

## UPDATE DECEMBER 2018

For the first time, a cancer patient was treated with InnoMedica's liposomal doxorubicin on November 12<sup>th</sup>, 2018 in the Cantonal Hospital of St. Gallen. Since then, the Ospedale Regionale di Bellinzona e Valli and the Cantonal Hospital of Graubünden have been officially opened as additional study centers and have started recruiting study patients. With the Inselspital in Bern and the University Hospital Basel, two more hospitals will follow step by step.

The achievement of this historic milestone was only possible due to the great efforts of InnoMedica's team and the continuous commitment of our investors. The capital increase in 2018 provided further funds of CHF 10.25 million and once again led to a substantial expansion of our shareholder base, which now includes more than 640 shareholders. A significant part of the new shares was subscribed to by existing shareholders, who further expanded their investment beyond their present shares.

The newly raised capital will allow the expansion of the production facility in Marly so that after completion of the clinical trial the cancer drug Talidox can be manufactured in sufficient quantities in the new clean room for market entry. At the same time, development of innovative pipeline products can be advanced, especially in neurology with further preclinical studies and the Talineuren toxicology study. The promising preclinical results in Parkinson's disease have now been complemented by a first study in a Huntington's animal model. In addition, a collaboration with the University of Bern in the field of amyotrophic lateral sclerosis (ALS) was initiated. In order to take full advantage of the potential of the protective effect of Talineuren, a collaboration was launched with the GM1 manufacturer TRB Chemedica in Geneva.



## Talidox: First Patient Treated

Launch of the clinical trial: The first patient was treated with InnoMedica's Talidox in the Phase I trial on November 12<sup>th</sup>, 2018 in the Cantonal Hospital of St. Gallen. Further suitable patients can be enrolled in the study at intervals of approximately three weeks.

Following the completion of a successful preclinical development, Swissmedic granted approval for the Phase I clinical trial with Talidox in summer 2018. In the following weeks, the product intended for clinical use was manufactured in compliance with good manufacturing practice (GMP) guidelines in the clean room of the company's own production facility in Marly, analyzed by quality control and finally released by quality assurance for the use in the Phase I study. Following Swissmedic's approval, SAKK prepared the first hospital in St. Gallen for the start of the study. The first Talidox delivery to the Cantonal Hospital of St. Gallen took place at the end of October and InnoMedica's medication was administered to the first patient on November 12<sup>th</sup>, 2018.

The purpose of the Phase I study is to test and confirm tolerability and to determine the optimal treatment dose of Talidox. Following a modern study design that allows a rapid dose escalation, the first patient receives a dose of Talidox corresponding to about a quarter of the dose used today in comparable doxorubicin applications. If no relevant doxorubicin-related side effects occur within three weeks after the first application, the patient receives the second of up to 9 treatment cycles and a next patient is included in the study at a higher dose level. This study design allows a rapid dose escalation to therapeutically effective dosages while exposing patients only to minimal risk. Finally, if significant side effects occur for the first time, further patients are treated at the same or a lower dose level according to an empirical model. That way, a dose can be determined that does not cause any significant side effects in 75% of patients.

The study managers expect that the recruitment of Phase I study patients will be comparatively easy, as both oncologists and individual patients already have medical experience with the use of the active substance doxorubicin contained in Talidox. Accordingly, the second patient could already be treated at the beginning of December.

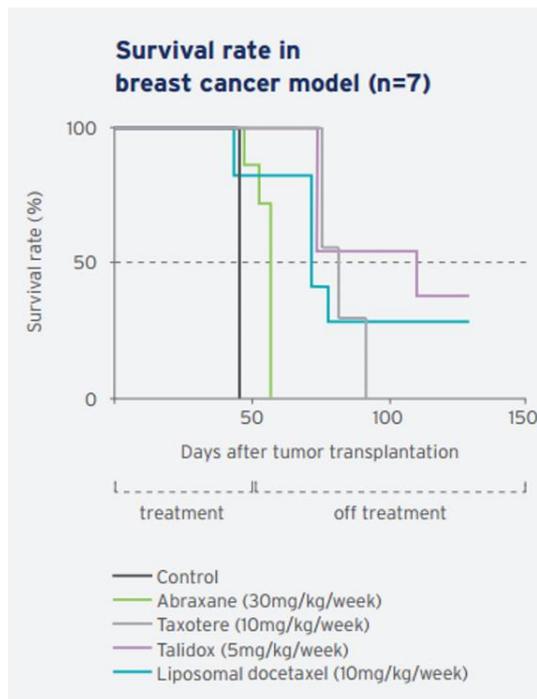
Patients are selected by the SAKK study physicians in the respective hospitals. Further information on the study and contact details of the responsible persons are provided by SAKK through the following link:



