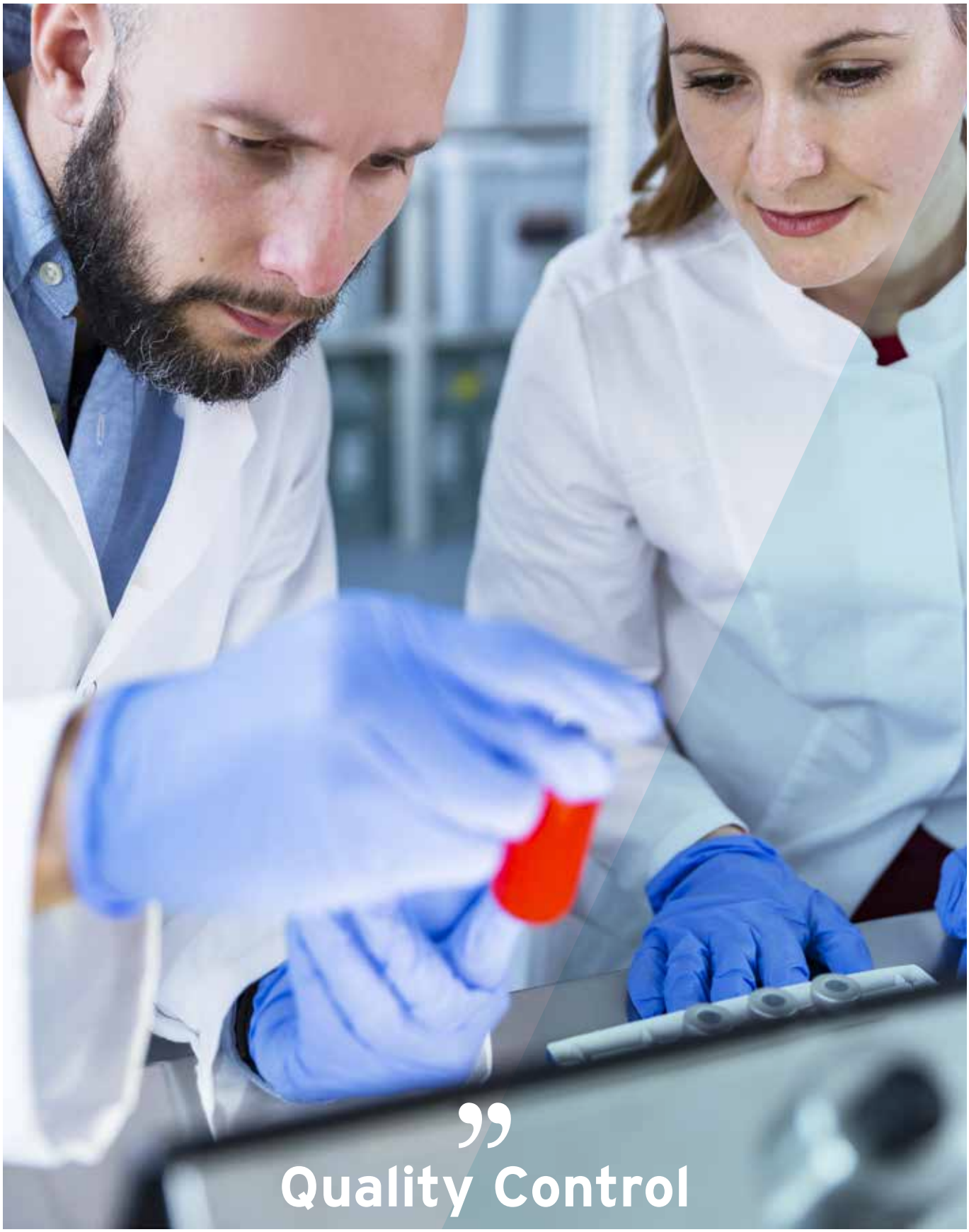
Business Plan Update

April 2019



The use of Talidox in patients in the phase I clinical trial gives more importance to quality assurance and requires comprehensive analyses during production and of the ready-to-deliver drug.

Executive Summary

With Swissmedic's approval of the phase I clinical trial in September 2018, InnoMedica reached an important milestone: the company now has its first product – Talidox – that is being tested in Swiss hospitals for tolerability, side effects and maximum dosage. As the trial is conducted directly in cancer patients, preliminary evidence of efficacy is much awaited. The stronger the initial indicative results, the easier it will be to design and perform subsequent clinical trials and the greater the chances of the product's success in obtaining fast approval from Swissmedic.

Preclinical development has rendered abundant evidence of the numerous advantages of Talidox with various comparative studies and the toxicology study. Furthermore, regarding the transferability of preclinical results to clinical application in patients, positive translational experiences with other liposomal formulations are already available. In order to meet high expectations in case of success, InnoMedica is currently focusing on the scale-up of the manufacturing process and the expansion of the new large clean room in Marly. To this end, the Marly Innovation Center (MIC) is renewing InnoMedica's clean air, hot and cold water supply. InnoMedica has already completed the renovation of the premises for process engineering and storage in line with current technical standards.

The planning and time-consuming infrastructure work must be initiated relatively early, so as to be aligned with the progress of clinical development and safeguard against delays due to supply bottlenecks. In scale-up, processes will be continuously optimized and production progressively stabilized in order to further increase batch size. The application of the drug in patients further highlights the importance of quality assurance and required comprehensive analyses both during the manufacturing process and of the ready-to-use product. The manufacturing team meets these high requirements and has further consolidated its competency in establishing routine processes. In the future, proven procedures will be automated whenever possible and simplified through technical measures. Only with these measures can the necessary throughput in batch production be achieved.

With the start of the clinical trial, the company's risk profile has shifted significantly. The focus is no longer on Swissmedic's approval of the study and the corresponding review of the preclinical research and production procedures, but instead the focus now lies on issues of cost, time required to expand production, and the further studies necessary for market approval.

The Business Plan Update 2019 will further elaborate these topics in the following. The planning of the phase II trials for Talidox is dependent upon the first meaningful results of the ongoing phase I trial, expected for autumn 2019. This is taken into account in the multi-stage phase IIa and IIb study approach, which weighs the evidence of an advantageous side effect profile and the evidence of equivalent or better tumor growth inhibition differently. Regarding Talineuren, the results of a first inquiry with Swissmedic will be discussed and the planning of the clinical trial in collaboration with Swiss neurologists will be presented. In addition to the use in Parkinson's disease, the use in Huntington's disease is being explored. Furthermore, a letter of intent for a long-term cooperation with the raw material supplier TRB Chemedica has been signed. With regard to production, the substantial investments in the infrastructure in Marly and the planning up to the commissioning of the new clean room are presented. Finally, an updated financial plan is presented and it is shown how the funds raised in the current capital increase will be used.

InnoMedica's remarkable operational results have been achieved by a highly motivated team of 25 people – supported by a broad shareholder base of over 650 shareholders. The management has been stable for over five years guaranteeing continuity. The mostly young employees ensure access to the latest technologies and scientific findings in biochemistry, structural biology, immunology, and chemistry, as well as familiarity with current medical practice. They are complemented by experienced managers who contribute valuable complementary expertise in areas such as contracting, financial planning, procurement, logistics, IT, infrastructure expansion, and automation.

InnoMedica remains committed to start-up culture and entrepreneurship. It is legitimate to take delight in the successes achieved and to draw confidence from them. But it is important to remain focused on the ambitious goals and to continue to tackle the great challenges with courage. Even with Talidox, the first product, already in use in five Swiss hospitals, InnoMedica will continue testing new ideas for the liposomal application of drugs in oncology: So far InnoMedica has consistently received positive and supportive signals from medical partners and authorities for its innovative approach.

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Talidox

Doxorubicin has been an invaluable part of the oncological treatment repertoire for approximately 30 years and is used in a broad spectrum of cancer types: Doxorubicin is widely used for the treatment of breast, ovarian and lung cancer, as well as lymphoma and soft tissue tumors. Its pharmacological effect is primarily based on the inhibition of cell division. In current applications, doxorubicin is administered intravenously either in its pure form or in a liposomal formulation. Therapy with free doxorubicin often causes severe side effects such as irreversible damage to the heart (cardiotoxicity). To avoid this, a liposomal formulation of the active substance was developed, which is used in hospitals under the name Caelyx/Doxil. Although this drug was able to reduce cardiotoxicity considerably, in many cases it led to an exceedingly unpleasant and debilitating hand-foot syndrome.

Talidox was developed by InnoMedica with the aim of preventing both cardiotoxicity and hand-foot syndrome. In the Talidox brochure of the Business Plan 2018, the potential benefits of the drug and the results of preclinical studies are discussed in more detail. Among other things, Talidox has been designed to enhance the exiting of the bloodstream and uptake into tumor cells. Talidox also has the potential to enhance synergies between chemotherapy and the immune system. On the one hand, Talidox induces immunogenic cell death in cancer cells, thereby stimulating the immune system to recognize and attack remaining cancer cells. On the other hand, Talidox protects immune cells circulating in the bloodstream and thus creates better conditions for the body's own cancer defense: a small liposome with great potential.

Clinical study phase I

First treatment of a patient with Talidox

After extensive preliminary work, the clinical trial with Talidox has been initiated: On November 12, 2018, the drug was administered for the first time in the Cantonal Hospital of St. Gallen.

As is common practice in a phase I clinical trial, a low starting dose was chosen for safety reasons and will be increased continuously as the trial goes on. In the case of Talidox, the starting dose of 10 mg/m² was approximately a quarter of the doxorubicin dose that would normally be administered during therapy using the approved reference drug Caelyx/Doxil. Over the course of the study, the Talidox dose will be increased over 5 further predefined dose levels up to the currently planned maximum dose of 40 mg/m² (Figure 1). The two highest dose levels (35 and 40 mg/m²) are comparable to the Caelyx/Doxil dose approved for the treatment of breast and ovarian cancer (±7%). Accordingly, the first indirect comparisons with the reference product Caelyx/Doxil, whose clinical use is significantly constrained by the frequently occurring hand-foot syndrome,

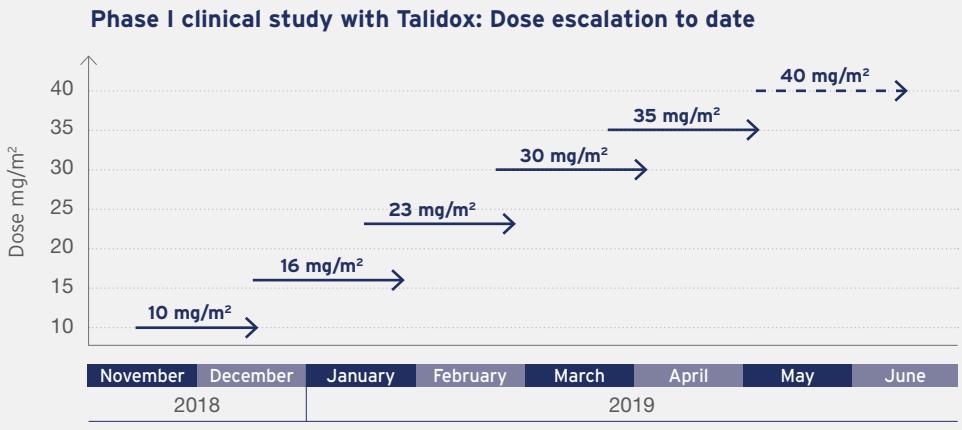


Figure 1: Phase I study history. In medicine, dosage data are always given in mg active substance per m² body surface area. An adult person' s average body surface area is between 1.7-1.9 m².

can be made after reaching this dose range. In addition to confirming the preclinical expectation that Talidox does not cause hand-foot syndrome, InnoMedica is also hoping for initial indications of the therapeutic effect of Talidox. The primary yardstick for this is the response rate, i.e. the proportion of patients with measurable tumor regression.

