

## PRESS RELEASE

NeuroVive Pharmaceutical AB (publ)  
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## NeuroVive's novel strategy for treatment of mitochondrial disease published in Nature Communications

**Lund, Sweden, August 9, 2016 - NeuroVive Pharmaceutical AB (Nasdaq Stockholm: NVP, OTCQX: NEVPF)**, the mitochondrial medicine company, today announces that research results from the NVP015 program investigating a novel pharmacological strategy for the treatment of mitochondrial disease has been published in Nature Communications, the third highest ranked multidisciplinary scientific journal in the world. The research was performed in collaboration between NeuroVive and Lund University, Newcastle University, Selcia/Mitopharm Ltd and Isomerase Therapeutics Ltd.

In the [Nature Communications](#) article, the team presents results from a novel therapeutic strategy in which succinate is delivered to cells with mitochondrial complex I dysfunction, a potential therapy for patients who suffer from mitochondrial disease related to complex I dysfunction.

Succinate, succinic acid, is normally not cell membrane-permeable and has limited uptake into cells. In the presented novel pharmacological strategy, succinate was, by using a prodrug technology, modified to become cell-permeable and thereby made available for the mitochondrion to use as fuel once inside the cell. In the study, isolated cells from healthy individuals and from a patient with Leigh's syndrome caused by complex I dysfunction were reported to increase energy production when treated with prodrugs of succinate.

*"The Nature Communications publication is a significant achievement for our team involved in mitochondrial disease research aiming at developing new therapeutic options for these serious diseases and reinforces the strength of our partnerships in advancing the research,"* commented NeuroVive's CSO Eskil Elmér. *"A new generation of succinate prodrugs is currently in development and we are very excited to see continued development of these drugs aiming at offering mitochondrial disease patients a beneficial treatment."*

The current compounds described in the Nature Communications publication are not suitable for use in more complex experimental models or in humans, due to low stability in plasma. To overcome this, the team at NeuroVive and Isomerase has developed a new series of succinate prodrugs within the NVP015 research program with increased plasma stability. The most promising lead compounds from this chemical series are currently being tested in various experimental models.

### **About NeuroVive's discovery program NVP015**

The NVP015 discovery program is based on a concept developed by NeuroVive's CSO, Dr. Eskil Elmér and his co-workers to create a cell-permeable prodrug of the endogenous energy substrate succinate. A prodrug is an inactive drug which is activated first when entering the cell and the chemical structure is altered. A successful candidate from this discovery program in mitochondrial disorders could classify as an orphan drug.

### **About complex I dysfunction**

One of the most common causes of mitochondrial diseases relates to complex I dysfunction, i.e. that the energy conversion in the first of the five protein complexes in the mitochondrion that are involved in effective energy conversion does not function normally. This is apparent in disorders including Leigh's Syndrome and MELAS, both of which are very serious diseases with symptoms such as muscle

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weakness, epileptic fits and other severe neurological manifestations. These diseases usually present early in life and deteriorate progressively.

### **About Nature Communications**

Nature Communications is an open access journal that publishes high-quality research from all areas of the natural sciences and has an Impact Factor of 11.3 according to the 2015 Journal Citation Reports® Science Edition (Thomson Reuters, 2015). This places Nature Communications third among all multidisciplinary science primary research journals, with Nature being first and Science the second. Papers published by the journal represent important advances within each field.

### **About NeuroVive**

NeuroVive Pharmaceutical AB (Nasdaq Stockholm: NVP, OTCQX: NEVPF) is a pioneer in mitochondrial medicine and a company committed to the discovery and development of highly targeted candidates that preserve mitochondrial integrity and function in areas of significant therapeutic need. NeuroVive's business approach is driven by value-adding partnerships with mitochondrial research institutions and commercial partners across the globe.

NeuroVive's portfolio consists of two clinical projects, one in acute kidney injury (**CicloMulsion®**) and one in traumatic brain injury (**NeuroSTAT®**). The candidate drug NeuroSTAT has orphan drug designation in Europe and in the US for treatment of moderate to severe traumatic brain injury and is currently being evaluated in the CHIC study. CicloMulsion is being evaluated in an on-going study, CIPRICS, in acute kidney injury during major surgery. Furthermore, the R&D portfolio consists of two late stage discovery programs and one compound in preclinical development.

NeuroVive is listed on Nasdaq Stockholm, Sweden, Small Cap, under the ticker symbol NVP. The share is also traded on the OTC Markets Group Inc market in the US. NeuroVive Pharmaceutical (OTC: NEVPF) trades on the OTCQX Best Market.

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