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COVIDAX (ACvac1)

Pluri-epitope peptide vaccine against COVID-19

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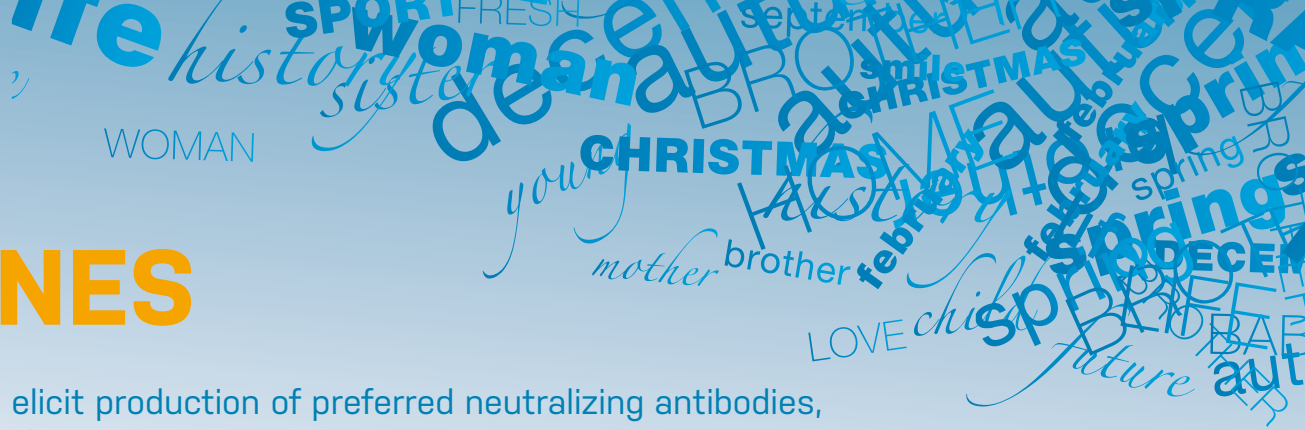
AXON Neuroscience (Axon) is developing **COVIDAX** – a vaccine candidate to protect against COVID-19, caused by the SARS-Cov-2 virus. Drawing on the expertise and know-how acquired during the development of its first-in-man Alzheimer's Disease vaccine AADvac1, Axon used its verified technology platform to develop a pluri-epitope peptide approach to neutralise the SARS-Cov-2 virus.

COVIDAX is a promising alternative to conventional vaccine approaches, particularly given its speed of development and ease of production. The vaccine induces highly specific antibodies that selectively target the vulnerable regions of the virus surface protein. The selectivity, specificity and safety of **COVIDAX** gives Axon a competitive advantage over conventional vaccine strategies.

> **COVID-19 may result in serious respiratory complications and pneumonia, which is particularly dangerous and lethal for elderly patients and people with immunodeficiencies.**



PEPTIDE VACCINES

Peptide vaccines use short protein fragments to elicit production of preferred neutralizing antibodies, consequently avoiding allergenic and/or reactogenic sequences.

The peptide-based approach is:

Safe
Peptide vaccines are designed to contain only selected epitopes on the virus that are required for its direct infection of human cells

Immunogenic
In combination with the proper carrier protein, a peptide vaccine is highly immunogenic and is able to stimulate an immune response even in subjects suffering from immunosenescence (such as the elderly population)

Easy to produce
Large quantity production is feasible with Axon's existing vaccine platform, which has already been scaled-up to early commercial batch size