In case no substantial side effects occur when reaching the highest dose level provided for in the study protocol, 40 mg/m^2, the study protocol would immediately be amended for additional higher dose levels. Such an increase in the maximum dose as a result of good tolerability together with concurrent signs of a good therapeutic effect would have a favorable impact on the anticipated benefit-risk profile of Talidox.

The clinical study is progressing well. Patient recruitment is on track and so far, there have been no dose-limiting side effects. While in many clinical trials recruitment progress is limited by the availability of suitable patients, in the clinical trial with Talidox all vacant positions could immediately be allocated to waiting patients. This is not only thanks to the properties of Talidox, but also to the good organization and coordination of the clinical trial by the trial team of the Swiss Group for Clinical Cancer Research (SAKK).

At the time of printing, a total of 5 patients had been treated with Talidox and the dose had been increased to 35 mg/m^2.

Further clinical development

Dependent upon good efficacy results, it is planned to directly expand the phase I clinical trial by 30 patients to a phase IIa trial with the indication breast cancer. This could demonstrate the expected equivalent or superior effect of Talidox in this first indication. In addition to phase IIa, the planning of the subsequent clinical phase IIb is already underway. Irrespective of the results of phase I/IIa and a possible approval, phase IIb is very likely necessary in order to obtain further indication-specific information and to draw conclusions on optimal treatment strategies. In collaboration with InnoMedica's clinical partner SAKK, the first indication has been identified as breast cancer. There are medical, epidemiological and regulatory reasons for using Talidox in breast cancer:

Medical efficacy: From a medical point of view, Talidox appears attractive for this indication because breast cancer in most cases responds favorably to therapy with doxorubicin. Accordingly, doxorubicin preparations are also frequently used for breast cancer therapy, often even as monotherapy. In this context, Talidox addresses the ongoing medical need for better treatment options for breast cancer patients in the form of new products with an advantageous efficacy/side effect ratio.

Epidemiology: Breast cancer remains by far the most common cancer among women worldwide, another reason why the development of Talidox as a breast cancer therapy first is advantageous. The high incidence suggests the potential for frequent use of the drug and facilitates rapid recruitment progress in clinical trials.

Lower regulatory hurdles: Regulatory considerations furthermore also support the development of Talidox as a breast cancer therapy. Given the number of approved products, the high efficacy of doxorubicin in the treatment of breast cancer is generally undisputed. In light of this, regulatory authorities may accept a much leaner submission dossier compared to new compounds, which would result in significant savings in terms of time and money up to approval.

Since InnoMedica is breaking new regulatory ground with Talidox, the regulator's guidelines however leave ample room for interpretation. Based on these considerations, InnoMedica is pursuing the following optimized clinical development strategy:

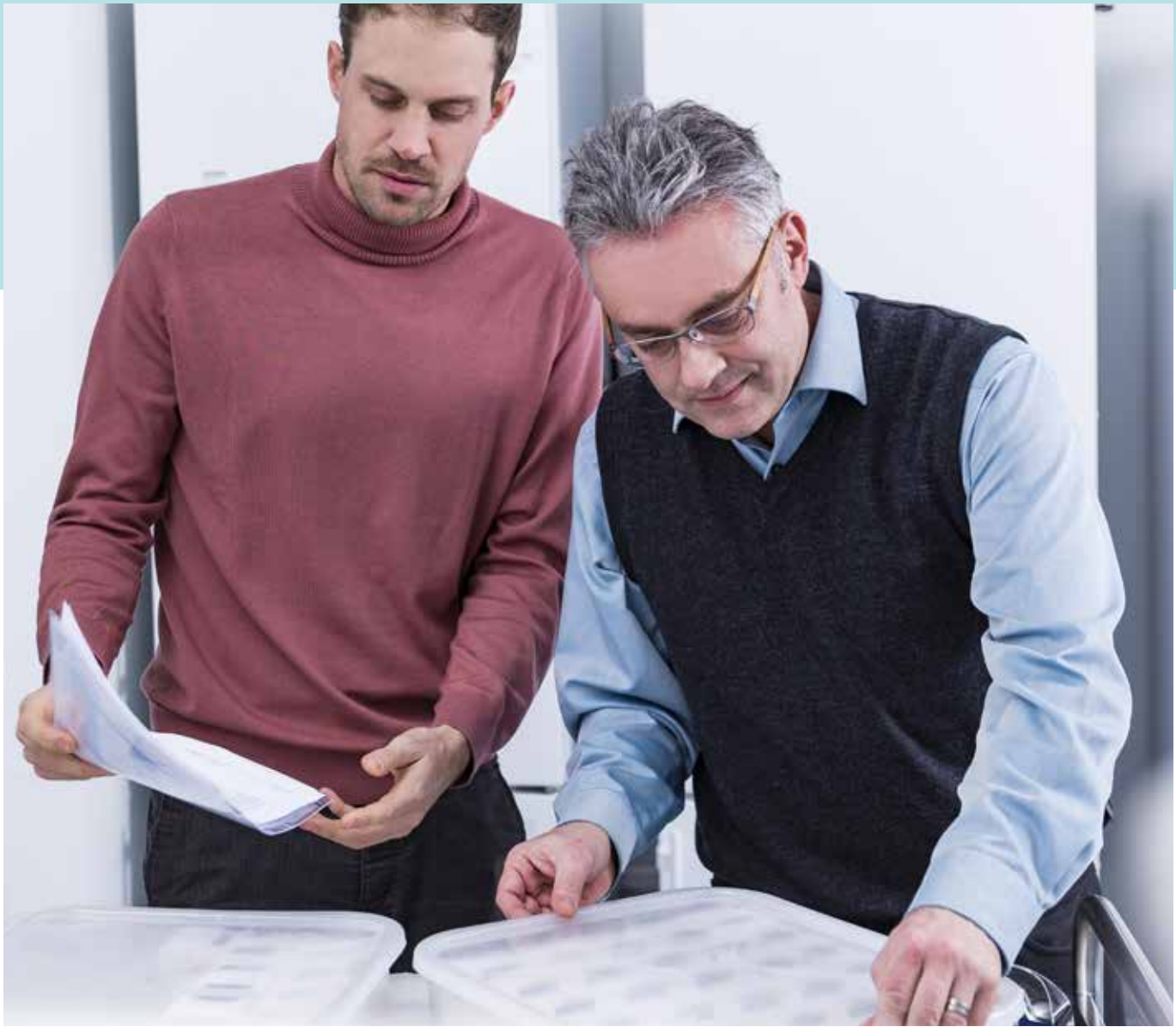
Clinical phase I/IIa: Bioavailability, dosage and tolerability

The phase I/IIa planning is based on three established issues emerging from the widespread use of doxorubicin in everyday clinical practice:

Equivalent but different: To date, three different formulations of doxorubicin have been approved. Free doxorubicin is marketed as Adriblastin (among others), while Caelyx/Doxil and Myocet refer to liposomal formulations of doxorubicin. The three preparations differ significantly in terms of bioavailability, dosage and tolerability, but the antitumoral effect in metastatic breast cancer is comparable in all three formulations.

Patient Safety

Each Talidox batch is released by the quality assurance team after verification of the GMP documents for the treatment of cancer patients in the phase I study. The drug can then be delivered to Swiss hospitals under controlled conditions.



Severe side effects: All three formulations leave substantial albeit different potential for improvement. While free doxorubicin has a strong dose-dependent cardiotoxic effect, Caelyx/Doxil frequently induces hand-foot syndrome. In many cases, a distinct weakening of the immune system is furthermore observed. Although Myocet has fewer side effects, it is a highly unstable formulation with the necessary preparation procedure in the hospital making administration extremely complicated.

Basic therapy: Doxorubicin-based chemotherapies remain crucial in the treatment of metastatic breast cancer, as well as many other forms of cancer, and still cannot be replaced by other therapies. In metastatic breast cancer specifically, also immunological or hormonal therapies benefit from the add-on of medications containing doxorubicin.

InnoMedica's preclinical data suggest that Talidox stands out positively from the three approved drugs in terms of bioavailability, dosage and tolerability. Several animal studies with Talidox provide evidence that certain side effects are significantly reduced. The clinical reasoning regarding the reduction of relevant side effects is comparatively simple and can largely be explained already on the basis of the data from the phase I study. Since the active substance of Talidox is in fact doxorubicin and there are no significant differences between the previously approved doxorubicin products with regard to the antitumoral effect in metastatic breast cancer, Talidox is also expected to have at least a comparable effect.

If the phase I results are positive, an extension of the ongoing study to a phase I/IIa study will be applied for. The additional 30 breast cancer patients will be treated with the optimal dose identified in phase I. While the primary focus of the phase I trial is on the tolerability of Talidox, the conversion to phase I/IIa will result in timely information on efficacy, especially since an extension of the trial only requires an adjustment of the trial protocol and not the submission of a completely new trial application. Should these data confirm an advantageous risk-benefit profile for Talidox, an application for approval can then be submitted.

Clinical phase IIb:
Bayesian study with control group

Talidox uses doxorubicin, an active substance for which there is a wealth of data available from clinical use. These empirical values on doxorubicin are taken into account in InnoMedica's phase IIb study design. A procedure according to Bayesian statistics is used, which allows the inclusion of these extensive clinical data on doxorubicin in the study evaluation. Based on these data, the expectations about effect and side effects of medications containing doxorubicin are used as a reference point for treatment with Talidox. In contrast to conventional statistical evaluation methods, these expected values do not have to be collected by including larger control groups in the clinical trial, therefore allowing a significant reduction of the sample size.

In order to create a current reference framework for the interpretation of the Talidox data – in addition to the historical data – a small control group with patients receiving conventional chemotherapy is recommended for calibration purposes. Even though the small control group planned for the phase IIb Talidox study does not suffice for a formal statistical comparison, it may render decisive information for the interpretation of the Talidox data. The comparison of the control group with the historical data shows whether the selection of study patients represents a typical patient group or whether the selection is particularly difficult or easy to treat. As such, the control group provides a validation for the unlikely but potentially critical event that the therapeutic success of the study patients would only have resulted from the selection of a particular patient group.

In contrast to comparative studies for new active substances, these considerations result in a much smaller, more cost-effective phase IIb study for Talidox. Given the extensive experience with the active substance doxorubicin, plans are based on the assumption that Talidox can in principle be expected to be effective and that consequently, a significantly reduced clinical development program in comparison to new active substances is adequate.

