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# ANNUAL REPORT



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## Immunicum at a glance

*Immunicum is a biomedical company that develops cancer immune therapies based on three different platform technologies: The COMBIG, CD70 and adenovirus vector platforms. The Company has five ongoing projects with a strong focus on the three based on the prioritised COMBIG platform, which is used to develop cancer immune actuators INTUVAX® and SUBCUVAX®.*

Data from a Phase I/II clinical trial with INTUVAX® in the treatment of 11 patients with metastatic renal cancer was most recently reported in September 2016. This showed a continuing more than doubled prolonged median survival rate for the entire patient group and a continuing more than tripled prolonged median survival rate survival for patients with a poor prognosis, compared with historical data.

In April 2016, Immunicum reported data from the ongoing Phase I/II clinical trials in the treatment of cancer of the liver which showed that the majority of fully treated patients showed an increased frequency of tumour specific CD8+ T cells in the blood after vaccination compared with before, an important biomarker for tumour-specific and systemic immune activation and that this could be linked to the prolonged survival. No confirmed serious vaccine-related side effects have been noted.

The Company's main focus in the immediate future is the implementation of a Phase II study concerning the treatment of renal cancer, as well as the completion of the ongoing Phase I/II studies concerning the treatment of primary liver cancer and gastrointestinal stromal tumours/GIST. In addition, the Company plans to commence two additional Phase I/II clinical trials within the indication malignant melanoma with the cancer immune primer INTUVAX® in combination with immune checkpoint inhibitors.

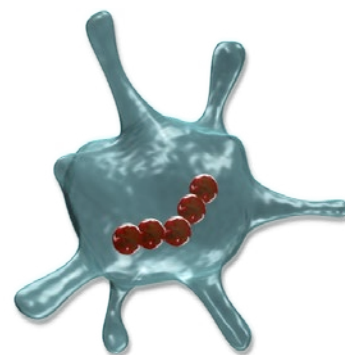
The Company's three technology platforms, as well as the production process for COMBIG, are protected by patents granted and patent applications in a total of seven patent families in several countries in Europe, Asia and the United States.

### STRATEGY

The Company's goal is to offer cancer patients treatment options which improve both prolonged survival as well as quality of life via developing effective and safe therapies that provide long-lasting and powerful immune responses to fight cancer. Since Immunicum's products are based on platform technologies, the Company is able to develop immune therapies against many different types of cancer.

Immunicum's strategy is to advance cancer immune therapies to the market together with a partner, via licensing agreements.

Immunicum intention is to position their main product INTUVAX® as the first choice for tumour-specific activation of the immune system in combination with various treatments that in different ways can combat immunosuppression.



## HISTORY

Immunicum AB (publ) was founded in 2002 as a spin-off from the Sahlgrenska University Hospital in Gothenburg. Its founders - three researchers Alex Karlsson Parra, MD PhD, who is the Company's Chief Scientific Officer, Bengt Andersson, MD PhD Sahlgrenska University Hospital, and Anna Carin Dag Wallgren, MD PhD, Karolinska University Hospital Stockholm - had been active in the field of immunology for many years and has studied the process of how the body to reject a transplanted organ. The basic idea was the first to try to inhibit this rejection process, when it was realised that it could instead be used to teach the body to also repel its own tumour transformed cells. As it was shown that the main reason for the rejection of transplanted organs is the accompanying white blood cells from the donor, allogeneic dendritic cells, researchers wanted to use these cells as immunopotentiators and in order to create cancer immune primers.

The founders formed a limited liability company and applied for the Company's first patent. Over the following five years, several test tube and animal experiments were conducted which confirmed the mechanism of action, and several articles were published in scientific journals. During 2007 and 2008, the Company was restructured with a new management, new members of the Board of Directors and a Scientific Advisory Board was established. Since then a number of important milestones have been reached.

Immunicum's project portfolio presently consists of five different projects, three of them are in clinic trials, which are protected by a number of patents granted and several patent applications within seven patent families.



