biacore) were used to investigate binding of BAN2401 and aducanumab to oligomers and to small and large protofibrils, as determined by size exclusion chromatography (SEC).
Protofibrils were defined as soluble aggregated Aβ species, >75 kDa, which do not pellet during 16000 *x g* centrifugation. Oligomers, defined as <75 kDa, were isolated using a Superdex 75 PC 3.2 column.
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.

Inhibition ELISA

Pre-incubation in solution | ELISA | Protofibril selective antibody binding to Aβ monomer and protofibril

Constant antibody concentration with increasing antigen (different Aβ species) concentrations

Free antibodies from pre-incubation step are detected by binding to the protofibril coat in the ELISA

Lower signal if the antibody prefers binding to the antigen in solution over binding to the protofibril coated plate

Results

Inhibition ELISA

BAN2401 exhibited similar binding strength to both small (IC50=1.6 nM) and large (IC50=1.7 nM) Aβ protofibrils, whereas the binding of aducanumab to both species was significantly weaker (IC50=171 nM and 27 nM, respectively). Thus, BAN2401 binds up to 100 times stronger to Aβ protofibrils, as compared with aducanumab. In addition, BAN2401 showed strong binding to cross-linked oligomers (<75 kDa), whereas only very weak binding was observed to these species with aducanumab.

Biacore

Interaction analysis of BAN2401 and aducanumab to protofibrils by SPR (Biacore) confirmed data from inhibition ELISA. Compared with aducanumab, BAN2401 exhibited stronger binding to protofibrils. Both antibodies had fast on-rates but BAN2401 had a considerably slower off-rate. Both antibodies showed very weak binding to monomers.

BAN2401 showed stronger binding than aducanumab to both small and large protofibrils by inhibition ELISA

Binding to small protofibrils | Binding to large protofibrils

Aβ protofibril conc (nM)

Antibody	IC50 (nM)
BAN2401	1.6
aducanumab	171.1
Fold difference	≈100

Antibody	IC50 (nM)
BAN2401	1.7
aducanumab	27.2
Fold difference	16

BAN2401 demonstrated stronger binding than aducanumab to cross-linked Aβ oligomers (<75 kDa) by inhibition ELISA

Protofibrils | Oligomers | Monomers

AU | Time [min] | Binding to oligomers | OD 450 nm | Aβ conc (nM) | BAN2401 | Aducanumab

BAN2401 showed much stronger binding than aducanumab to soluble aggregated Aβ species by SPR

	Monomers	Small protofibrils	Large protofibrils	Fibrils
BAN2401	K_D: 3980 nM	K_D: 1.32 nM	K_D: 0.54 nM	K_D: 6.82 nM
aducanumab	K_D: >5000 nM	K_D: 138 nM	K_D: 45 nM	K_D: 31.2 nM
Fold difference:	-	105	83	4.4

References

1. Tucker S., et al., The murine version of BAN2401 (mAb158) selectively reduces amyloid-beta protofibrils in brain and cerebrospinal fluid of tg-ArcSwe mice. *J Alzheimers Dis* 2015; 43: 575-88.
2. Magnusson K., et al., Specific uptake of an amyloid-beta protofibril-binding antibody-tracer in AbetaPP transgenic mouse brain. *J Alzheimers Dis* 2013; 37: 29-40.
3. Nilsberth C., et al., The 'Arctic' APP mutation (E693G) causes Alzheimer's disease by enhanced Abeta protofibril formation. Nature Neuroscience 2001; 4: 887-93.
4. Sehlin D., et al., Large aggregates are the major soluble Abeta species in AD brain fractionated with density gradient ultracentrifugation. *PLoS One* 2012; 7: e32014.

As presented at Alzheimer's Association International Conference July 2019

Full poster available on BioArctic website www.bioarctic.com

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BAN2401 additional data accepted for oral presentation at Clinical Trials on Alzheimer's Disease (CTAD) in December 2019

BioArctic oral presentation

Additional data on the binding profile of BAN2401

"Binding profiles of BAN2401 and aducanumab to different amyloid-beta species"

Eisai late-breaking oral presentation

Additional data from Phase 2b study with BAN2401

"Persistence of BAN2401-Mediated Amyloid Reductions Post-Treatment: A Preliminary Comparison of Amyloid Status Between the Core Phase of BAN2401-G000-201 and Baseline of the Open-Label Extension Phase in Subjects with Early Alzheimer's Disease"

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ABBV-0805: potential disease modifying antibody for Parkinson's disease with strong preclinical results now in Phase 1

High unmet medical need

No disease-modifying treatment

- 2nd most common neurodegenerative disease
- 6.2 million people with Parkinson's in 2015
- Younger patient group, still at working age