Talidox on its way to market approval

InnoMedica plans to apply for market approval in the indication of metastatic breast cancer directly after phase I/IIa if the study results are sufficiently conclu-

sive. The phase IIb and further clinical trials in breast cancer or additional indications would then take place after initial approval. The extent to which the data from the phase I/IIa study provide a sufficient basis for regulatory review depends primarily on the extent to which the available clinical data on Talidox allow a reliable assessment of the benefit-risk profile in view of the broad experience with doxorubicin. In the assessment of Talidox, the focus is less on the efficacy of doxorubicin than on the change in the efficacy-side effect profile due to the new liposomal formulation and the transferability of the benefits documented in the preclinical phase to humans. The following central questions come up:

Compared to free doxorubicin and Caelyx/Doxil, can Talidox transport more active substance into the tumor in humans?
The biological distribution of free and liposomal doxorubicin in the human body is relatively well researched. Based on this prior knowledge, InnoMedica was able to optimize the decisive parameters – in particular the size and composition of the liposomes – in the development of Talidox specifically for use in patients. In the animal model, it was then shown that Talidox liposomes effectively bring more active substance into the tumor. The probability that this will also be the case in humans is therefore relatively high.

Can Talidox improve the release of the loaded doxorubicin in the tumor?
The relationship between the size of a nanoparticle and its uptake into cells (endocytosis) has been well explored scientifically. The size of Talidox was designed according to the described optimum for endocytosis of 60 nanometers. The substantially improved uptake of Talidox by tumor cells compared to Caelyx/Doxil was proven in cell experiments.

Can Talidox eliminate the relevant side effects of today's doxorubicin-based formulations?
The damage to the heart muscle caused by free doxorubicin occurs only to a very small extent in Caelyx/Doxil due to the liposomal shell. A comparable reduction of this side effect is therefore expected for Talidox. According to the results of the toxicology study, the hand-foot syndrome caused by Caelyx/Doxil should also drop to a negligible level due to the optimized biological degradation processes of Talidox.

Can therapy with Talidox be continued over a longer period of time?
While the duration of therapy with free doxorubicin is usually limited by the risk of irreversible heart muscle damage, the use of the liposomal doxorubicin product Caelyx/Doxil is often limited by the occurrence of hand-foot syndrome. For Talidox, a simultaneous reduction of both above-mentioned side effects would lead to the prospect of treating patients for correspondingly longer periods of time. Furthermore, there is reason to believe that the liposomal formulation of Talidox also has advantages from the point of view of resistance: Many tumors develop resistances over the course of therapy with conventional chemotherapeutic agents, leading to associated loss of efficacy. Liposomal formulations in many cases seem to circumvent the relevant resistance mechanisms. If Talidox can be administered for longer because of its good tolerability and remains more effective thanks to the suppression of resistance, a substantial efficacy advantage could be achieved compared to previous chemotherapy approaches.

First evaluations of the clinical results will allow conclusions regarding the tolerability and side effects of Talidox. The latter are key aspects of any chemotherapy. InnoMedica has demonstrated in preclinical studies that the number of neutrophil immune cells responsible for the defense against acute infections remains unexpectedly high. This suggests that the liposomal structure of Talidox results in a measurable protection of the neutrophil immune cells. The neutrophil immune cells make up around 60 percent of all immune cells in the blood. Their number and function are of particular importance for cancer patients:

- The larger the number of functional neutrophil immune cells circulating in the blood, the lower the risk of the cancer patient suffering severe complications due to acute bacterial infections.

- An intact immune system can lead to a better immune response against cancer. This is of particular importance for therapies containing doxorubicin, as these cause immunogenic cell death. Tumor cells that die through the influence of doxorubicin trigger the immune system and provoke a certain immune reaction against cancer. In therapy with free doxorubicin, however, the active ingredient damages the immune cells circulating in the blood in such a way

that it suppresses the immune system and makes a proper immune reaction against the dying tumor cells less likely. Therapy with free doxorubicin, so to speak, prevents an important part of its own success. In addition, in treatment with free doxorubicin compared to Talidox, less active substance reaches the tumor, which reduces the number of dying immunogenic tumor cells. Talidox in contrast exploits the potential of doxorubicin by transporting larger amounts of the drug to the tumor while protecting the immune system in the blood from its unwanted side effects.

To summarize, there is reason to assume that also in humans Talidox …

… accumulates better in the tumor
… protects the immune system
… allows treatments over longer periods of time
… causes immunogenic cell death and benefits from synergies with the immune system

The aim of the ongoing clinical studies is to prove these claims in the patient.

Talineuren

The Talineuren project has produced some very promising results since its beginning in the summer of 2016. Talineuren opens new perspectives in the treatment of Parkinson's and other neurodegenerative diseases. Detailed information on Talineuren can be found in the according brochure of the Business Plan 2018. The positive preclinical results encouraged InnoMedica to press ahead the translation of Talineuren. The following three levels of action are crucial:

Preclinical research: In preclinical research, questions of efficacy, dosage, administration form, and tolerability are investigated using animal models. The preclinical results are summarized in an Investigator's Brochure.

Pharmaceutical production: The production of medical grade Talineuren is a central requirement for the start of the first clinical study. Compliance with the Good Manufacturing Practice (GMP) guidelines is binding and documented in the Pharmaceutical Quality Dossier. Furthermore, the production quantities required for the study need to be ensured with an appropriate scaling concept.

Clinical study: The study protocol provides a detailed description of the clinical trial's course of action. The most important parameters include the definition of the endpoints, dosages, inclusion criteria, study centers, and physicians, as well as the selected method for evaluating the collected study data.

Preclinical research

The first administration of Talineuren to patients in the clinical study depends upon toxicological testing in addition to existing efficacy and dosage studies.

Toxicology study

Preclinical tests for acute and chronic toxicity, conducted under Good Laboratory Practice (GLP) conditions, will determine the maximum administered dose for Talineuren. The tests furthermore enable conclusions regarding the dose-dependent tolerability. The starting dose for the first clinical trial is then calculated based on these findings.

Drugs with new active substances usually require a toxicological test in at least two mammalian species. Since the active ingredient of Talineuren, GM1, has already been tested in various animal models, as well as in a number of clinical studies, Swissmedic considers a simplified toxicity test in only one mammal species as conceivable in principle. Such a simplification would bring substantial financial savings and markedly accelerate the completion of the preclinical phase.

Potential in different indications

Several academic animal studies show that the active substance GM1 contained in Talineuren, in addition to its clinically proven benefit in the treatment of Parkinson's disease, also has therapeutic potential in other neurodegenerative movement disorders: For example, the direct injection of GM1 into the brain in the Huntington's mouse model led to promising results up to complete remission of various symptoms. However, the route of direct injection into the brain used in these animal studies is extremely invasive and not feasible for long-term, broad clinical use. With the liposomal transport system, Talineuren could cross the blood-brain barrier even in an orally ingestible formulation. This would enable an incomparably better and safer

Huntington's disease

Huntington's disease is a dominantly inherited neurodegenerative disease caused by mutations of the Huntington's gene. The mutation leads to the production of a faulty protein in neurons in the brain of affected persons. The defective proteins continually form neurotoxic aggregates, which lead to the long-term death of neurons. The disease manifests itself through progressive motor, cognitive, and psychological impairments.

Initial symptoms usually occur in the form of subtle personality changes, perception disorders, and jerky, involuntary movements. These are followed by increasingly impaired psychomotor functions such as chewing and swallowing difficulties, as well as gait disorders, which lead into general neuropsychiatric abnormalities such as anxiety, depression, and obsessive-compulsive behavior, then to reduced cognitive abilities and memory disorders, and ultimately dementia.

Current treatments provide only temporary relief for only some of the symptoms, while often causing severe side effects. Approximately 400 people with Huntington's disease live in Switzerland. The average age at diagnosis is 40 years. The disease usually leads to death within an average of 15 years.

Talineuren scale-up

As Talineuren is based on InnoMedica's technology platform, already for Talidox established production processes and scale-up concepts can be used: Investments made for Talidox also pay off for Talineuren.

GM1 therapy. With this in mind, InnoMedica has decided to investigate the effect of Talineuren not only in Parkinson's but also in Huntington's disease. In the fourth quarter of 2018, a first Huntington's study with Talineuren was conducted, which rendered first potential evidence to the desired effect. Based on these findings, a follow-up study has been initiated, addressing questions such as optimal dosage and the best starting point for treatment. The results of this study are expected in the second quarter of 2019.

Based on the existing preclinical data on GM1 in Huntington's models, there is reason to assume that Talineuren may facilitate an effective therapy for this rare, as yet virtually untreatable disease. Should the preclinical data on Talineuren support this assumption, InnoMedica will gain attractive access to the *Orphan Disease* programs of various registration authorities (see Clinical Study).

Pharmaceutical production

Talineuren's approval for clinical trials depends on production in accordance with pharmaceutical guidelines of Good Manufacturing Practice (GMP). InnoMedica has at its disposal the company's own production facility in Marly, certified by Swissmedic, together with the GMP system in use in the production of Talidox. While this will allow accessing existing resources, implementation of Talineuren production requires important additional steps:

Suppliers: Some of the raw materials for Talineuren are much more difficult to procure as compared to Talidox. Notably the active ingredient GM1 and components of the liposome shell are expensive and often are not available on call in industry-standard quantities. InnoMedica has managed to secure a reliable source for the most important component of Talineuren. TRB Chemedica produces the active ingredient GM1 in Switzerland, the availability of which has been contractually agreed upon it in a letter of intent between TRB Chemedica and Innomedica.

Scale-up: In addition to securing the necessary raw materials, processing them in larger quantities is a key prerequisite for the future market entry of Talineuren. Since Talidox and Talineuren are both based on InnoMedica's technology platform, the production of Talineuren is analogous to production processes established with Talidox and similarly can fall back on already developed scale-up concepts. Hence, investments made for Talidox will also pay off for Talineuren. In case of a potentially fast-growing number of patients, the production volume can be increased promptly. In September 2018, a first batch of Talineuren in the expected final formulation was successfully produced on a large scale of up to 4 liters.

Stability: After successful adaptation of the manufacturing process to the needs of clinical development, the biochemical stability of the resulting product must be demonstrated. A provisional shelf life is determined on the basis of test production batches, which is later conclusively determined on the basis of the batch effectively used for clinical purposes.

Cooperation with TRB Chemedica: securing the supply chain and developing an international distribution network

In June 2018, InnoMedica and TRB Chemedica signed a Letter of Intent for a long-term collaboration that underlines the strategic importance of a partnership for successful clinical translation and industrial manufacturing of Talineuren.

TRB Chemedica is specialized in large-scale pharmaceutical purification of glycolipids from biological sources. InnoMedica further processes these glycolipids in liposomal formulations and so opens up new areas of medical application. By combining the two technologies, nanostructures can be made pharmaceutically viable close to their natural form. The combination of the core technologies of TRB Chemedica and InnoMedica can lead to synergies and a multitude of new innovative products.

TRB Chemedica is a pharmaceutical company headquartered in Geneva with more than 900 employees worldwide. The company specializes primarily in ophthalmic and antirheumatic drugs, which are marketed through 18 foreign subsidiaries and a network of distributors in approximately 70 countries. Thus, InnoMedica can also benefit from TRB Chemedica's large international distribution network for fast market access. TRB Chemedica's patented proprietary GM1 extraction processes qualify the company to market its high-quality GM1 product in China, Brazil and Argentina. InnoMedica sees clear advantages for product development and marketing of the drug in cooperation with TRB Chemedica. Following regulatory approval of Talineuren, TRB intends to immediately increase GM1 production substantially.

Quality assurance: InnoMedica can also benefit from the experience gained in Talidox production with regard to quality assurance. In particular with regard to important aspects of patient safety, such as sterility and endotoxin control, this extensive prior knowledge is an advantage. Additional work is therefore limited primarily to those process steps that deviate from Talidox production. Furthermore, the clear spatial separation of Talineuren and Talidox production must be implemented in order to rule out contamination of Talineuren by cytostatic agents.