YEAR	MILESTONES	FINANCING*
2008	> Immunicum implements an emission of new shares	SEK 5 million
	> Research funding is granted	
	> A Scientific Advisory Board is established	
	> Victory in Venture Cup West	
	> The plan for conducting clinical trials concerning SUBCUVAX® is interrupted, due to that the production facility is not up to the required standards	
2009	> CD70 Cancer is developed and a patent application is submitted	
	> The COMBIG Platform is developed and successful in vitro studies are completed	
2010	> Immunicum implements an emission of new shares	SEK 6 million
	> Major funding from VINNOVA is granted	SEK 3.5 million
	> A patent application for COMBIG is submitted	
	> Successful concept test with INTUVAX® on rats is carried out	
	> Professor Rolf Kiessling becomes a member of the Scientific Advisory Board and Agneta Edberg assumes the office of Chair of the Board of Directors (COB)	
2011	> Successful toxicity study and biodistribution study of INTUVAX® is carried out	
	> The Swedish Medical Products Agency gives the green light for clinical trials concerning the treatment of renal cell carcinoma (RCC)	
	> The European Patent Office (EPO) grants patent protection for the COMBIG platform	
	> CD70-Viral and CD70-CD3 are developed and patent applications are submitted	
2012	> Immunicum implements an emission of new shares	SEK 6.3 million
	> Clinical Phase I/II study for the treatment of RCC begins	
2013	> Immunicum implements an emission of new shares	SEK 30.2 million
	> Immunicum is listed on First North	
	> Immunicum receives approval to initiate a Phase I/II clinical trial concerning the treatment of HCC	
	> The last patient in the Phase I/II clinical trial underway concerning the treatment of RCC receives their concluding dose	
	> Immunicum®, SUBCUVAX® and INTUVAX® receive trademark protection in Europe	
	> Immunicum receives a grant from Vinnova for Optimisation of the Production Process	SEK 0.47 million
	> Clinical Phase I/II Study in the treatment of HCC begins	
	> The U.S. Patent and Trademark Office (USPTO) grants patents for the COMBIG platform	
	> Immunicum presents promising survival data from the RCC Phase I/II Study at the Informas Immunotherapy Conference in Brussels	
2014	> Immunicum publishes promising data for CD70	
	> Immunicum presents its final report for the Phase I/II study concerning the treatment of RCC, the data from which shows positive results	
	> Immunicum presents data from the Phase I/II study concerning the treatment of RCC at the ASCO conference held in Chicago	
	> Immunicum implements a directed share issue	SEK 56 million
	> Immunicum implements a preferential share issue, which is oversubscribed	SEK 44 million

YEAR	MILESTONES	FINANCING*
	<ul style="list-style-type: none"> <li>&gt; Immunicum's Research Manager, Alex Karlsson-Parra, is awarded the Athena Prize, healthcare's most significant award for clinical research</li> <li>&gt; The USPTO announces its intention to grant Immunicum's patent applications in respect of genetically modified adenovirus vector and ways to activate the immune activator cells</li> <li>&gt; The EPO announces its intention to grant Immunicum's patent application in respect of the production method of the Company's therapeutic cancer immune activator</li> </ul>	
2015	<ul style="list-style-type: none"> <li>&gt; The first patient receives treatment in the Phase II Study of INTUVAX® treatment with patients with metastatic renal cancer (The MERECA Study)</li> <li>&gt; Immunicum presents continuing improved Phase I/II survival data for renal cancer patients put on treatment with INTUVAX®</li> <li>&gt; Immunicum presents updated safety and survival data in a Phase I/II Study for liver cancer patients (HCC) put on treatment with INTUVAX®</li> <li>&gt; Immunicum delivers genetically modified adenovirus vectors to the Frederick National Laboratory for Cancer Research (FNLCR) in the U.S.</li> <li>&gt; The technology behind INTUVAX® is presented at a conference at the Karolinska Institute together with the world's leading immunologists</li> <li>&gt; Immunicum supplies Ad5PTDf35 adenovirus technology Rutgers Cancer Institute of New Jersey</li> <li>&gt; Immunicum and the Karolinska Institutet submit a joint application to the Swedish Medical Products Agency concerning the initiation of a Phase I/II study of INTUVAX® for GIST patients</li> <li>&gt; The EPO announces its intention to grant Immunicum's patent application concerning INTUVAX®</li> <li>&gt; Immunicum presents continuing improved Phase I/II survival data for renal cancer patients put on treatment with INTUVAX®</li> <li>&gt; The Japanese Patent Office (JPO) announces its intention to grant Immunicum's patent application concerning INTUVAX®</li> <li>&gt; Immunicum releases updated data from the Phase I/II study for those being treated with INTUVAX®</li> <li>&gt; The Swedish Medical Products Agency and Ethical Vetting Board approves the extension of the Phase I/II Study concerning the treatment of six new liver cancer patients with INTUVAX®</li> </ul>	
2016	<ul style="list-style-type: none"> <li>&gt; Immunicum completes a significant adjustment of the manufacturing process for INTUVAX®, which allows the product to be used directly in hospital without preparation at a local pharmacy</li> <li>&gt; Immunicum presents a status update from the ongoing Phase II Study, MERECA</li> <li>&gt; The transfer of production to the GMP-certified production unit Eufets GmbH is made in Germany and vaccine cell handling is simplified for greater availability in hospitals.</li> <li>&gt; Immunicum presents updated immunological data from the first part of the HCC study, which shows that the increase in tumour specific T cells in the blood seem to correlate with improved survival</li> <li>&gt; The Chinese patent office SIPO announces that it intends to grant the patent application concerning INTUVAX®</li> <li>&gt; The Company files for a listing on Nasdaq Stockholm's Main Market and is listed on First North Premier as a part of this process</li> <li>&gt; Immunicum announces its joint cooperation with Accelovance and the Midwest Melanoma Partnership for future clinical studies in the United States</li> <li>&gt; Immunicum implements a preferential rights share issue, which is oversubscribed.</li> <li>&gt; Peter Suenart, M.D., Ph.D., is hired as Chief Medical Officer.</li> <li>&gt; The IND application is submitted to the U.S. Food and Drug Administration (USFDA).</li> <li>&gt; The CD70-patent is to be granted in the United States and China.</li> <li>&gt; Immunicum reports positive follow-up survival data from the Phase I/II study in the treatment of renal cancer</li> <li>&gt; Records with HCC I/II data are approved for presentation to the annual meeting of the Society of Immunotherapy for Cancer in November.</li> <li>&gt; Carlos de Sousa is appointed as new Chief Executive Officer.</li> </ul>	SEK 128 million