<https://www.sakk.ch/en/trial/phase-i-trial-tld-1-novel-liposomal-doxorubicin-patients-advanced-solid-tumors>

## Prospect of Cancer Treatment with Less Risk of Relapse: Preclinical Studies on Long-term Effects of Liposomal Chemotherapy

Promising long-term effects: InnoMedica's liposomal formulation of doxorubicin (Talidox) and docetaxel completely suppressed tumor growth in one third of preclinical cases and prevented tumor growth even after the end of treatment.



InnoMedica's liposomes allow for intelligent packaging of a wide variety of drugs to alter their distribution throughout the body. With Talidox, the first oncology application is in the clinical phase and is being used in patients for the first time. In addition to doxorubicin, which is wrapped in Talidox, other widely used chemotherapeutics could also benefit from liposomal packaging. Hence, a liposomal formulation of docetaxel which exceeded the effect of approved docetaxel preparations in initial preclinical studies has been added to InnoMedica's pipeline.

Further preclinical studies investigated the effect of Talidox (5mg/kg/week) and the liposomal formulation of docetaxel (10mg/kg/week) in a breast cancer model and compared these with treatments with free docetaxel (10mg/kg/week, Taxotere) and Abraxane (nano-albumin paclitaxel, 30mg/kg/week). A three week treatment period was followed by an observation period to assess tumor growth and survival rates. 3 out of 7 subjects treated with Talidox and 2 out of 7 subjects treated with the liposomal

formulation of docetaxel showed complete disappearance of the tumor. None of the approved drugs (Taxotere, Abraxane) was able to produce such a positive long-term effect, even if higher drug doses were administered. The beneficial long-term effect is also confirmed in the survival rates: 100 days after the start of treatment, only animals that had received InnoMedica's liposomal formulations of doxorubicin and docetaxel survived.

## Talineuren: Swissmedic Offers Prospects for Facilitation of Preclinical and Clinical Trials

Scientific Advice: Swissmedic accepts toxicological testing of the drug in only one single species and in principle regards the simultaneous testing of the drug in patients with different indications (Parkinson's, Huntington's, ALS) in a first Phase I clinical trial as feasible.

In preclinical Parkinson's disease studies, InnoMedica has already demonstrated that Talineuren liposomes are able to cross the blood-brain barrier and deliver the protective substance GM1 to dying brain cells. For the further development of the drug, InnoMedica requested Scientific Advice from Swissmedic to clarify the prerequisites that must be fulfilled for a swift clinical translation and the first use of Talineuren in patients.

Although Talineuren transports an active substance into the brain, Swissmedic allows a simplified preclinical safety testing prior to the start of the clinical trials. This means that Talineuren only needs to be tested in a single animal species for safety. In contrast, new drugs often have to be tested in at least two mammalian species (e.g. dogs and primates). As with Talidox, Swissmedic shares InnoMedica's view that this is not necessary for Talineuren in view of existing clinical data on the active substance GM1. This will have a positive effect on the costs of the preclinical toxicology study and should significantly accelerate the time to clinical trials.

Swissmedic also offers the prospect, subject to strong preclinical results, that the first clinical trial with Talineuren could be conducted directly with patients instead of healthy volunteers. This allows to expect early efficacy relevant results and thus further accelerates clinical development.