Clinical study

As with Talidox, information was obtained from Swissmedic during the conceptualization of the clinical study strategy for Talineuren and taken into account in the study design. If strong preclinical data are available, it is in principle possible also for Talineuren to conduct the first clinical study directly with patients instead of healthy volunteers. This procedure generates early results on efficacy and promotes rapid progress in clinical development.

Scientific findings prove that the active substance GM1 used in Talineuren is involved in various essential functions such as the development, differentiation, and survival of nerve cells, particularly in the central nervous system. Animal experimental data and clinical studies even point to rehabilitative effects of GM1. This suggests that Talineuren could be therapeutically effective in various neurodegenerative diseases. Based on this prospect, InnoMedica plans to include both Parkinson's and Huntington's disease patients in the first clinical trial.

On the part of the regulator, a study design that includes several indications is basically possible. Provided there is appropriate preclinical proof of concept, the potential of Talineuren could thus be investigated in both a large indication such as Parkinson's and a rare disease such as Huntington's disease all in one single study. Such an approach is exceptional in that two different neurodegenerative diseases can be treated with the same drug.

Due to its high degree of innovation, Talineuren is likely to qualify for an accelerated approval procedure for the treatment of Huntington's disease in Switzerland as well as in the EU and the USA. In doing so, the authorities specifically promote drugs that address rare and insufficiently treatable diseases (*orphan diseases*). Should Talineuren be recognized as an *orphan drug*, the authorities can provide extensive support for the further development of the drug until its market launch. These include a shortened assessment period on the part of the EU regulatory authority, regular scientific advice, support in drawing up the clinical development strategy, major fee reductions, an accelerated assessment of the approval application, and the prospect of ten years of market exclusivity after market entry. Once *orphan drug* status has been granted, a conditional marketing authorization can be applied for on the basis of initial successful clinical trials, allowing early marketing of Talineuren. The clinical data required for the unrestricted, indefinite approval could then be collected in parallel and submitted later.

Also beyond the *orphan diseases* category, support services in the form of regular consultations and accelerated procedures are offered for drugs with substantial potential for improvement. These regulatory support measures could therefore technically also be requested for approval applications in larger indications such as Parkinson's disease.

Cooperation with neurologists

For the planning and implementation of the clinical study with Talineuren InnoMedica is working with PD **Dr. med. Michael Schüpbach**, consultant physician at the Inselspital Bern and head of the Neurological Institute Konolfingen. The experienced neurologist most recently headed the Centre for Movement Disorders and the Deep Brain Stimulation Unit (DBS) at the Neurological Clinic at the Inselspital in Bern before taking up his practice at the Neurological Institute Konolfingen (BE) and at the Joint Practice for Neurology in Bern in 2017. After studying medicine in Bern, Atlanta and Boston, he first worked as an assistant at the Physiological Institute in Bern and then completed specialist training as a neurologist in Bern. Then followed several years of research work in Paris, which was continued part-time after returning to the Inselspital in Bern. He can draw on many years of experience both in clinical research and in his work as a clinician and brings in a great deal of expertise in Parkinson's and Huntington's disease. He also holds the office of Vice President of the Swiss Movement Disorder Society (SMDS) and continues to maintain a scientific cooperation with the Hôpital de la Pitié-Salpêtrière in Paris.

The clinical strategy for Talineuren plans to apply for *orphan drug* status for Huntington's disease after completion of the preclinical studies in this indication. The tolerability and efficacy of Talineuren can then be evaluated in a phase I/IIa study simultaneously in both Parkinson's and Huntington's indications. Should relevant data which indicate a substantial improvement compared to existing therapies already be available from phase I, an application for an accelerated approval procedure will be submitted in Switzerland and the EU for the respective indication.

InnoMedica plans to act as the institution responsible for the study for the first clinical trial with Talineuren. With Talidox, this function was taken on by SAKK. As for Talineuren, there are advantages for InnoMedica in acting as a study sponsor itself. This will save both costs and time while ensuring more immediate control and greater flexibility in the realization of the study.

Reconstruction Clean Room II

In order to meet the high expectations in the event of success, InnoMedica is currently fucusing on the scale-up of the manufacturing process and the expansion of the new large clean room. The expansion of production is thus fully in line with the clinical progress of Talidox.

Manufacturing

The molecular class of phospholipids - a combination of phosphates and fats - is of great importance for organic life on earth, since phospholipids form the spatial boundary and organizational structure of every higher cell.

To date, there are only a few drugs that specifically use the mechanisms of biological differentiation and cell organization in their treatment concepts. It is too complex and technically demanding to combine pharmaceuticals with phospholipids and there is too little knowledge about the functional relationships of different phospholipids, their nanostructure, their distribution in the body, or their therapeutic potential.

To combine phospholipids with active pharmaceutical substances and turn them into drugs several important technical challenges have to be mastered:

- Production must be cost-effective and operable at scale.
- The end products must be sterile and stable.
- The biological functionality of the drug must be described in a precise manner.

Considering the complexity of such tasks, it seems obvious to outsource the production to a specialized partner. However, in doing so, a large part of the core technology and thus important know-how is lost for the company, which as a consequence is left with limited potential for further development of its process technology in production, and likewise severely restricted opportunities to further develop the basic understanding of liposomal design.

From the outset, InnoMedica relied on operating its own production facility. This enabled prompt and flexible testing of development findings in technologically optimized manufacturing processes, as well as subsequently feeding knowledge thus gained back into development. Setting up the company's own production facilities initially entailed a considerable additional risk, higher investment costs, and somewhat slower project progress. As we can now see however, this strategy bears clear long-term advantages regarding fundamental technological concerns. InnoMedica has been able to position itself well in a very competitive international environment thanks to the know-how it has acquired in manufacturing, pharmaceuticals, and nanobiochemistry, with a broad pipeline of new products and international patents in liposome technology and its application. Highly qualified employees continuously contribute to new applications and optimized, innovative process technologies.

By now, InnoMedica has been able to set up a fully functional production facility that covers the entire value chain according to the latest guidelines of Good Manufacturing Practice (GMP), from the procurement of raw materials and consumables, to production, all the way to the stable, sterile, injectable end product. This current production facility is capable of meeting the demand for Talidox in ongoing clinical trials, but is not designed for the volumes required after marketing approval. For this reason, and in view of the fact that setting up pharmaceutical production in compliance with the guidelines takes a lot of time, InnoMedica began planning the industrial-scale production of Talidox at the end of 2017. The first construction activities began in the summer of 2018 with the installation of storage facilities and a process engineering laboratory. With the start of the phase I clinical trial, construction began on a second, much larger clean room, which will significantly expand InnoMedica's production capacity (Table 1).

Clean room II

At the time of printing, the construction of InnoMedica's new clean room II is nearing completion. It is based on the following room concept:

Production facilities: Large batches of InnoMedica's liposomes are produced in separate production rooms for Talidox and for Talineuren, respectively. In particular, this constellation facilitates preventing contamination in the manufacture of different drugs.

Sluices: In the new concept, the personnel and material sluices are spatially separated. Staff reaches the production rooms via a three-stage staff sluice, the material is fed via a single-stage material sluice.

Peripheral rooms: The monitoring and supply technology was each implemented in a separate control and technical room. The control room allows the production steps to be monitored and the production team to be actively supported during production. The technical room contains all equipment and machines that do not necessarily have to be placed in the production rooms. The clean room zone is supplied with the required infrastructure services from there via supply lines.

A complex air pressure cascade concept allows the production of sterile, injectable cytostatic products in the ISO 7 (Class C) classified clean room without contamination of the environment and with optimal protection of employees. The new clean room II uses only fresh air that has been filtered and processed in accordance with pharmaceutical guidelines. The reuse of exhaust air is deliberately avoided in order to prevent contamination with cytostatic particles. The energy required for air purification is to be significantly reduced by means of heat exchangers. The infrastructure work in the air treatment system and supply system will be carried out by the landlord, the Marly Innovation Center, in parallel with the ongoing clean room installation.

After completion of the construction phase, the room qualification as well as the installation and qualification of production equipment will take place in the second half of 2019. This will be followed by the manufacture of the first trial batches on a larger scale and the approval of the entire production concept by Swissmedic. The new clean room will then be able to produce larger GMP-compliant Talidox batches for the first time in the phase IIa clinical trial.

Commissioning of new process engineering

In the fourth quarter of 2018, the premises of the process development laboratory were completely gutted, enlarged, and upgraded to the new standard. The bright, large rooms are now equipped with precisely dimensioned ventilation and technical facilities, which create conditions in line with pharmaceutical standards for the future process optimizations. In particular, the new process engineering rooms enable testing and optimizing production technologies used in clean room II in advance, but also more precise analysis and improvement of existing process steps. (Figure 2).

Investment overview (Table 1)
Estimates are shown in italics.

Investments	Expenses (CHF)	Commissioning
GMP storage Sample drawing area	120,000	Oct 2018
Process engineering	120,000	Nov. 2018
Cold storage room +5°C	*80,000*	*Jun 2019*
Clean room cover	*500,000*	*2019/H2*
Clean air, heat recovery, heating/cooling system	*750,000**	*2019/H2*
Reactors, production equipment	*500,000*	*2019/20*

* Investment by landlord following InnoMedica's initiative

Expansion and commissioning of GMP storage facilities

The new storage rooms were additionally rented from the landlord and rebuilt according to InnoMedica's specifications:

GMP warehouse with controlled conditions: The pharmaceutical warehouse has already been put into operation. Storage at controlled temperature and humidity as well as in an area with slight overpressure enables securing the quality of raw materials, consumables, intermediate and finished products (Figure 4). The warehouse provides sufficient storage space under controlled conditions at 20 °C, 5 °C and -20 °C for the continuation of phase I and II clinical trials. The new GMP warehouse includes an integrated room for sampling with an overpressure sluice (Figure 5). This room, qualified as class D (ISO 8), has a laminar flow bench which allows sampling under sterile conditions. In accordance with the new GMP guidelines, an exemplary and future-proof investment has been made in this sample draw room, which also permits the professional handling of cytotoxic raw materials while avoiding cross-contamination as well as environmental and personal hazards.

High rack warehouse: To relieve the load on the GMP warehouse, a high rack packaging material warehouse was put into operation in autumn 2018, used for primary, secondary, and tertiary packaging materials, as well as accessories.

Cold storage space: With the expected increase in demand for Talidox as part of ongoing clinical development and subsequent market entry, the current cold storage capacity will quickly be exceeded. This capacity is currently limited to five qualified refrigerators and cannot be further expanded at the current location in the GMP warehouse. In December 2018 it was therefore decided to build a new GMP cold storage facility, which will be constructed using the pro-

Figure 2: New process engineering laboratory, built to meet pharmaceutical standards.

ven room-in-room technology. The cold storage room will be operated at +5 °C using two redundant cooling units and will have its own emergency power supply in order to protect InnoMedica's products and intermediate products from temperature fluctuations if necessary. This is particularly important since Talidox may no longer be used as a medication if the temperature specification is violated. With a volume of 46.8 m^3, the new cold storage room allows proper storing of intermediate products until further processing, of stability samples, and of finished packaged dosage forms until their temperature-controlled transport to the hospitals. The new cold storage facility is scheduled to go into operation in the first half of 2019 and is designed for the storage requirements of Talidox as well as other liposomal products – in particular Talineuren.