Unique profile

Unique and targeted binding profile

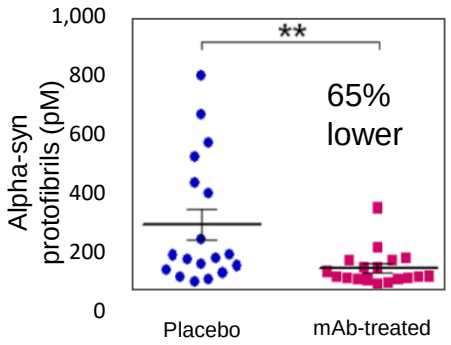
- Highly selective for toxic forms of misfolded alpha-synuclein (oligomers/protofibrils)

Built on genetic and pathology rationale

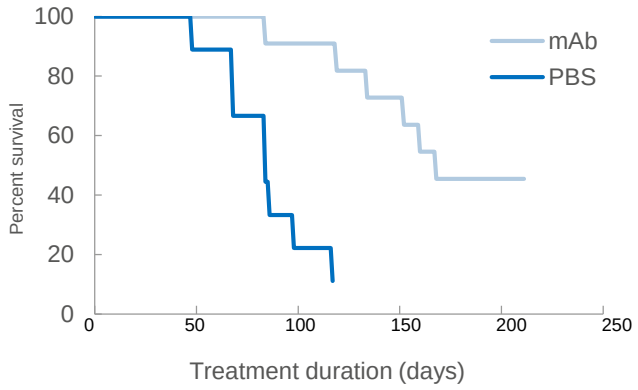
- Alpha-synuclein mutations lead to Parkinson's
- Alpha-synuclein oligomers/protofibrils are elevated in Parkinson's

Preclinical proof of concept

Reduction of neurotoxic alpha-synuclein oligomers/protofibrils



Delays disease progression and increases lifespan



ABBV-0805 in clinical development

- Phase 1 with ABBV-0805 ongoing by AbbVie
- BioArctic will deliver follow-up antibodies in the continued collaboration with AbbVie

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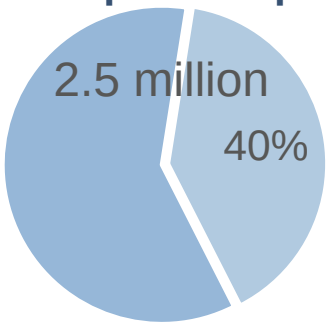
SC0806: potential regenerative treatment for Complete Spinal Cord Injury in Phase 2

High unmet medical need

No treatment for chronic injury

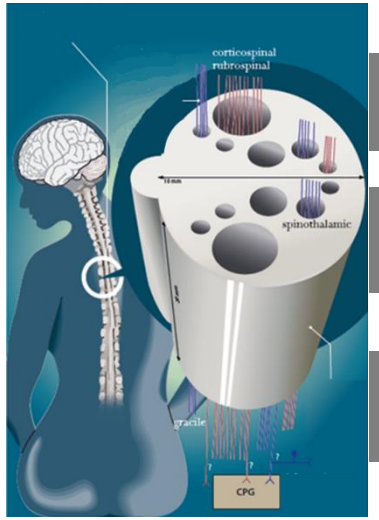
People with paralysis



of which complete spinal cord injury

- Significant qualify of life issues
- More common among younger men
- Orphan Drug designation in US and EU for SC0806

SC0806 makes nerve regeneration possible



Growth factor FGF1

Peripheral nerve autografts

Biodegradable device

Preclinical proof of concept and initial clinical safety

Preclinical model showed [1]:

- Nerve regeneration
- Electrophysiology restored
- Motor function improved

Phase 1 in patients:

- Safety evaluation supported progression into Phase 2

SC0806 in Phase 2

- Phase 2 ongoing in patients with Complete Spinal Cord Injury
  - Interim analysis expected 4Q 2019/1Q 2020
- EU Horizon 2020 research and innovative program [2]

