

Newsletter

May 2017

KL1333 – a new exciting project in NeuroVive's project portfolio

On May 2, NeuroVive was happy to announce that a project for the treatment of genetic mitochondrial diseases was in-licensed from the South Korean company Yungjin Pharm. The in-licensed candidate drug KL1333 is a perfect fit with NeuroVive's cutting-edge expertise in mitochondrial medicine and its own projects in genetic mitochondrial diseases. The project also fits perfectly with NeuroVive's business model in which orphan drug projects are developed in-house through the clinical development all the way to the market.

We have spoken to NeuroVive's CEO **Erik Kinnman** and the company's chief medical officer **Magnus Hansson** about the latest news.

We begin by asking Magnus Hansson a few questions.

Can you tell us more about the in-licensed compound and genetic mitochondrial diseases?

The compound KL1333 is a novel small molecule drug which has shown several effects very well suited to address the dysfunctions of genetic mitochondrial diseases. The mitochondria of patients affected by genetic mitochondrial disorders are like very weak car engines. The engines may be sufficient for travelling at low speed, but if you need to go uphill the power is insufficient, even if you press the gas pedal to max. In patients with mitochondrial disorders, the body's organs may need more energy than the mitochondria can produce when they for instance have a viral infection or when they need to walk upstairs. In severely affected patients, the mitochondrial function may be insufficient even without increased energy demand and their body's organs deteriorate.

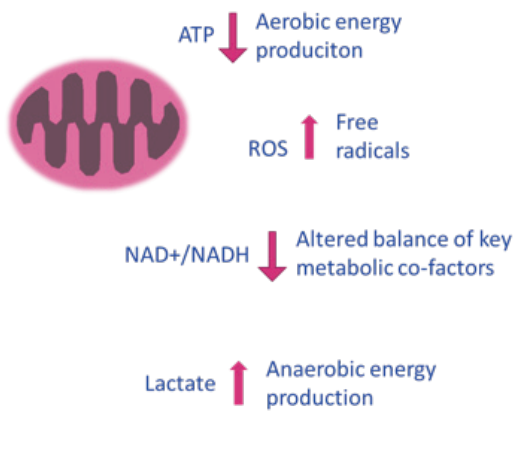
How does the compound KL1333 work?

KL1333 increases the cells' energy output in three ways. First, it restores and increases the availability

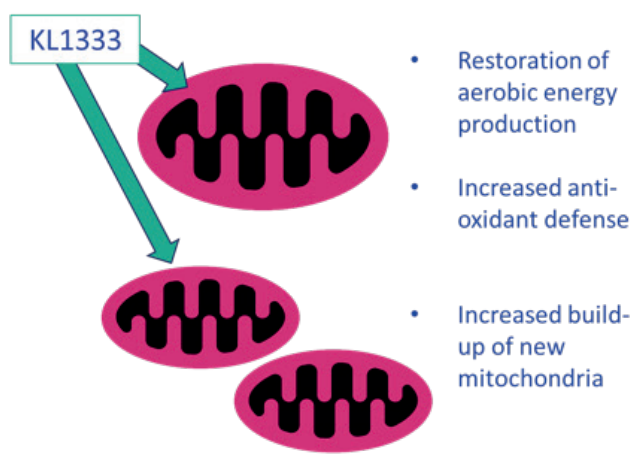


of NAD+, a key metabolic co-factor in the break-down of nutrients. This enhances the availability of energy substrates without production of lactate, which the cells otherwise produce if energy output is insufficient. Secondly, it directly transfers energy from the cell's cytoplasm to the last parts of the mitochondrial electron transport chain, bypassing the most common sites of dysfunctions. Thus, KL1333 functions like a turbo on an engine, enhancing the power output by optimizing the fuel utilization. Thirdly, increasing NAD+ enhances the cells' production of new mitochondria, a process called mitochondrial biogenesis. This is like increasing the number of cylinders in the engine or increasing the number of engines. A fourth important effect of KL1333 is upregulation of antioxidant defense mechanisms. Dysfunctional mitochondria produce more reactive

Dysfunctions in genetic mitochondrial disorders



Improved energy balance and mitochondrial health with KL1333



oxygen species. This is like exposing cars to salt water. KL1333 increases the glutathione levels, one of the cell's most important defenses against oxidative stress, analogous to ensuring a car has adequate rust protection. KL1333 thus have the potential to overcome several of the hallmarks of genetic mitochondrial disorders.

What kind of disease/indication do you aim for?

The project is directed towards genetic mitochondrial disorders such as MELAS, KSS, CPEO, PEO, Pearson, MERRF and Alpers syndrome. We will have to come back with a more detailed outline on which of these indications and which manifestation of the diseases we will focus on initially in the clinical development.

Will you need large and expensive studies?

Since these are orphan indications, the documentation need for market approval is more limited and the clinical studies will be considerably smaller than average and thus the path to the market will be faster and less costly compared to common diseases. Clinical studies in orphan indications such as genetic mitochondrial disorders have their own challenges, and successful development requires close interaction with the specialized clinical researchers in the field as well as with the patient advocacy groups. We have already started these important interactions and NeuroVive is well positioned to develop the project in a timely and cost-effective manner led by our experienced experts, agile team, and partners in our network.

When and where will the next clinical study start and what is the timeline for finalizing it?

An IND (Investigational New Drug) application and a clinical trial application for the Korean Phase I study has been approved by the Korean regulatory authorities and will start within a couple of months. The study is estimated to be completed during next year.