Scale-up and process optimization

The multi-stage production process has been further stabilized and now permits routine GMP production of Talidox on a 6-liter scale. In production it is now essential to make the process more efficient and prepare for a further scaling step and transfer to clean room II. The measures taken include:

Production reactors and scale-up: 2017, in the first scaling phase to 6-liters, small mobile glass reactors with volumes of 5 to 50 liters were implemented (Figure 3). For the further scale-up of the production batches from the 6- to an 18- then 36-liter scale, industrial reactors made of stainless medical steel are now being introduced, which have the advantage of improved heat conduction and temperature control compared to the previous glass containers. In addition to the reactors, the specifications of the other necessary equipment are currently being revised in cooperation with InnoMedica's suppliers and adapted to the requirements of the scale-up.

Supply security: In 2018, supplier relationships for key raw materials, important consumables, and analytical services were further consolidated. Where necessary and possible, backup suppliers were qualified according to GMP, for example for the active substance doxorubicin. For the most important raw material for the production of injectable sterile solutions, sterile water, an experienced supplier from the region was contracted.

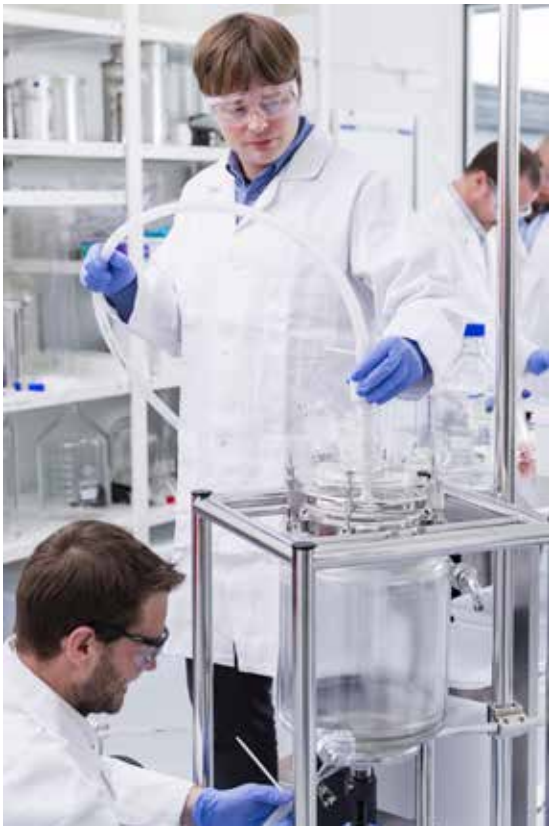


Figure 3: Cleaning mobile glass reactors

Figure 4: New process engineering laboratory, built to meet pharmaceutical standards.

Automation: In 2019, it is planned to switch from manual filling to semi-automatic filling using a small robot specially designed for InnoMedica. Filling must take place in the isolator under conditions of the highest purity class A and is therefore very time-consuming. By switching to semi-automatic filling, the filling time can be reduced by a factor of four and the operating time of the isolator can be shortened accordingly. In a second step, the filling process is to be converted to fully automatic by means of tailor-made robots with efficiency gains.

Logistics: The existing ERP system was further parameterized and allows efficient warehouse management as well as tracking, which is particularly important for pharmaceutical products, with proof of which raw materials were used for which products. ERP also supports the labelling of all raw materials and finished products as well as the creation of delivery documents. A system with recyclable cool boxes was procured for the cold shipment of products and analysis samples, which is to be implemented in the second quarter of 2019.

Production at InnoMedica made great progress in 2018. The planning phase of the expansion was completed and the construction phase started. A process-oriented perspective was implemented such that the expansion is aligned with the industrial scale-up. All production steps, from purchasing and storage capacities to efficient production and end product storage, were taken into account in the planning. With the start of the clinical trial, expectations are growing that Talidox will also be available in larger quantities, which is why the expansion of the production plant should not be delayed. In this respect, the expansion of production is optimally aligned with Talidox's clinical development progress.

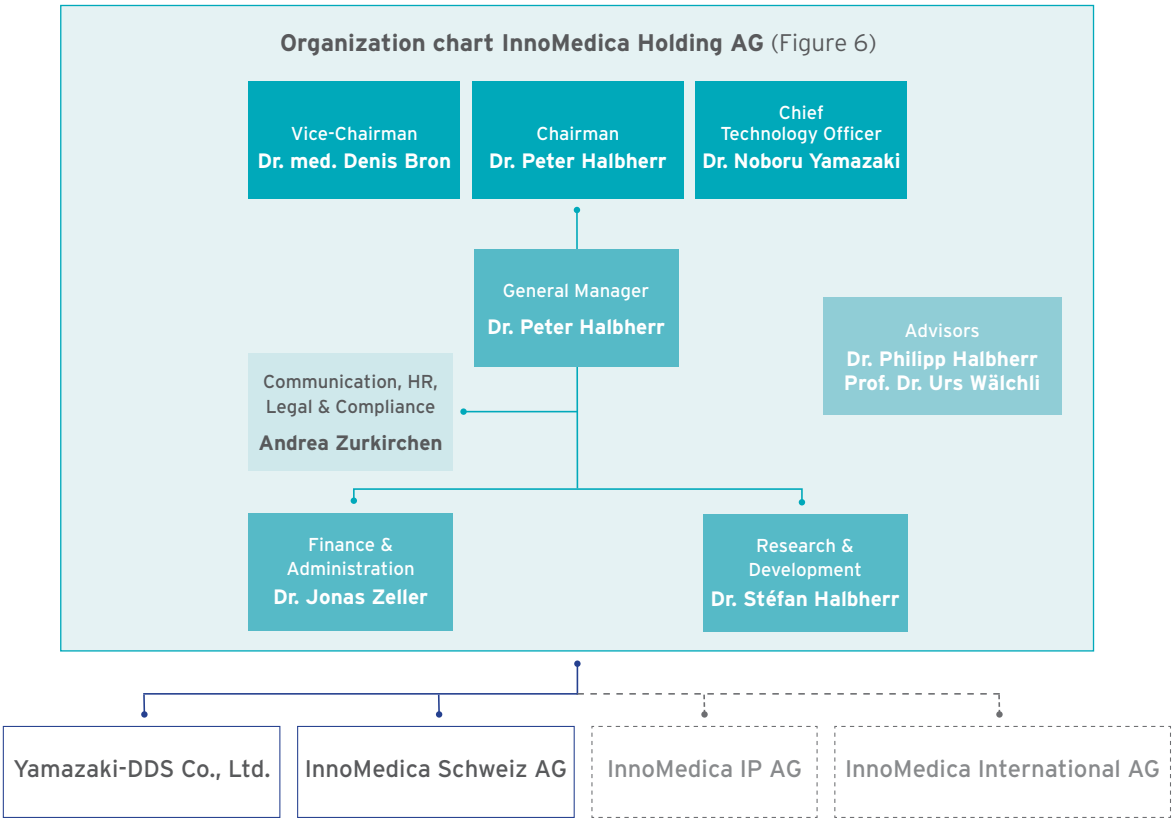
Figure 5: Sample drawing room in GMP warehouse with laminar flow bench

Team

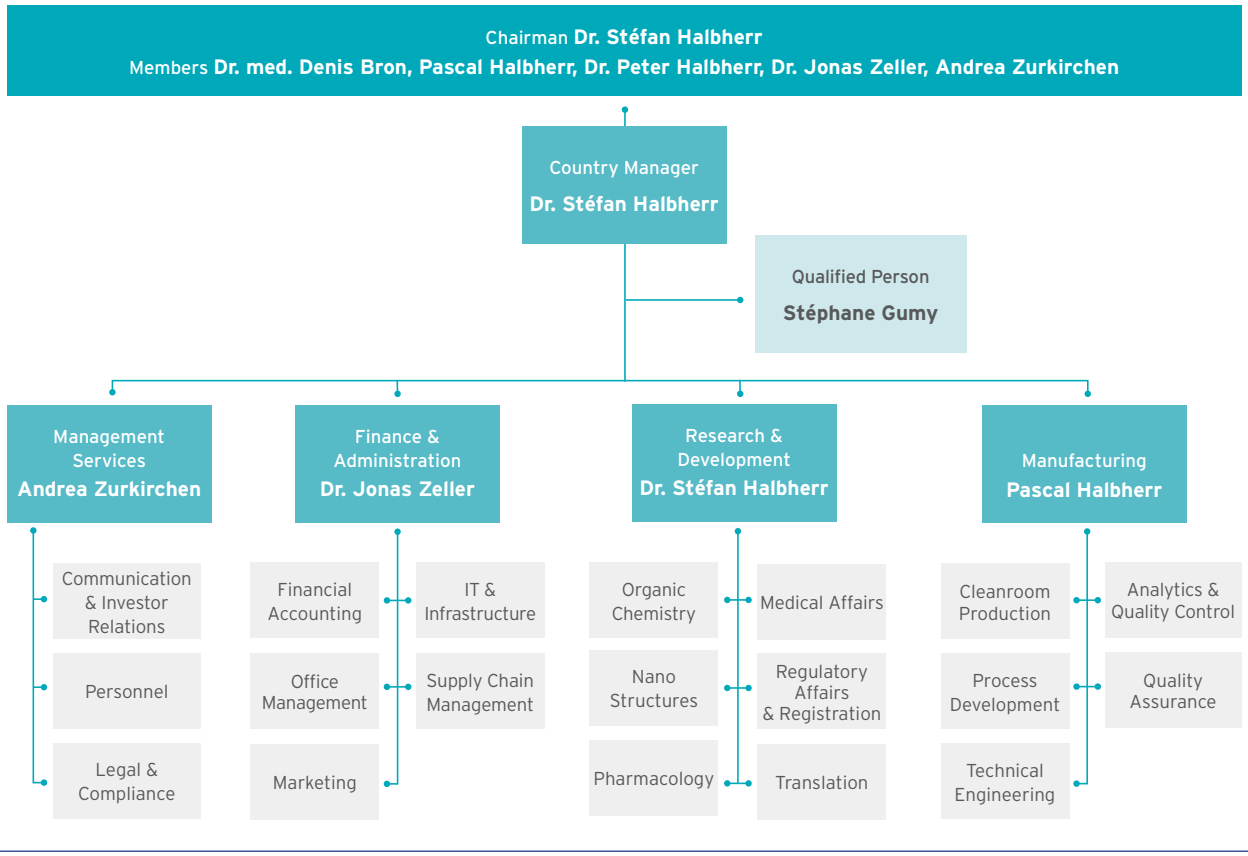
What began in the basement at Gesellschaftsstrasse as a start-up project of a few innovative minds has now grown into a young company with 25 employees - with its own production, analytics and quality assurance, a medical affairs team with a first product in the clinical phase, and a research department with more new and promising products in the pipeline.

Building and safeguarding the valuable know-how of the people involved in InnoMedica within the company has been a key element of InnoMedica's success since the beginning of the project. Following the acquisition of the patents for the liposomal drug transport system in 2013, Dr. Noboru Yamazaki was a member of InnoMedica's Board of Directors, where he was also involved in operations in the beginning and passed on his experience to the founding team. Dr. Denis Bron was elected to the Board of Directors and appointed Vice-Chairman at the 2018 Annual General Meeting. As a medical consultant he was associated with the company for many years and had already contributed patents in liposome technology to InnoMedica in 2010. Dr. Peter Halbherr's central role as a link between the Board of Directors and the operational management is reflected in his function as Chairman and Delegate of the Board of Directors. Particularly in the initial phase of the project, his company IPAG Inter Personal AG absorbed large parts of the incubation risks through personnel financing and the provision of office and IT infrastructure and made a significant contribution to InnoMedica's lean cost structure.

