Drug candidate with potential to **slow Parkinson's disease**

BioArctic's selective antibodies for misfolded alpha-synuclein have the potential to be efficacious disease-modifying treatments for synucleinopathies such as Parkinson's disease. In 2023, BioArctic decided to conduct a Phase 2a study in-house with its most advanced antibody, exidavnemab (formerly BAN0805).

Synucleinopathies are a group of rare diseases that are associated with abnormal aggregation of misfolded forms of the protein alpha-synuclein, which is the cause of several diseases such as Parkinson's, Parkinson's dementia, Lewy body dementia and multiple system atrophy (MSA). BioArctic has decided to initiate an in-house Phase 2a study of exidavnemab in patients with Parkinson's disease. The study, which is expected to commence in the second half of 2024, constitutes the basis for the possibility of continued studies in several conditions with synucleinopathy. For some of these conditions, such as Parkinson's disease dementia and Lewy body dementia, no clinical studies with antibodies that target alpha-synuclein have either been conducted nor commenced within the research field.

Parkinson's disease is the second most common neurodegenerative disease after Alzheimer's disease, and the most common disease in the group of alpha-synucleinopathies. Today, 10 million people are living with the disease and the number of patients continues to increase[1]. The affected patient population is relatively young and most are still of working age when they fall ill, which means that the costs to society are significant.

The disease is caused by misfolded alpha-synuclein.

The motor functions of the body depend on the signal substance dopamine, and Parkinson's disease emerges when the nerve cells that produce dopamine cease functioning. This in turn is due to the protein alpha-synuclein beginning to misfold and aggregate in the nerve cells. Misfolded alpha-synuclein first forms aggregates that are soluble – oligomers and protofibrils – and subsequently, insoluble aggregates that are called Lewy bodies. The soluble aggregate is believed to be the most harmful to nerve cells. These harmful forms of alpha-synuclein can also spread to both neighboring cells and other areas in the brain, which could explain how the disease develops and causes new symptoms.

1) Parkinson's Foundation - Understanding Parkinson's, Statistics 2020

Selective antibodies against alpha-synuclein protofibrils

BioArctic, in partnership with Uppsala University, has developed antibodies that selectively bind to the toxic aggregates of alpha-synuclein. Currently, the company is conducting four antibody projects aimed at synucleinopathies such as Parkinson's disease: exidavnemab, PD1601, PD1602 and PD-BT2238. The antibodies make it possible for the body's immune system to detect and eliminate the harmful accumulations of alpha-synuclein, and the progress of the disease can hopefully be slowed.

BioArctic will evaluate exidavnemab in an Phase 2a study

Preclinical data shows that BioArctic's most advanced drug candidate, exidavnemab, is highly selective against aggregates of alpha-synuclein and spares the basic physiological form of the protein. The antibody is thus expected to impact the underlying pathology for diseases that are caused by alpha-synuclein aggregates and slow the progress of these diseases. Data from studies of brain samples from patients with Parkinson's disease also shows that the antibody binds to pathological alpha-synuclein. Analyses of the Phase 1 study show a favorable pharmacokinetics and safety profile for the antibody. All together, all the data points to continued clinical development, and BioArctic is preparing for the start of a Phase 2a study in the second half of 2024, with exidavnemab being administered to patients intravenously. In parallel, the company is investigating partnership potential for further development at a later clinical stage.

Three preclinical projects

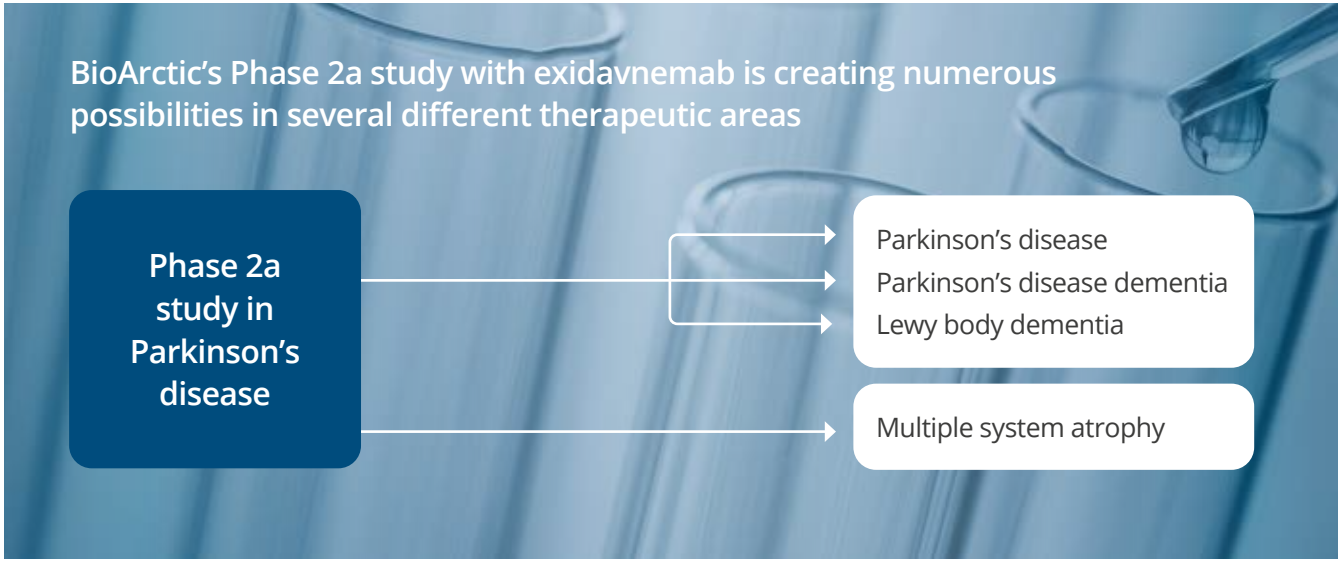
In addition to exidavnemab, BioArctic has antibodies PD1601 and PD1602, which also target aggregate forms of alpha-synuclein. Drug candidate PD-BT2238, which is also being developed for Parkinson's disease, is a combination of a highly selective alpha-synuclein antibody and BioArctic's BrainTransporter technology, which facilitates greater exposure to the antibody in the brain.

Parkinson's disease – the most common synucleinopathy

Parkinson's disease is normally detected around the age of sixty, and approximately one percent of the world's population over the age of 60 will be affected. The initial symptoms are often impaired sleep, mild tremors in one hand, or a decreased sense of smell. As the disease progresses, the tremors worsen, movements become slower and the body's muscles stiffen. Further, the risk of cognitive impact also occurs in approximately half of the patient population over an illness period of 10-15 years. Current treatments only alleviate the symptoms and are often most efficacious in the early stages of the disease. In pace with disease progression, the treatments lose their effect and the patient is gradually forced into a more limited lifestyle. In its later stages, living a normal and independent life becomes increasingly difficult.

54 billion USD

In estimated annual costs for Parkinson's disease in the US alone. One half of these costs comprises the cost of direct care, and the other half indirect costs[2].



2) Yang, W. et al. Current and projected future economic burden of Parkinson's disease in the U.S.