Over to Erik Kinnman, CEO at NeuroVive:

What does the agreement mean to NeuroVive?

We have now added a project with a high potential value - at a relatively low upfront cost - to our portfolio. Furthermore, the addition of KL1333 is perfectly in line with our business model focusing on rare diseases and the development of orphan indication projects all the way to the market. Moreover, the project fits very well with our existing genetic mitochondrial disease project. I.e., we have considerable increase our opportunities at a small initial cost and diversified the portfolio.



Who is Yungjin? Is it a big corporation?

Yungjin Pharm. Co., Ltd., established in 1952, has been playing a major role as a forerunner in the Korean pharmaceutical industry for half a century. It has previously mainly been a branded generics company in Korea, but now has the ambition to develop and market new innovative drugs and expand its international footprint. It has about equal sales in the domestic market as through international sales. Yungjin is listed on the South Korean stock market with a current market cap of \$1.4bn.



When can there be a product on the market and what is the market potential?

Since this is orphan indications with a faster route to market, a market approval is possible already in 2022. We estimate peak year sales to exceed \$1bn.

Who are your competitors, are there any drugs on the market today?

There is only one approved treatment for one of all existing genetic mitochondrial disorders in EU, Leber's hereditary optic neuropathy (LHON) (idebenone, Santhera). Other than this there are only a few projects in development for genetic mitochondrial diseases.

On what projects will NeuroVive put its focus going forward?

Besides KL1333, we will focus internal development resources on our other clinical asset, NeuroSTAT for TBI and the early project NVP015 for genetic mitochondrial disorders. In parallel we will drive the common disease projects for NASH and HCC with full speed to complete documentation packages for out-licensing agreement discussions during second half of 2017 and during 2018 respectively.

NeuroVive's partner Isomerase Therapeutics receives prestigious award in the UK

In April 20, NeuroVive's partner Isomerase Therapeutics announced that the company is the proud winner of a Queen's Award for Enterprise in International Trade 2017. The Queen's Award is the most prestigious corporate achievement that any UK business can attain and is a seal of approval for outstanding performance.

Dr Matt Gregory (CEO) and **Dr Steven Moss** (CTO) co-founded and have managed the company from its formation in 2012 to its current position. The company's overseas sales have grown by over 600% during the last three years with strong relationships built with companies across the globe. It employs over 20 highly skilled staff working from the company's facility at Chesterford Research Park, near Cambridge. The team at Isomerase works with partners to help them discover and develop Microbial Natural Products.

Dr Matt Gregory commented "The Queen's Award reflects the exceptional science we do and our commitment to innovation, investment in UK science and in global collaborations."

<http://isomerase.co.uk/index.php/news/46-isomerase-wins-prestigious-queen-s-award-for-international-trade>

In brief

About KL1333

KL1333 is a potent modulator of the cellular levels of NAD⁺, a central coenzyme in the cell's energy metabolism. KL1333 has in preclinical studies been demonstrated to increase mitochondrial energy output, reduce lactate accumulation, diminish the formation of free radicals, and to have long-term beneficial effects on energy metabolism. It is in clinical development stage for chronic oral treatment of primary genetic mitochondrial

disorders such as MELAS, KSS, CPEO, PEO, Pearson, MERRF and Alpers syndrome. Its mode of action is complementary to that of NVP015, which is intended to alleviate acute episodes of energy crises in genetic mitochondrial disorders with dysfunction in respiratory complex I and to NVP025, intended to protect the mitochondria in skeletal muscle from dysfunctional calcium handling and consequential muscle wasting.

About mitochondrial diseases

Approximately 12 in every 100,000 people suffer from a genetic mitochondrial disorder. Mitochondrial disorders usually present in early childhood.

KL1333 qualifies for orphan drug designation in the US and Europe during clinical development, enabling a faster and less costly route to market, and a higher price.

In 2016, the orphan drug market amounted to USD 114 billion and in the same year, the average annual cost for the treatment of a single patient was an estimated USD 140,443 (approx. 1.3 million SEK).¹

1. Evaluate Pharma Orphan Drug Report 2017

Conference participation

Investor meetings

- BioTrinity London 8-10 May. Company showcase presentation & meetings.
- Aktiedagen, Stockholm, 15 May. Company presentation.
- BioEquity, Paris 21-23 May. Company presentation & meetings.
- Rodman and Renshaw, New York 10-12 September. Company presentation & meetings.
- Nordic Life Science Days, Malmö 12-14 September. Company presentation/meetings.

Scientific conferences

- EuroMIT Cologne 11-15 June.
- 2017 UMDF (United Mitochondrial Disease Foundation) Mitochondrial medicine congress 28 June – 1 July. Presentation by Johannes Ehinger, Research scientist at NeuroVive.
- NeuroTrauma Washington 9-12 July.

ABOUT NEUROVIVE

NeuroVive Pharmaceutical AB is a leader in mitochondrial medicine. The company is committed to the discovery and development of medicines that preserve mitochondrial integrity and function in areas of unmet medical need. The company's strategy is to take drugs for rare diseases through clinical development and into the market. The

strategy for projects within larger indications outside the core focus area is out-licensing in the preclinical phase.

NeuroVive is listed on Nasdaq Stockholm, Sweden (ticker: NVP). The share is also traded on the OTCQX Best Market in the US (OTC: NEVPF).