At the 2018 Annual General Meeting, Dr. Peter Halbherr was elected Chairman of the Board of Directors following Dr. Herbert Früh, who held this office from 2003 to 2018. In mid-January 2019, Dr. Herbert Früh and Manuel C. Frick announced their resignations from the Board of Directors of InnoMedica. The change in the Chairman's Office and the resignations took place in the context of differing views on the strategic orientation and corporate culture of the company, in particular with regard to the separation of the Board of Directors and the Executive Board and the formation of a Group structure. The resignation of the two members of the Board of Directors brings a clarification of responsibility and ensures the efficient management of the company by the Board of Directors. The remaining members of the Board - Dr. Peter Halbherr, Dr. Denis Bron and Dr. No-



Organization chart InnoMedica Schweiz AG (Figure 7)



boru Yamazaki - are well acquainted with the young team and management dynamics and have played a key role in building the company through active participation over extended periods. The Board of Directors will submit a proposal for the expansion of the Board to the next Annual General Meeting.

In view of the company's increasing financial strength and upcoming development, the outsourcing partner IPAG Inter Personal AG was acquired by InnoMedica Holding AG at book value as of January 1st, 2019 and will be integrated into the parent company after being renamed InnoMedica Schweiz AG. This concludes the incubation phase and simplifies the development of a holding structure for InnoMedica. The takeover was accompanied by Prof. Dr. Urs Wälchli as consultant and by Deloitte with a high-level due diligence. The holding structure now permits the operational business and current contracts to be combined in the subsidiary InnoMedica Schweiz AG. This helps to limit risks. At holding level, Dr. Peter Halbherr will continue to act as General Manager of the company. Dr. Stéfan Halbherr (Research & Development), Dr. Jonas Zeller (Chief Financial Officer) and Andrea Zurkirchen (Communications, HR, Legal & Compliance) will now exercise their functions both in the holding company and in the subsidiary (Figure 6).

Dr. Stéfan Halbherr, Dr. Jonas Zeller, Pascal Halbherr, Andrea Zurkirchen, Dr. med. Denis Bron and Dr. Peter Halbherr together form the new Board of Directors of the subsidiary InnoMedica Schweiz AG. This is chaired by Dr. Stéfan Halbherr, who has a central role in the company due to his expertise and his contribution to the development of the products and at the same time takes over the management of the operative business of the subsidiary as Country Manager. One of the company's goals is to place particular emphasis on professional expertise when filling management positions and also to offer development opportunities to younger managers within the company. This applies not only to management functions, but also to the Board of Directors level. Thus, a younger generation shall be built up for the succession and an independent development shall be ensured in the longer term (Figure 7).

After doubling the headcount from 11 to 22 employees in 2017 and taking into account the result of the financing round in spring 2018, InnoMedica has

pursued a more moderate personnel growth. In the context of the positive preclinical results for Talineuren and the ongoing phase I clinical trial with Talidox, additional recruitment in production and research and development became necessary at the beginning of 2019. Further expansion of quality assurance is also planned. The InnoMedica team was presented in the Business Plan 2018. There have been personnel changes in the meantime: Dr. Fabiola Schorer (GMP Quality Design), Andreas Inderbitzin (Technical Engineering) and Vanessa Ackermann (Office, Legal & Compliance) have reoriented themselves. The manufacturing team was expanded by the recruitment of Dr. Dominik Waluk, Dr. Matthias Burgener and Michael Aeberhard in Process Engineering Pharma Production and Dr. Borka Jojic in Quality Control and Analytics. Dr. Adeline Colussi joined the development team and the finance team was further expanded with the addition of Dr. oec. Martin Stähle. From June 2019, Noëmi Müller will also be responsible for office management and will complement the Legal and Compliance division as a lawyer. In April/May 2019, Philipp Steffen and Dr. Caroline Dafflon-Urech will be two further important new hires in quality assurance.

The management has been stable for over five years and provides continuity. We give particular value to professional competence when staffing management positions, and younger managers are given the opportunity to develop within the company.

Michael Aeberhard
Technical Engineering Architect FH, Bern (The transition from public zone to private space in residential construction)
previously: Project Manager and Architect

Dr. Matthias Burgener
Process Engineering Pharma Production PhD in Chemistry and Biochemistry, University of Bern (Polarity Formation in Molecular Crystals, Inorganic-Organic Composites and Natural Tissues)
previously: Analyst at Geistlich Pharma AG

Dr. Adeline Colussi
Research & Development MSc in Structural Biology and Biophysics, ETH Zurich; PhD in Molecular Biology, University of Cambridge (Measuring Protein Curvature Sensitivity and Membrane Remodelling in a Single-Particle Solution Assay)

Dr. Caroline Dafflon-Urech
Quality Assurance MSc in Life Science, University of Oxford and EPFL; PhD in Oncology, EPFL (Identification of Tumor-Stroma Interactions Crucial for the Establishment of Liver Metastasis)
previously: PostDoc at Novartis Institutes for Biomedical Research (NIBR)

Dr. Borka Jojic
Quality control & Analytics MSc in Cellular & Molecular Neuroscience, University of Tübingen; PhD in Molecular Biology and Biochemistry, University of Bern (Characterization of the Translationally Controlled Tumor Protein in Trypanosoma brucei)
previously: PostDoc at University of Bern

Noëmi Müller
Office, Legal & Compliance MLaw, University of Lausanne (Insolvency of natural persons); Admitted to the Bar of the Canton of Bern
previously: Lawyer in the Tax Administration and the Health and Welfare Directorate of the Canton of Bern, Faculty of Advocates in Edinburgh, Kellerhals Carrard

Dr. Martin Stähle
Accounting & Controlling Dr. oec., University of Hohenheim (Essays on the Informational Sufficiency of Accounting Data)
previously: Management consultant and lecturer at the University of Bern

Philipp Steffen
Quality Assurance MSc in Chemistry & Molecular Sciences, University of Bern (Intra- and Intermolecular Excited State Dynamics in the Condensed Phase. MALDI Matrix 2,4,6-Trihydroxyacetophenone and Nucleobase Cytosine)
previously: Quality Management Validation for CSL Behring

Dr. Dominik Waluk
Process Engineering Pharma Production MSc Biochemistry, , Lund University SWE; MSc in Chemistry, Jagiellonian University, Krakow; PhD in Molecular Genetics, Stockholm University (Biosynthesis and Physiological Functions on N-acyl Amino Acids)
previously: Project Manager at Inselspital Bern, Associate Scientist at ETH Zurich and the University of Stockholm

Prof. Dr. rer. oec., University of Bern
Advisor

Prof. Dr. Urs Wälchli has advised the Board of Directors of InnoMedica since 2018, primarily on governance, strategy and financial issues. He is a visiting professor at the Simon Business School of the University of Rochester, New York, Deputy Academic Director of the Rochester-Bern Executive Program and SFI Adjunct Professor. The focus of his research, teaching and consulting activities is the financing and management of innovative companies.

Urs Wälchli studied economics at the University of Bern, where he also completed his doctorate on "Corporate Governance of Swiss Boards of Directors". He has researched and taught at various American universities (NYU, Wharton, Purdue University) and was assistant professor at the University of Bern from 2008 to 2014.

Finances

Current strategic situation

For the financial evaluation of InnoMedica's technology platform and in particular its first two drugs Talidox and Talineuren, a continual review of the validity of the strategic assumptions underlying the financial planning is vital. The evaluation carried out as part of this update to the Business Plan 2018 shows that these assumptions remain valid.

Innovation in chemotherapy – untapped market potential

Innovative capacities in medical oncology mostly focus on immunotherapeutic approaches, particularly cell and gene therapy. Over the past decade, research in this field has led to numerous new drugs and new treatment options. However, it also shows that the majority of these drugs are only successfully used in a small number of patients and cannot be used as a basic therapy in a broad patient population. Statistics show that cancer continues to be the leading cause of death in industrialized countries from the age of 40 onwards. Table 2 shows the current figures for new cases and deaths in Switzerland. With around 40,000 new cases and 16,500 deaths per year, the cancer-induced mortality rate is 40 percent. The typical oncological treatment scheme for this group is almost exclusively chemotherapy. For the remaining 60 percent of the patient population, chemotherapy also plays a central therapeutic role. Approximately 35 percent of all cancer patients can be treated with the chemotherapy doxorubicin contained in Talidox.

A major unresolved problem of chemotherapy is the related severe toxicity. Even after numerous innovation efforts aiming to reduce these side effects, a major breakthrough is still missing. However, even comparatively small improvements in the efficacy-side effect profile are in great demand among patients and physicians, quickly leading to sales in the billions of CHF, as demonstrated impressively by the example of Celgene's Abraxane. With Talidox, InnoMedica offers a new solution with great potential in the low-innovation field of chemotherapy.

Simplified clinical development becomes a reality – rapid market approval ahead

From a regulatory point of view, the risks associated with innovations in chemotherapy are comparatively low due to the many years of experience with this therapeutic approach. As a result, in a scientific advice inquiry, the Swiss Agency for Therapeutic Products (Swissmedic) has classified Talidox as a 'known active substance with innovation' as opposed to a new active substance. This classification significantly lowers the requirements for clinical testing and InnoMedica alongside SAKK have planned the clinical development of Talidox accordingly.

Figures on cancer in Switzerland. (Table 2)

Indication	Cancer patients (diagnosed since <5 years)	Newly diagnosed diseases (per year)	Mortality (per year)
Total	**115,000**	**40,011**	**16,533**
Total doxorubicin indications	**41,200**	**14,349**	**5,890**
Lung	12,000	4,174	3,159
Bone	300	91	44
Breast	17,100	5,957	1,364
Ovary and uterus	5,000	1,754	705
Testicles	1,300	444	11
Urinary bladder	3,400	1,174	543
Thyroid gland	2,200	755	64

Source: Federal Office of Statistics

The dose escalation in the phase I study focuses on the reduction of side effects. In this setting, a comparatively small number of patients has sufficient explanatory power to estimate the extent to which Talidox can reduce the side effects as compared to free doxorubicin and Caelyx/Doxil. In phase I/IIa, the number of patients will then be increased in order to directly investigate the efficacy of Talidox with respect to specific indications without interrupting the study. If, as a result, InnoMedica and SAKK conclude that the study results of the phase I/IIa should be assessed by the health authorities, InnoMedica will submit a first market application dossier to Swissmedic.

Regardless of such considerations, clinical development of Talidox will continue as outlined in the Business Plan 2018, and a phase IIb study including a control group is planned to further consolidate the evidence. With respect to the financial update in this document, the recent progress of clinical planning will allow a more accurate cost estimate of the clinical development program.

Successful financing model – cost awareness through milestone financing

InnoMedica has successfully relied on a milestone financing model right from the start. The step-by-step financing in line with the growing track record has the following advantages: Dilution for incumbent shareholders is minimized, while cost awareness within the company is continuously maintained at a high level.