Cost effective
Using synergies within Axon's vaccine pipeline

A COMPARISON OF COVID-19 VACCINES IN DEVELOPMENT

	PEPTIDE VACCINE COVIDAX	MRNA VACCINE	DNA VACCINE	CONVENTIONAL VACCINE
IMMUNOGENICITY IN GENERAL POPULATION	high[1]	low[2]	usually low[3]	usually high
IMMUNOGENICITY IN ELDERLY POPULATION	high[1]	low[4]	usually low[5]	low-high depending on the type of vaccine
POSSIBLE UNINTENDED EFFECTS	unlikely *targeted epitope approach*	likely *multi-epitope approach*	likely *multi-epitope approach*	likely *multi-epitope approach*
SAFETY	safe[6] *targeted epitope approach*	adverse effects cannot be excluded *RNA sequence of the entire S protein is used as an immunogen*	adverse effects cannot be excluded *DNA sequence of the entire S protein is used as an immunogen*	adverse effects cannot be excluded *S protein or whole virus is used as an immunogen*
DELIVERY	subcutaneous	intramuscular intradermal	intramuscular special devices are required	subcutaneous intramuscular intradermal
DOSE	µg	µg	mg	µg
STABILITY	stable at 2-8°C	mainly frozen	frozen	mainly frozen
MANUFACTURE	rapid	rapid	rapid	time-consuming

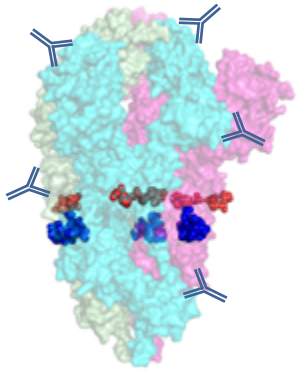
1. AXON peptide vaccine AADvac1 was highly immunogenic, with patients developing a geometric mean IgG antibody titre of 7318 after two doses and 18 382 after three doses in elderly population in Phase I clinical trial (Novak et al., 2016, 2018).
2. Zhang et al., 2019; vaccine against Zika - mRNA1893. developed a geometric mean IgG antibody titre up to 1500 after two doses in Phase I clinical trial.
3. Hobernik and Bros, 2018
4. Vaccine against influenza - mRNA 1777, developed geometric mean IgG antibody titre up to 1000 after three doses in elderly population in Phase I clinical trial.
5. Carter et al. 2019
6. No safety signals were reported in standard laboratory assessments, on vital signs, in neurological examination, MRI, in general physical examination, or in ECG assessment in Phase I clinical trial on AADvac1 (Novak et al., 2016, 2018). The vaccine was safe and well tolerated also in the Phase II study (Novak et al., 2020).

EXCEPTIONAL SAFETY PROFILE

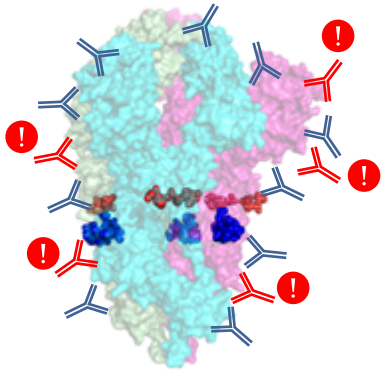
Targeted versus multi-epitope approach

RNA, DNA, recombinant protein-based, live attenuated, inactive virus, or subunit vaccines contain hundreds of antigenic epitopes (Calloway, 2020). Some of those immunodominant epitopes serve as false beacons directing an immune response to nonessential regions, and may even be detrimental or induce allergenic or reactogenic responses as was shown in SARS-CoV and MERS-CoV vaccines (Tseng et al., 2012; Liu et al, 2019).

In contrast, **COVIDAX** contains only selected peptides that were designed to contain a combination of B cell and T cell epitopes that instruct the immune system to generate specific antibodies to neutralize the viral activities required for efficient infection of human cells. All of the selected peptides have sequences dissimilar to those found in human proteome.



Targeted approach of AXON`s COVIDAX vaccine



Multiple-epitote approach other vaccines

The safety of Axon's vaccine platform was clearly demonstrated in Phase I and Phase II studies of the AADvac1 vaccine.

No significant differences in laboratory safety parameters (haematology, coagulation, chemistry, and urinalysis) and vital signs were observed.

No vascular oedema was observed in MRI. In general, the AADvac1 vaccine was safe and well tolerated, and no safety signal emerged (Novak et al., 2016, 2018, 2020).