Since InnoMedica believes that patients with different neurodegenerative diseases could benefit from treatment with Talineuren, it is intended to test Talineuren simultaneously in several neurological conditions. Therefore, InnoMedica conducted a first preclinical study on Huntington's disease in addition to the preclinical studies in models of Parkinson's disease. InnoMedica also initiated a collaboration with the University of Bern on amyotrophic lateral sclerosis (ALS), another disease in which nerve cells degenerate. Subject to the approval of the Ethics Committee, Swissmedic considers it possible to include patients with Parkinson's, Huntington's and ALS in the first clinical trial. This way, the potential of Talineuren can be investigated both in large indications such as Parkinson's and in rare diseases such as Huntington's or ALS in a single study. This exceptional approach is possible because the "neuroprotective" effect of GM1 can be used to treat various neurodegenerative diseases.

The indications Huntington's disease and ALS are recognized as orphan diseases due to their rare occurrence and lack of treatment options. Thus, an orphan drug application can be filed for Talineuren in these indications. Benefits associated with the status include a direct contact with the regulatory authorities, facilitated approval conditions and ten years of market exclusivity in the EU.

Further preclinical studies are currently being conducted in the above indications. In a first trial for the treatment of Huntington's disease, a preliminary positive effect on the course of the disease by oral administration of Talineuren was observed. Subsequently, follow-up questions on dose and frequency of administration will be addressed. Huntington's disease is an incurable, genetically caused disease of the nervous system in which a dominantly inherited gene defect leads to the death of certain brain cells. Onset of the disease is usually between the ages of 35 and 50. If the genetic disorder is present, the affected person will become symptomatic with certainty and with a 50 percent probability will pass the gene on to children. The disease manifests itself both in physical and mental impairments. Those affected suffer from restlessness, involuntary spasmic movements and difficulties speaking and swallowing. In addition, personality changes often occur, which can lead to slight irritability, indifference, depression, loss of mental abilities and social withdrawal. About 15 years after the first symptoms the disease leads to death.



Roughly 400 people in Switzerland are affected by Huntington's disease. This small patient population gives InnoMedica access to the "orphan disease" programs of various authorities (EMA, US-FDA and Swissmedic). Should Talineuren be recognized as an orphan drug, the prospect of conditional approval on the basis of initial successful clinical studies exists. The former allows InnoMedica to market Talineuren at an early stage and to submit the clinical data required for a regular approval later.

InnoMedica has established a robust and cost-efficient supply chain in order to meet Swissmedic's positive feedback, so that the drug can be produced in Switzerland under high quality standards. At the same time, the process engineers have adapted the Talidox manufacturing process so that Talineuren can now also be manufactured under cGMP conditions in the clean room. This is a clear advantage of InnoMedica's technology platform, which allows the production of Talineuren with the same infrastructure as already used in the production of Talidox. Large production volumes for a large number of patients can thus be achieved more quickly and existing investments can be used more efficiently.

## Letter of Intent signed with Swiss GM1 Manufacturer TRB Chemedica

InnoMedica and TRB Chemedica will enter into a long-term partnership for the extraction and processing of GM1 and other glycolipids for product development in neurological diseases such as Parkinson's disease, Huntington's disease, ALS, multiple sclerosis and spinal cord injury.



In June 2018, InnoMedica and TRB Chemedica expressed their intention to cooperate in a letter of intent. A long-term collaboration with the GM1 manufacturer is considered strategically important for successful clinical translation and large-scale manufacturing of the product Talineuren. TRB Chemedica is a pharmaceutical company headquartered in Geneva with more than 900 employees worldwide. The company manufactures products in ophthalmology and rheumatology, which it markets itself through 18 foreign subsidiaries and a network of distributors in approximately 70 countries.

TRB Chemedica has patented proprietary processes for the production of GM1 and has strong marketing experience in China, Brazil and Argentina and Central America. InnoMedica already uses TRB Chemedica's GM1 for the production of Talineuren and believes that the

continuation and intensification of the cooperation will provide crucial advantages for product development and marketing of the drug. For example, TRB Chemedica agrees to a substantial scale-up of GM1 production as soon as Talineuren can be registered by InnoMedica and is approved by the regulatory authorities.