\* All amounts are approximate amounts.



## PROJECT PORTFOLIO

**Immunicum has five ongoing projects with a strong focus on the three based on the priority COMBIG platform, which is used to develop cancer immune actuators INTUVAX® and SUBCUVAX®.**

### INTUVAX® - RCC

Immunicum is presently conducting a European Phase II study (MERECA Study) where a total of 90 newly diagnosed renal cancer patients are to be included. Sixty patients will receive treatment with INTUVAX® in combination with subsequent contralateral nephrectomy (the removal of the tumour affected kidney) as well as the standard treatment with tyrosine kinase inhibitor Sutent (sunitinib). Thirty patients in the control group will undergo only contralateral nephrectomy and standard treatment with Sutent.

The primary objective of the MERECA Study is to examine the median survival rate of patients with a poor prognosis and the survival rate after eighteen months for patients with an intermediate prognosis. In addition to these primary effect parameters, the Company will also study the objective tumour response after reintroduction of Sutent and study the intratumour infiltration of CD8+ T-cells in primary tumours and accessible metastases, compared with normal tissue.

The Company has submitted an Investigational New Drug application ("IND Application") to the U.S. Food and Drug Administration (USFDA) in order to be able to begin with the treatment of renal cell cancer patients in the United States this year.

### INTUVAX® - HCC

Immunicum has an ongoing Phase I/II clinical trial concerning the treatment of patients with primary cancer of the liver (Hepatocellular Carcinoma - HCC). The primary objective of the clinical trials is to examine not only whether INTUVAX® is safe, but also the immunological response to it. In addition, any prolonged survival will be evaluated. The first part of the study includes twelve patients who have stopped responding to standard treatment and who receive INTUVAX® as a second line treatment as mono therapy.

Based on the good safety profile and the promising survival data reported in the treatment of cancer of the liver, the Company has also received approval from the Swedish Medical Products Agency to provide INTUVAX® as a primary treatment in combination with standard treatment. Up to six patients will receive INTUVAX® as the primary treatment in combination with standard treatment, and the first patient in the other part of the study has been recruited.

On 18 April 2016, the Company presented updated immunological data from the first part of the HCC study, which shows that treatment with INTUVAX® leads to an increase of tumour specific CD8+ T cells in the blood, an important biomarker for immunological activity with the majority of the fully treated patients, and that this increase appears to correlate with an improved survival.

### INTUVAX® - GIST

Immunicum is presently carrying out a Phase I/II clinical trial with INTUVAX® concerning the treatment of patients with incurable gastrointestinal stromal tumours (GISTs). Twelve patients who have stopped responding to standard treatment, and who normally would have concluded their treatment, were referred being treated with INTUVAX® in combination with Sutent (sunitinib). The study is being carried out in cooperation with the Swedish medical university, Karolinska Institutet. The first patient has commenced their treatment, but no data reporting has occurred yet.