EXCELLENT IMMUNOGENICITY

Vaccine for vulnerable populations

Since elderly individuals and people with immunodeficiencies are the most vulnerable to develop serious respiratory complications and pneumonia caused by SARS-CoV2, it is important to develop vaccines that protect this segment of the population. In general, older individuals typically do not respond well to vaccination due to immunosenescence. Only a limited number of vaccines and an even smaller number of platforms have been tested in this population. It is therefore difficult to predict whether vaccines lacking an adjuvant would be successful in generating of an effective immune response in elderly people. Protecting the elderly population might require higher neutralization titres as compared to that required in younger individuals.

Axon's peptide-based vaccine platform has been shown to induce extensive production of high-affinity antibodies in the elderly population recruited and studied in previous clinical trials. **COVIDAX** may thus represent the right solution for the group that is particularly vulnerable to COVID-19 infections.

Axon´s AADvac1 PHASE II study | Antibody response in elderly population

HIGH TITRES
Geometric mean of titres after six doses – **17 350**
Geometric mean of titres after three doses – **8 868**

EXCELLENT AFFINITY
The majority of patients developed affinity in the range of **1 – 0.01 nM**

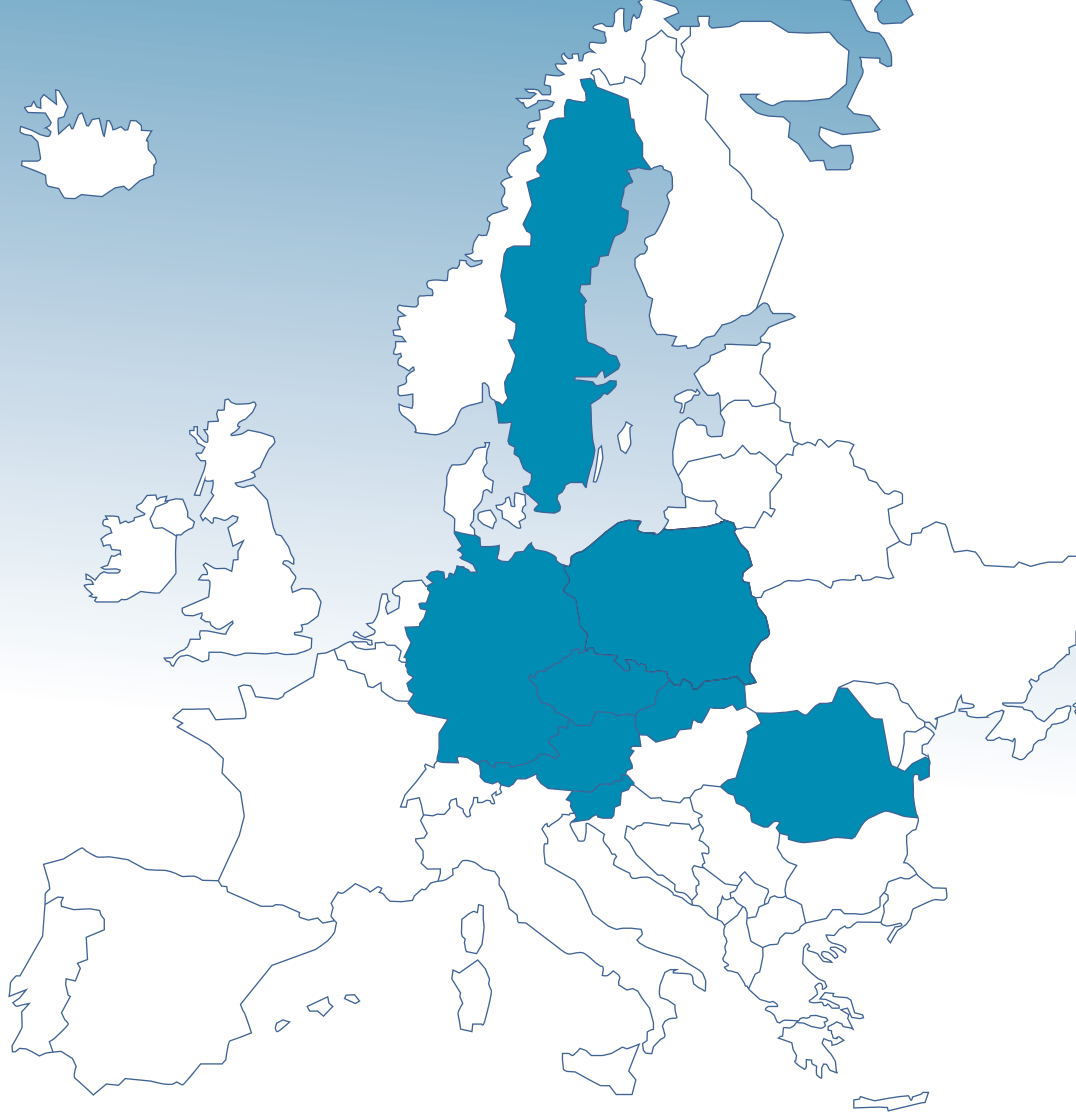
CLINICAL DEVELOPMENT EXPERIENCE

AXON platform was fully validated in the Phase II clinical trial

The Axon peptide vaccine platform was successfully validated with the Alzheimer's Disease peptide vaccine AADvac1, which was designed to reduce tau pathology, relieve the symptoms in patients, and even prevent the onset of the disease.

The Phase 2 study demonstrated that AADvac1 is exceptionally safe and well-tolerated. The vaccine induced a robust production of antibodies with high affinity in the elderly population. It exhibited a disease-modifying effect confirming its therapeutic potency.

Currently, it is the most clinically-advanced tau therapy in development for treating and preventing Alzheimer's Disease, moving to a pivotal confirmatory study.