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

2) Grant Agreement No. 643853 of MEUR 6.4

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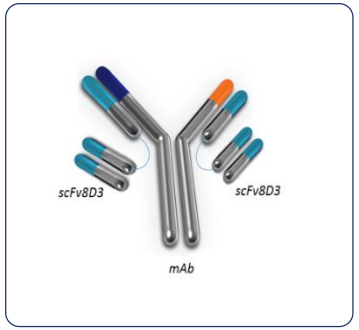
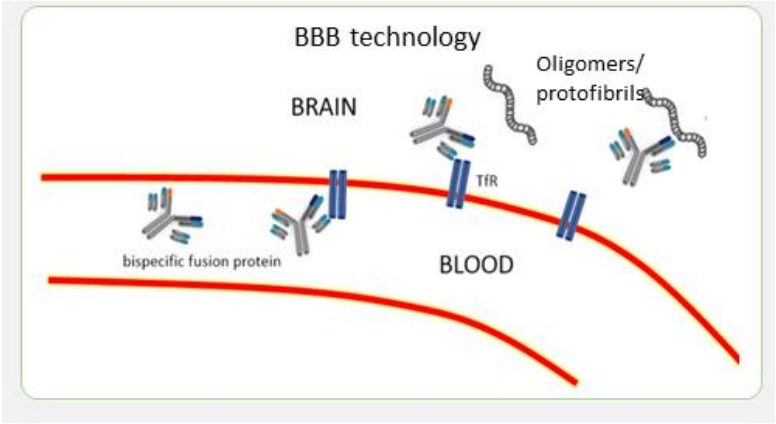
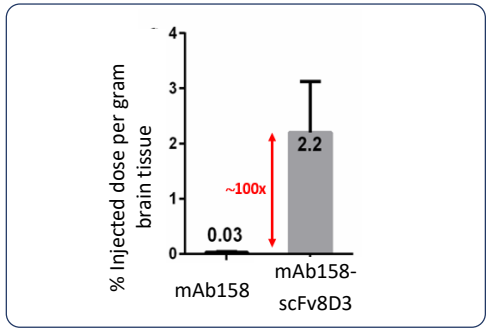
Advancing technology platforms and diagnostics to fuel pipeline

BLOOD-BRAIN BARRIER TECHNOLOGY PLATFORM



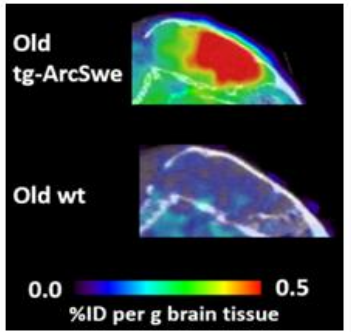


Substantially increased antibody brain uptake by BioArctic's brain shuttle technology



DIAGNOSTICS

Antibody-based imaging (PET)



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

Biochemical biomarkers

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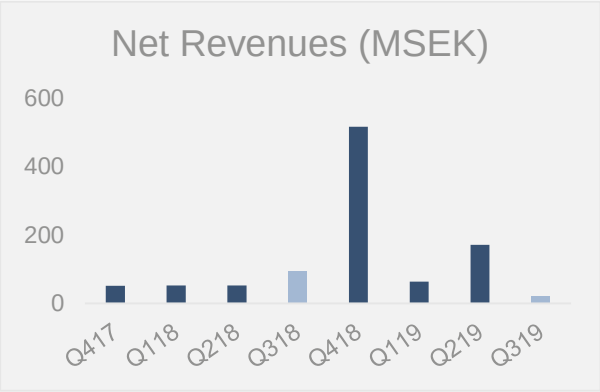
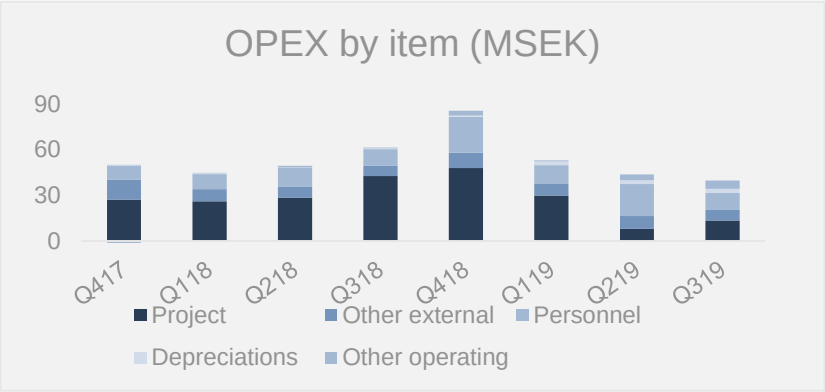
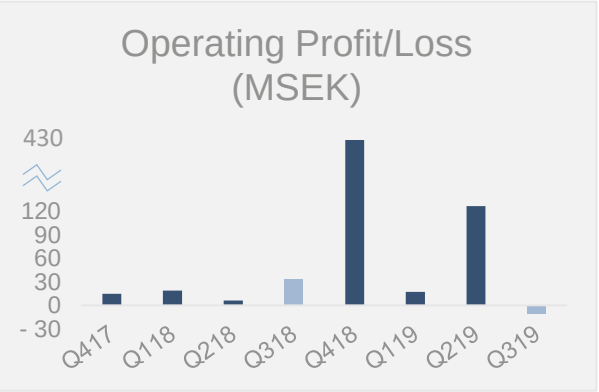
Finance Summary

Revenues and operating profit Q3 2019







- Net revenues decreased to 20.6 MSEK (94.0)
- The Parkinson's project has progressed into clinical phase resulting in lower revenues from the research collaboration with AbbVie versus previous year