### INTUVAX® - MELANOMA

Immunicum plans to carry out an additional two Phase I/II clinical trials, one in Sweden and one in the United States, concerning the treatment of melanoma. The patients are to be treated with INTUVAX® in combination with various immune checkpoint inhibitors in where one study will be focused on first-line treatment and the other study on second-line treatment. These plans are subject to change, based primarily on the responses from the governmental agencies.

The Company believes that immune checkpoint inhibitors will receive, to an ever-increasing extent, marketing approval in various indications, and in this manner the Company will have an opportunity to possibly confirm a synergistic effect in combination with a new product category that is likely to be an important part of the future standard treatment for cancer.

Furthermore, the Company makes the assessment that melanoma is a particularly relevant indication to focus on for the study of important immunological parameters that are otherwise difficult to implement in other indications.





COMBIG	Pre-clinical stage	Phase I/II	Phase II	Phase III
INTUVAX-RCC	COMPLETED	COMPLETED	UNDERWAY	
INTUVAX-HCC	COMPLETED	UNDERWAY		
INTUVAX-GIST	COMPLETED	UNDERWAY		
INTUVAX-MEL USA	COMPLETED	SCHEDULED		
INTUVAX-MEL SWE	COMPLETED	SCHEDULED		
SUBCUVAX	UNDERWAY			
<b>CD70</b>				
CD-101	UNDERWAY			

#### SUBCUVAX® and Ad5PTDf35 adenovirus vector

Preclinical studies with the Ad5PTDf35 vector for the development of SUBCUVAX® are in progress in cooperation with the University of Uppsala and Professor Magnus Essand. The objective is to examine the possibilities of using the vector for the production of relevant tumour antigens to be used in the SUBCUVAX® vaccine cells. Professor Magnus Essand's group has also initiated a Phase I/II clinical trial with the vector for oncolytic treatment of neuro endocrine tumours. Immunicum does not own the rights to this indication, however does own the rights to all subsequent indications. The Company follows the developments with great interest due to that it can confirm the vector as being also useful for oncolytic treatment.

#### CD70

Immunicum's CD70 platform works for adaptive immunotherapy, which is a treatment strategy where the patient T cells are isolated and in some cases genetically manipulated to specifically recognise cancer cells. In order to obtain a sufficient number of tumour-specific T cells, an expansion period in the test tube is required before the cells are injected back to the patient. There are currently two established expansion methods: *rapid expansion protocol* and *bead expansion protocol*.

Today, the development with the CD70-concept continues in joint collaboration with Professor Magnus Essand's research group at the Department of Immunology, Genetics and Pathology, Rudbeck Laboratory, Uppsala University. In a publication entitled "*Allogeneic lymphocyte-licensed DCs expand T-cells with improved anti-tumour activity and resistance to oxidative stress and immunosuppressive factors*", which was published on March 6, 2014 in the American journal *Molecular Therapy - Methods & Clinical Development* (published by Nature Publishing Group in cooperation with the American Society of Gene & Cell Therapy), Professor Essand's research group compared Immunicum's patent-pending expansion protocol, referred to as "CD70-CD3" with established expansion protocols.

In the article, it emerges that T cells, including the CAR-transfected T cells which expanded with Immunicum's CD70 protocols, compared to the established protocols, show a better survivability capacity, better ability to kill tumour cells in the test tube, and better capability to begin to expand once again upon contact with tumour cells when the cells are subjected to immunosuppressive factors that reflect the "hostile" tumour environment. Immunicum's goal is to establish the CD70-concept as an expansion protocol for CAR T cells (adaptive immune therapy) for the treatment of solid tumours.

## OBJECTIVES

Below is a follow up report on the nine main objectives established for 2016, along with a presentation of the Company's objectives for 2017.

### FOLLOWING-UP THE NINE MAIN OBJECTIVES FOR 2016:

1. Report the follow-up of the survival data from the Phase I/II clinical trial concerning the treatment of patients with metastatic renal cancer.

**Follow-up:** During the year, the Company has reported positive follow-up survival data.

2. Effective recruiting of patients for the Phase II study (MERECA) for the treatment of patients with metastatic renal cancer.