In 2018, InnoMedica reached significant milestones and, as shown in Table 3, used a total of CHF 5.4 million in cash and cash equivalents as follows:

CHF 390,000
Start of phase I clinical trial for Talidox in collaboration with SAKK in five Swiss hospitals

CHF 880,000
Research expenditure and coverage of personnel expenses in research and development

CHF 160,000
Continuation of preclinical development and planning of phase I trial for Talineuren

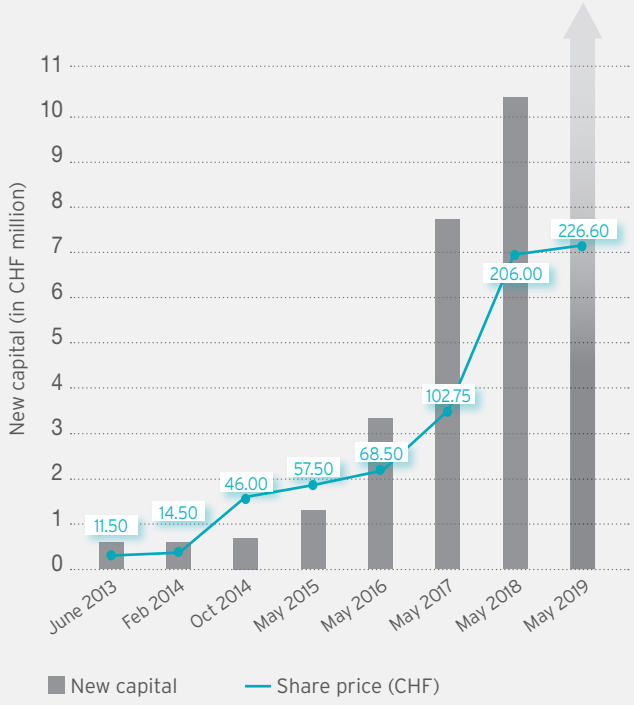
CHF 570,000
Investments in the expansion of the production infrastructure at the Marly site

CHF 2.3 million
Production costs and scale-up of Talidox as well as coverage of personnel expenses in production

CHF 1.1 million
Personnel expenses in finance, administration and management as well as expenses associated with the capital increase (CHF 380,000)

InnoMedica's recent financing round in 2018 yielded an amount of CHF 10.2 million in new capital. Taking into account the existing liquidity reserves of CHF 7.0 million less the CHF 5.4 million used last year, financial resources at the beginning of the year 2019 amounted to CHF 11.8 million. Figure 8 summarizes the historical financing rounds and the planned capital increase in the second quarter of 2019.

InnoMedica's financing steps to date and planned capital increase in 2019
(Figure 8)



Income statement

Talidox Division	*2018*	2019	2020	2021	2022	2023
Number of patients (clinical trials)	2	30	300	650	800	800
Number of patients (market)			950	4,250	7,500	14,000
Price/treatment (CHF)			23,000	23,000	23,000	17,500
Margin (retail price vs. factory selling price)			86%	86%	86%	86%
Earnings			18,791,000	84,065,000	148,350,000	210,700,000
Production	*2,285,404*	3,800,000	7,000,000	21,000,000	26,000,000	35,000,000
R&D expenditures	*877,022*	1,400,000	3,000,000	4,000,000	5,000,000	7,000,000
Clinical trials	*392,189*	1,790,000	3,000,000	6,500,000	8,000,000	8,000,000
Finance/admin./sales/registration	*1,126,694*	1,600,000	5,000,000	21,000,000	35,000,000	50,000,000
Depreciation (20%)	*219,401*	515,521	1,012,416	1,509,933	1,907,947	2,926,357
Employees manufacturing	*10*	15	25	70	75	100
Employees R&D, clinical trials	*6*	8	15	18	21	25
Employees fi nance/admin./sales/registration	*6*	8	20	70	108	143
Expenditures	***4,900,709***	**9,105,521**	**19,012,416**	**54,009,933**	**75,907,947**	**102,926,357**
EBIT	***–4,900,709***	**–9,105,521**	**–221,416**	**30,055,067**	**72,442,053**	**107,773,643**

Talineuren Division	*2018*	2019	2020	2021	2022	2023
Number of patients (clinical trials)			60	200	350	550
Number of patients (market)					1,000	3,000
Price/treatment (CHF)					54,750	54,750
Margin (retail price vs. factory selling price)					91%	91%
Earnings					**49,822,500**	**149,467,500**
Production		250,000	1,400,000	4,000,000	24,000,000	47,000,000
R&D expenditures	161,798	700,000	700,000	1,700,000	4,000,000	7,000,000
Clinical trials		200,000	1,000,000	2,000,000	3,500,000	5,500,000
License fees				0	2,366,569	7,099,706
Finance/admin./sales/registration		200,000	500,000	2,000,000	14,000,000	27,000,000
Employees manufacturing		1	3	7	42	67
Employees R&D, clinical trials		4	4	9	20	31
Employees fi nance/admin./sales/registration		1	3	8	47	83
Expenditures	***161,798***	**1,350,000**	**3,600,000**	**9,700,000**	**47,866,569**	**93,599,706**
EBIT	***–161,798***	**–1,350,000**	**–3,600,000**	**–9,700,000**	**1,955,931**	**55,867,794**

Financial planning

InnoMedica has updated the financial planning based on its current strategic planning (Table 3). The figures for 2018 correspond to the actual figures from InnoMedica's 2018 Annual Report. The target figures for the years 2019 to 2023 assume a successful translation of the preclinical results into the phase I/IIa clinical trial with Talidox and a subsequent approval by Swissmedic. In comparison to the business plan of March 2018, the following changes are relevant:

2018: The cash flow statement shows that in 2018 the outflow of cash and cash equivalents totaled CHF 5.4 million - CHF 2.0 million less than projected in the financial statement of the Business Plan 2018. This is mainly due to a more conservative expansion of staff. Following the 2018 capital injection of CHF 10.2 million, growth expectations were moderately revised downwards and a clear strategic prioritization was made in favor of the Talidox project. With respect to the balance sheet, the 2018 actual figures differ from the target figures mainly in terms of cash and cash equivalents. For the estimate of the target figures, a full subscription of the 2018 capital increase had been assumed, which would have led to a significantly higher inflow of funds.

2019: After consultation with SAKK, InnoMedica has good reason to believe that existing study data on free doxorubicin and Caelyx/Doxil could be included in a future clinical study, hence significantly reducing the number of patients to be included in the study. This is expected to lead to cost savings, especially during study phases I/IIa and IIb. According to the current planning of this business plan update, the 305 trial

Balance sheet

Year	*2018*	2019	2020	2021	2022	2023
Cash and cash equivalents	*12,033,478*	23,850,204	18,041,204	36,406,204	105,712,135	267,779,929
Manufacturing facilities	*877,603*	2,062,082	4,049,666	6,039,733	11,131,786	12,705,429
Subsidiaries (YDDS)	*200,000*	200,000	200,000	200,000	200,000	200,000
Total equity	***13,111,081***	**26,112,286**	**22,290,870**	**42,645,936**	**117,043,921**	**280,685,358**
Liabilities	*212,437*	212,437	212,437	212,437	212,437	212,437
Share capital	*1,296,484*	1,400,000	1,400,000	1,400,000	1,400,000	1,400,000
Reserves from capital contributions	*23,363,467*	46,716,677	46,716,677	46,716,677	46,716,677	46,716,677
Other reserves	*1,826,043*	1,826,043	1,826,043	1,826,043	1,826,043	1,826,043
Previous years	*–8,524,843*	–13,587,350	–24,042,870	–27,864,287	–7,509,220	66,888,765
Annual results	*–5,062,507*	–10,455,521	–3,821,416	20,355,067	74,397,985	163,641,437
Total liabilities	***13,111,081***	**26,112,286**	**22,290,870**	**42,645,936**	**117,043,921**	**280,685,358**
Remarks on the balance sheet:						
Capital increases:						
Number of newly issued shares	*49,756*	103,516				
Price per share	*206.00*	226.60				
Total capital increase	***10,249,736***	**23,456,726**				

Cash flow

Year	*2018*	2019	2020	2021	2022	2023
EBIT (cumulative)	–5,062,507	–10,455,521	–3,821,416	20,355,067	74,397,985	163,641,437
+ Depreciation	219,401	515,521	1,012,416	1,509,933	1,907,947	2,926,357
Operative cash flow	***–4,843,106***	**–9,940,000**	**–2,809,000**	**21,865,000**	**76,305,931**	**166,567,794**
- Investments	*565,281*	1,700,000	3,000,000	3,500,000	7,000,000	4,500,000
Free Cash Flow	***–5,408,387***	**–11,640,000**	**–5,809,000**	**18,365,000**	**69,305,931**	**162,067,794**
Change in liabilities	*–35,447*					
Change due to capital increase	*10,249,736*	23,456,726				
Additional change in equity	*618*					
Change in liquidity	*4,806,520*	11,816,726	-5,809,000	18,365,000	69,305,931	162,067,794
Developments cash	***12,033,478***	**23,850,204**	**18,041,204**	**36,406,204**	**105,712,135**	**267,779,929**

Table 3: Financial planning before and including 2023 with information on the income statement, balance sheet and cash flow. For 2018, the effective values are shown in italics.

patients previously planned for treatment in 2019 can be reduced to 78. This will lead to savings of CHF 2.8 million in the projected direct study costs and CHF 2.2 million in the production of Talidox for the study. These significant changes in our projections are welcome in terms of financial savings, but more importantly raise the prospect of an accelerated approval and thus a timelier improvement of cancer therapy for patients at large.

In addition to the clinical planning, the current financial planning projects investments in the sales organization not before 2020, saving further CHF 1.4 million in costs in 2019, relative to projections in the previous business plan. Adjusting the depreciation schedule accordingly, the planned expenditure for Talidox will decrease by a total of CHF 6.8 million, from originally CHF 15.9 million to CHF 9.1 million.

Due to the moderate growth in personnel, InnoMedica slightly decelerated the development of Talineuren, which leads to cost savings of CHF 2.4 million. The start of the clinical trial was postponed until 2020, saving another CHF 800,000 in clinical trial costs in 2019. For the preclinical studies, InnoMedica expects costs of CHF 200,000 in 2019. CHF 1.3 million will be saved in manufacturing Talineuren and CHF 300,000 from postponing market registration.

As a result of this more precise cost estimate and the partial rescheduling of cost items to the years 2020 and 2021, liquid funds of InnoMedica in 2019 will be higher by CHF 10.6 million than projected in the Business Plan 2018. However, the projection only holds under the assumption of a cash inflow of CHF 23.5 million from the capital increase 2019.

2020 to 2023: The current planning of the clinical development of Talidox also has an impact on subsequent years. Due to the lower number of study patients in phases I/IIa and IIb, clinical trials will become more cost-effective. In addition, due to the timely deferral of the studies, the number of patients in 2020 is expected to fall from 2,500 to 950. InnoMedica expects 4,250 paying patients in 2021, given market entry in Germany, which will increase projected revenues from around CHF 18.8 million to CHF 84.1 million. The forecasts for the last two years in the five-year plan remain mostly unchanged compared to forecasts for the last two years of the Business Plan 2018.

The rescheduling also implies that the investment costs of CHF 16.5 million for the expansion of the production facilities spread over four instead of three years. This approach is less risky than the approach according to last year's planning and complies with a current, more risk-averse investor sentiment.