- Project expenses decreased to 13.5 MSEK (42.7) due to lower external expenses in the Parkinson's project versus previous year
- Other operating expenses increased to 5.5 MSEK (0.4) and relates to exchange rate losses

- Operating profit decreased to -10.5 MSEK (33.1)

Operating expenses are expected to be in the range of 190 - 210 MSEK for the fiscal year January - December 2019

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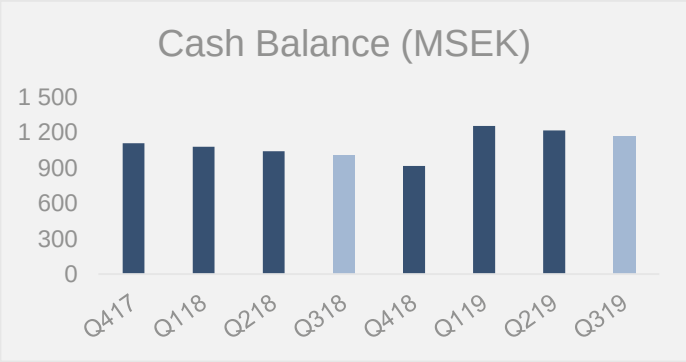
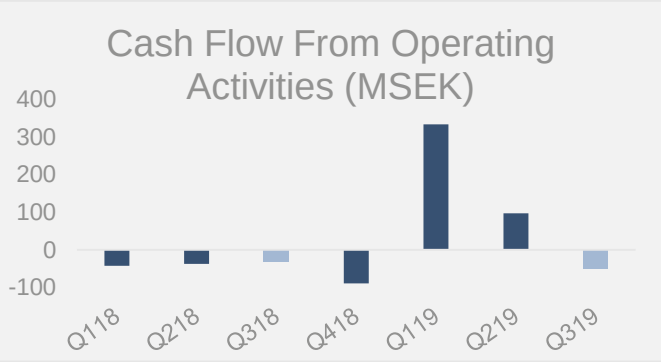
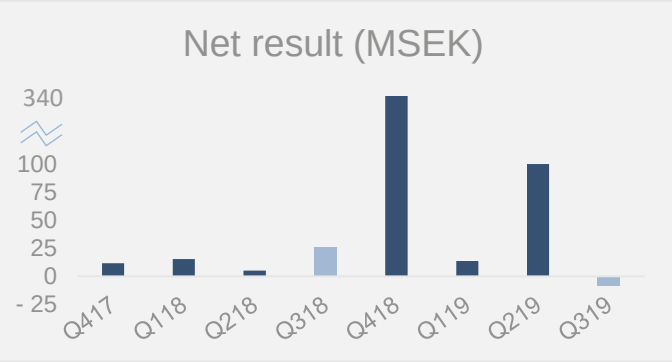
Cash related and net profit Q3 2019







- Cash balance amounted to 1,170.2 MSEK (1,008.5) at the end of the quarter

- Operating cash flow amounted to -49.4 MSEK (-31.5) during Q3

- Profit for the period decreased to -8.3 MSEK (25.9) during Q3
- The decrease of net result is attributable to lower revenues from the research collaboration in the Parkinson's project

To sum up, BioArctic continues to have a strong financial position

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Upcoming news and closing remarks

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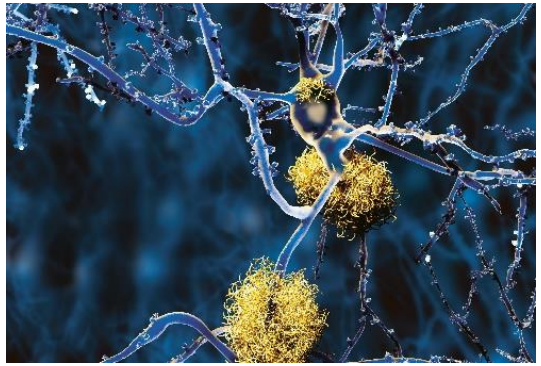
Upcoming news flow

Alzheimer's Disease



BAN2401 (Eisai)
- To present data at international congresses incl. CTAD December 2019
- Phase 3 confirmatory study results 2022
- Phase 2b open label extension study results
- Secondary prevention study start 2020

Discovery stage programs
- Advance into preclinical development

Parkinson's Disease

ABBV-0805 (AbbVie)
- Complete Phase 1 study

Discovery stage projects
- Continue development in AbbVie collaboration

Complete Spinal Cord Injury

SC0806
- Phase 1/2 study interim analyses of safety and efficacy 4Q 2019/1Q 2020

Diagnostics and Technology

Blood-Brain Barrier Technology Platform
- Expansion and continued development

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GUNILLA OSSWALD, CEO

JAN MATTSSON, CFO

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- **Next Report:**
  Full Year Report 2019 on February 6, 2020
- **Contact:**
  +46 8 695 69 30
  ir@bioarctic.se

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