**Follow-up:** The MERECA Study has been delayed by approximately 9 months, due to an extensive transfer of the production process to a larger GMP facility located in Germany, our efforts to develop a much simpler product that is easier for the hospitals to manage, and the protracted evaluation process of the applications to start the clinical trials in most of the European countries. The latter is due to that INTUVAX® is an entirely new type of advanced cell therapy, which therefore requires special evaluation and assessment by the public authorities. The Company presently has approval for the start of the recruitment of seven of the eight planned countries in Europe, and Immunicum expects to begin the process of recruiting patients in the U.S. during the year, provided that the IND application is approved.

3. Initiate the treatment of renal cancer patients in the United States within framework of the MERECA study.

**Follow-up:** The Company submitted an IND application to the USFDA during the summer and assuming a positive response is received, which is expected shortly, the Company can begin the recruitment process of kidney cancer patients in the United States during the latter part of the year.

4. Initiate Phase I/II clinical trials concerning the treatment of patients with GIST.

**Follow-up:** The first patient has commenced treatment, however no data reporting has taken place yet.

5. Initiate Phase I/II clinical trials concerning the treatment of melanoma in the United States and Sweden, in combination with various immune checkpoint inhibitors.

**Follow-up:** Provided that the IND application is approved, Immunicum then intends to also apply for approval to commence melanoma clinical trials with INTUVAX® in the U.S. and in Sweden during the year, in combination with immune checkpoint inhibitors. These plans may however be changed, primarily based on the response from the public agencies.

6. Advance the CD70 platform vis-à-vis clinics, or alternatively, assess the potential and possibility of licensing the technology platform.

**Follow-up:** The Company is currently evaluating the possibilities for clinical production of CD70 cells.

7. Complete the recruitment of hepatic cancer patients who will be receiving INTUVAX® as first-line treatment in combination with standard treatment.

**Follow-up:** Treatment has been initiated with the first patient, and the Company is optimistic concerning the possibilities to complete the recruitment over the remainder of the year concerning all the required patients.

8. Conclude the preclinical studies of SUBCUVAX® in combination with the Ad5PTDf35-adenoviral vector in order to determine whether SUBCUVAX® can be taken to clinical trials.

**Follow-up:** The Company is optimistic concerning the possibilities of finishing the preclinical studies during the year concerning SUBCUVAX®.

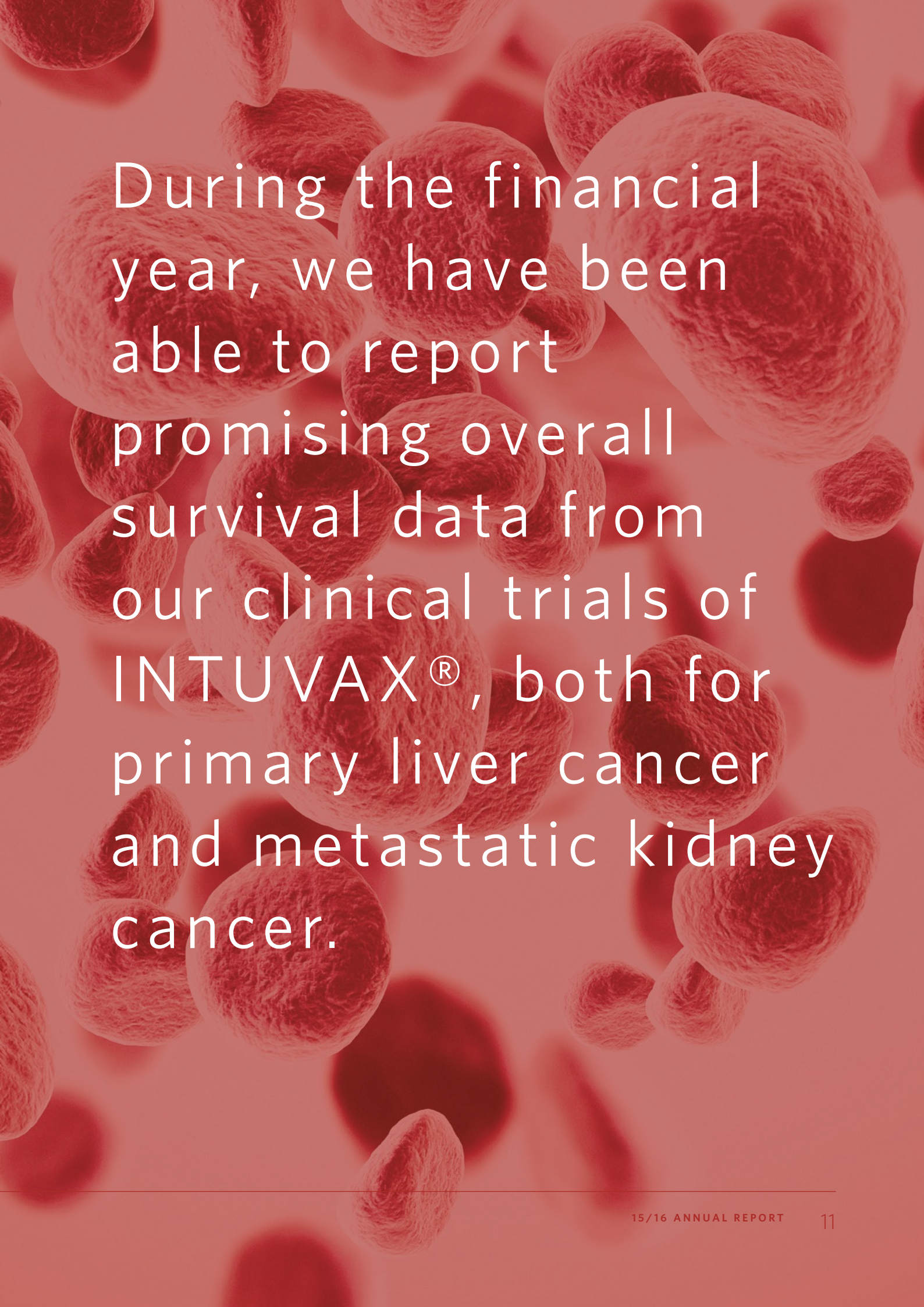
9. Advance the discussions with potential commercial partners relating to joint cooperation concerning INTUVAX® to the next level.