Phase II study (24-month randomised, placebo-controlled, parallel group, double-blinded, multi-centre on AADvac1 in patients with mild Alzheimer's disease) was conducted in 8 European countries and 40 investigational sites: Austria, Czech Republic, Germany, Poland, Romania, Slovakia, Slovenia, Sweden.

FLEXIBLE AND RAPID MANUFACTURE

Strategic collaboration with the global leader in peptide vaccine manufacturing

Conventional vaccine manufacture is limited to producing only a narrow range of vaccines. Individual processes of manufacture need to be developed for each individual vaccine, making development costly and time consuming. The advantage of the Axon peptide vaccine platform is a flexible, rapid and low cost manufacturing process.

The platform is highly customizable to display a variety of antigenic peptides. The Axon peptide vaccines can be manufactured using the synergies of an established and scalable process. Axon's longstanding strategic collaboration with the European-based global leader in peptide manufacturing enables Axon to enter into clinical trials in autumn 2020.

ADVANTAGES OF THE AXON PEPTIDE VACCINE PLATFORM

	PEPTIDE VACCINE COVIDAX	LIVE / ATTENUATED VACCINE	NUCLEIC ACID VACCINE
TARGET SELECTION	Identify epitopes	Identify pathogen	Identify pathogen
Produce selected antigens	**Standardized:** • peptides synthesis (g scale) • API manufacture (sub-kg scale) • Established formulation	**Identify pathogen-specific optimized cultivation** ⧖ **Develop & Establish:** • pathogen-specific attenuation or inactivation • specific manufacture & controls • formulation $$$ ⧖	**Standardized plasmid & mRNA** **Standardized** **mRNA (mg scale)** **DNA (kg scale)**
PHASE 1			
Scale-up	Established peptide& API manufacture (kg scale)	Perform pathogen-specific manufacture scale-up $$	Standardized scale-up (kg scale)
PHASE 2/3	Safety ✓ Efficacy ✓	Safety ! Efficacy ✓	Safety ! Efficacy !
Commercial scale manufacture	Standardized syringes	Pathogen-specific commercial manufacture $$	Standardized syringes (RNA) Specific cartridges (DNA)
MARKET	Simple application	Simple application	Simple application Specialized delivery (DNA)

Manufacture · Clinical trials · $$$, $$ Increased cost · ⧖ Time consuming processs · Saved time · ! Possibility of unfavourable outcome · ✓ Verified outcome · Application by syringe · Application by special device

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