Talidox is expected to break even in 2020. Liquidity at an amount of CHF 18.0 million at the end of 2020 may suggest that InnoMedica has a relatively low liquidity requirements for break even. However, it should be noted that the market entry for Talidox is not planned before the second half of the year and that the respective operating costs and the development of a sales organization will have to be pre-financed. As for prior year's business planning, InnoMedica projects that liquid funds will never fall below CHF 9 million at any time.

The financial performance of InnoMedica is fostered by its discipline on the cost side. InnoMedica has been able to complete the entire preclinical development of an innovative cancer drug and to initiate a clinical trial with comparatively low financial resources and independently of large pharmaceutical companies. In addition, by constructing its own production facilities, InnoMedica has created the potential for an international market presence. Accordingly, InnoMedica has entered into an initial, long-term valuable partnership for international marketing with TRB Chemedica.

Capital increase

According to the Business Plan 2018, InnoMedica intends to raise further capital of CHF 31.6 million to finance the Talidox and Talineuren projects. The capital increase in spring 2018 already generated CHF 10.2 million in new capital for the company. Despite liquidity reserves of CHF 11.8 million at the end of 2018, InnoMedica is planning to raise additional capital in spring 2019 for the further clinical development of Talidox. The public offering of additional shares for a broad public, calls for a minimum subscription of 60 shares or CHF 13,596. In the run-up to the capital increase until March 28, 2019, InnoMedica offered subscription rights to larger investors. Investors subscribing to packages of at least 500 shares during that time were able to benefit from a guaranteed full allotment via subscription rights of the pool shareholders. Subscriptions of shares can be placed with InnoMedica by completing the subscription form and paying the corresponding amount into an escrow account. After May 31st, 2019, the shares will be allocated by the Board of Directors and transferred to the investors.

The share price for the 2019 capital increase was set by the Board of Directors at an amount of CHF 226.60 per share based on the company's valuation, corresponding to an increase in share value of 10 percent compared to the 2018 price. Accordingly, 103,516 authorized shares will be issued. Detailed information on the offering can be found in the prospectus.

InnoMedica updated the valuation relative to the Business Plan 2018 in order to determine the subscription price:

- The comparable valuation shows that comparable preclinical companies have an average valuation of USD 433 million and a median of USD 487 million. For the phase I companies, the respective values are USD 505 million and USD 535 million, which corresponds to an increase in value from the preclinical phase to phase I of 16 and 10 percent, respectively. InnoMedica has moved from the preclinical phase to phase I with the start of the clinical trial in November 2018. According to the comparable valuation model, the reach of this milestone justifies a 10 percent increase of share price.

- The second valuation method using discounted cash flows is based on the projected free cash flows in Table 3 and a discount rate of 30 percent per year. From 2023 onwards, a 10-year competitive advantage period with a growth rate of 10 percent per year

is assumed. The continuing value estimate is based on an annual growth rate of 3 percent. Taking into account an additional liquidity discount, the pre-money valuation is CHF 294 million.

Use of capital

- Implementation of phase I/IIa and phase IIb clinical trials and filing for market authorization
- Market entry of Talidox and creation of a sales organization in Switzerland and Europe
- Completion of preclinical work with Talineuren and start of clinical trial with Parkinson patients and possibly additional neurological indications
- Commissioning of the production plant and further automation steps in production
- Coverage of operating costs until Talidox enters the market

Risk management

Swissmedic's approval of the phase I clinical trial has fundamentally changed the risk profile of InnoMedica:

Reduction of core risk by means of reviews by the SAKK and Swissmedic

Swissmedic, as a neutral and experienced regulatory authority, has examined the Talidox product in terms of product design, treatment concept, preclinical studies, manufacture and quality controls on the basis of a comprehensive dossier and found it to be good for initial use in patients. Swissmedic also reviewed and approved the study concept with the data to be collected and the scientific evaluation. Prior to submission to Swissmedic, the documents were discussed in detail with the SAKK oncologists and many suggestions and objections were considered. This is a clear first statement in favor of Talidox and InnoMedica by two important bodies in Switzerland.

Solid preclinical and toxicological data

Even if these tests are to be regarded as very valuable, there are still risks regarding proof of success in the patient. However, these risks have also been significantly reduced by the numerous preclinical studies and the toxicology study. With regard to the efficacy, the reference product Caelyx/Doxil was excelled in many cases, while the toxicology study was able to show that, for example, the side effect hand-foot syndrome did not occur in Talidox. In addition, InnoMedica has new products in the pipeline for use in oncology that could complement Talidox as a combination therapy to further increase efficacy. This demonstrates the vitality of the development department and the continued high innovative strength of the research team.

Proven translation to humans

There is experience in translating free doxorubicin as well as various liposomal formulations from preclinical into clinical application. Current study analy-

ses show that doxorubicin has an inhibitory effect on tumors in practically all variants of free or liposomal administration. It is therefore unlikely that Talidox will not inhibit tumor growth at least equally well. Preclinical studies and analyses of biodistribution provide evidence that the tumor-inhibiting effect of Talidox could be even better.

Reduced manufacturing risk

The scale-up to larger batches represents a serious challenge for InnoMedica. The risk primarily relates to the engineering effort required and the costs associated with it. However, the manufacturing process as such is now well established and a number of innovative approaches have already proven themselves in practice. Production is complemented by efficient and experienced batch control analytics, which have defined clear limits and monitor them in the individual production steps and in the finished product.

Only slightly reduced financing risk

On a positive note, InnoMedica had more liquid funds than ever before at over CHF 11 million at the beginning of the year. At the same time, costs and above all personnel growth as the most important cost driver were kept within reasonable limits. This ensures stability and the ability to respond to various scenarios. With the start of the clinical trial, InnoMedica qualifies for an even larger number of investors, which should increase the chances of success of the planned capital increase as of May 31st, 2019. Remaining as high risks are the costs for the phase IIa and IIb clinical trials, which are substantially reduced overall but still relatively high, and the duration of the trial still to be determined. In relation to the processing period for the future marketing application of up to 12 months, this may keep the costs up at a critical level until market launch and break-even.

Structural reform reduces risks

The new holding structure and the outsourcing of operating activities to the subsidiary InnoMedica Schweiz AG have had a positive effect on the company's risk profile. So far, all contracts have been drawn up directly by the holding company, whereas InnoMedica Schweiz AG will now take over. The cash reserves are protected in the holding company, a monthly amount of money flows into the Swiss company. The strategically important intellectual property will remain in the holding company for the time being and will be outsourced to a separate company, InnoMedica IP AG, in a second step. This reduction in entrepreneurial risk was previously ensured structurally by the incubator IPAG Inter Personal AG and can now be continued by InnoMedica itself.

Personnel risks further reduced

The young executive management has further consolidated its role in the management and has proven its worth even under greater pressure. The Executive Board has been operating in this form for several years and now has the necessary management experience. With the separation of the holding company and the Swiss company, the management team is increasingly taking over the management of the Swiss company autonomously. In addition to the Executive Board, other employees take on demanding management tasks that are of great value to the company. Staff turnover is very low overall, even though salary levels are not yet at industry-standard levels. Recruitment continues to attract highly qualified candidates. This shows that the employees' identification with the project is high and that the team trusts in the success of the project.

Compliance moderately implemented

The streamlining of the Board of Directors with the resignation of two members has contributed to clarifying the strategic direction and significantly improved the cooperation between the Board of Directors and the Executive Board. An increasing separation of strategic tasks at the Board of Directors and Holding level from operational management in the Swiss company has largely been implemented. However, the complete separation of the Board of Directors and Executive Management from each other at this point in time would rather jeopardize this very positively developing process and would incur significant additional costs. Furthermore, there are legitimate doubts as to whether managers with the necessary expertise can be found on the labor market at all. In keeping with InnoMedica's innovative character, these will continue to be built up internally and gradually familiarized with management tasks.

Outlook

The wish for better chemotherapy is great and can be sensed everywhere. Not only investors and employees are focusing their attention on the study results of phase I clinical trials, but also patients or persons from their immediate environment are asking whether results from use in hospital are already available and whether Talidox could already be used in cancer therapy. Many patients have to stop treatment because of side effects and find themselves in a hopeless situation. The great demand for innovations is also reflected in the recruitment of patients, which has allowed the study to progress according to plan. These are all tangible indications of considerable potential for success and a lack of competition. A replacement is being sought for the two products currently available, Myocet and Caelyx/Doxil, and Talidox is a promising candidate that is already well advanced in development.

Understandably, information on progress in the clinic is in demand and the desire to proceed as quickly as possible is omnipresent. However, too much pressure is not appropriate. Patients receiving Talidox in the phase I trial have advanced cancer and usually not many options available. Doctors and patients must gradually familiarize themselves with InnoMedica's new drug and gain experience. This process can only be accelerated to a limited extent. Every single use must be carefully checked for appropriateness. The study protocol requires a large amount of measurement data to be collected during treatment, which means a great deal of effort for the hospital. Patience and a certain restraint are necessary for the study to be completed properly.

Together with the SAKK oncologists, InnoMedica is currently investigating ways of shortening the study duration for phases IIa and IIb and at best also reducing necessary sample sizes. For ethical reasons, the control groups in particular should be kept as small as possible, because the use of drugs with such severe side effects should be avoided as much as possible. A further strategy may be emphasizing the advantageous side effect profile of Talidox as the relevant innovation, while arguing that the efficacy of Talidox is at least equivalent to that of doxorubicin.

With regard to the market launch – both in Switzerland and internationally – InnoMedica is interested in solid study results. These are a prerequisite for efficient cooperation with oncologists and the relevant authorities. They create safety, reduce risks, and form the basis for opening up a broader market. Based on the experience thus far, the authorities have rarely been a limiting element in InnoMedica's progress. A much more critical role came to progress in production, needing to evolve towards production of larger volumes. Both aspects – the approval process and the manufacturing process – together require a balanced consideration. This is the only way for InnoMedica to succeed in the face of a larger number of patients and sustainably improve their often difficult situation today.

With Talineuren, InnoMedica has a second product, whose market potential could even significantly exceed that of Talidox. Like Talidox, Talineuren addresses indications where satisfactory drug treatment is still lacking. Both products are therefore associated with high expectations on the patient side. Ideally, InnoMedica will be able to finance the clinical development of Talineuren with initial proceeds from Talidox. For the time being, however, it will be necessary to supplement the first preclinical results with additional studies and to test the tolerability in a toxicological study. Only then will the pathway to the patient be open also to Talineuren. Since Talineuren could qualify for *Orphan Drug* status in an indication such as Chorea Huntington, preliminary information from the authorities indicates that in this case a faster progress might be expected.

The effort that InnoMedica has to make for both products nevertheless remains considerable. Depending on the resources available, InnoMedica will have to set priorities and focus on the success of the company. Careful use of the funds entrusted to InnoMedica, smart investments, and lean structures are key elements of the success to date and must be maintained. It is on these elements that the trust of already more than 650 investors in InnoMedica is built. With the existing and new investors as partners, InnoMedica will finally be able to realize both projects and achieve the planned profitability: Proof that innovation is not only an important element of entrepreneurial dynamism, but also pays off for those who dare something new.

Today, the start-up project of a few innovative minds is a young company with 25 employees: with its own production, analytics and quality assurance, a medical affairs team with the first product in the clinical phase and a research department with promising products in the pipeline.

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The English version of InnoMedica's Business Plan Update 2019 was translated from the original German version which shall be binding in case of disparities.