## Expansion in Marly and Consolidation of the Company

More growth at the Marly site: In order to manufacture Talidox for clinical applications and at the same time develop more pipeline products, InnoMedica is further expanding its infrastructure in Marly, investing in the automation of filling processes and driving forward moderate personnel growth.

The start of the clinical phase with Talidox as well as the positive results with Talineuren, which after completion of further preclinical trials will also be prepared for pharmaceutical production, require a substantial expansion of InnoMedica's Marly facility. The warehouse has been enlarged to meet the increasing space requirements and the planning of a cold store has begun. A larger process engineering

laboratory has also been put into operation in order to test the larger production equipment required for industrial scale-up and make it implementable in the new clean room at a later date. The order for the reconstruction of the new larger clean room was placed and is expected to be completed by spring 2019. This will permit InnoMedica to quickly adapt the infrastructure to larger production volumes if the Phase I clinical trial with Talidox is successful or if Talineuren is designated an orphan drug.



The plans for expansion also take into account the growth in personnel with a focus on the entry into the clinical trial and the expanded production capacities. In view of last year's doubling of the workforce from 11 to 22 employees and the result of the financing round in spring 2018, InnoMedica initially pursued moderate growth. With over CHF 10 million in new capital, a new record in fundraising was achieved. Nonetheless, slight adjustments of the growth speed set in the business plan proved necessary. Further recruitment is currently planned in the context of the continuously strong preclinical results and the ongoing Phase I clinical trial. InnoMedica is pursuing moderate growth that does not jeopardize financing through equity. In the development, engineering and production areas, first positions have already been taken and further positions are planned for 2019, especially in quality assurance.

At the 2018 Annual General Meeting, the shareholders of InnoMedica elected Dr. Peter Halbherr as Chairman of the Board of Directors of InnoMedica. The Board of Directors also confirmed him in his function as General Manager. This dual function ensures lean and competent management in the dynamic startup phase, in which no operating income is generated yet.

With the election of Dr. Denis Bron, the Board of Directors is extended by an additional member. Dr. Bron, who serves as Vice Chairman of the Board of Directors, has been Medical Advisor to InnoMedica in an



advisory role since 2005. As an inventor he, together with InnoMedica, holds an early patent of the targeting approach regarding the dosage form of pharmaceutical agents, which he brought into the company in 2010. Dr. Bron is Chief of Aeromedical Medicine Air Force of the Aeromedical Institute FAI and heads the Aeromedical Center (AeMC) in Dübendorf. He previously worked in neurology at the Harvard Medical School in Boston, the University Hospital of Basel and the Cantonal Hospital of Aarau. Dr. Bron completed his medical studies at the University of Basel in 1997. He contributes to InnoMedica his broad network in the medical sector and his experience in working with doctors and hospitals.

## Financial Planning

Authorized Capital: InnoMedica plans to place additional shares to fund Talidox' Phase IIa clinical trials and the Talineuren project.

According to the 2018 Business Plan, InnoMedica needs capital of CHF 31.6 million to finance the Talidox and Talineuren projects. The capital increase in spring 2018 raised CHF 10.25 million in new capital for the company. Of the authorized capital, 103,516 shares are still available to InnoMedica for a financing

round in spring 2019. This will again be carried out in a two-stage approach with a preliminary round aimed at larger qualified investors and a public campaign.



With funding needs of approximately CHF 7 million for 2019, which includes all costs incurred including production and conducting the Phase I clinical trial, InnoMedica is well financed for the time being with an expected cash reserve of approximately CHF 12 million by the end of 2018. Depending on the results of the ongoing Phase I clinical trial with Talidox, a transition to a Phase IIa is possible, which could significantly accelerate the clinical development, but will also cause

further costs of approximately CHF 2 million. In addition, planned preclinical studies with Talineuren in various indications are to be carried out and possibilities for achieving orphan drug status are to be examined, particularly in the case of Huntington's disease. To avoid jeopardizing what has been achieved by a lack of liquidity, InnoMedica is planning to secure the outstanding CF 21.35 million at due time. Swissmedic's positive responses to Talineuren, as well as the progress made in production and the start of the clinical trial, once again provide a good basis for the further commitment of numerous existing and new shareholders.