**Follow-up:** Several Big Pharma companies have shown interest in INTUVAX® during the year, and Immunicum is presently conducting ongoing talks with potential collaborative partners. However the Company cannot provide any forecasts as for when, or if, a license agreement will be entered into.

### PRIMARY OBJECTIVES FOR 2017

1. Report the follow-up survival data from Phase I/II clinical trials concerning the treatment of kidney and liver cancer, and for GIST.
2. Conclude the recruiting of patients for the MERECA Study.
3. Commence melanoma clinical trials with INTUVAX® in combination with immune checkpoint inhibitors the United States and Sweden.
4. Decide whether or not to conduct clinical trials with CD70 and/or evaluate and appraise the possibilities of a licensing out of the technology platform.
5. Make decisions concerning the continued development of SUBCUVAX®.
6. Implement the listing of the Company on Nasdaq Stockholm's Main Market.





During the financial year, we have been able to report promising overall survival data from our clinical trials of INTUVAX<sup>®</sup>, both for primary liver cancer and metastatic kidney cancer.

## A few words from the CEO

*With the great progress we have reported during the financial year, Immunicum made it clearly evident that we can play an important role in the development of next-generation treatment cancer therapies. The primary focus is on clinical trials with INTUVAX®.*

During the financial year, we have been able to report promising overall survival data from our clinical trials of INTUVAX®, both for primary liver cancer and metastatic kidney cancer. At the most recent update in September 2016, data from the completed renal cancer study showed concerning a continuing more than doubled prolonged median survival rate for the entire patient group and a continuing more than tripled prolonged median survival rate for patients with a poor prognosis. In the clinical trials of patients with primary liver cancer, we have shown that treatment with INTUVAX® increases the frequency of tumour-specific CD8+ T cells in the blood of the majority of the fully-treated liver cancer patients, and that this appears to correlate with prolonged survival.

We have also received approval, and have initiated treatment of a further six liver cancer patients who are receiving INTUVAX® as first-line therapy in combination with standard treatment that can remove immunosuppression. The 12 patients in the first part of the study were treated with INTUVAX® monotherapy when they no longer responded to approved first-line therapy.

In December, we received the go-ahead to launch our fourth clinical trial with INTUVAX®. The clinical trial includes 12 patients at the Karolinska University Hospital in Stockholm with gastrointestinal stromal tumours (GIST). The clinical trials have commenced, but so far no reporting of data has occurred. If the study delivers positive data, we will seek an orphan medicinal product for human use designation for INTUVAX® in the treatment of GIST.

Our ongoing Phase II study of renal cell cancer patients – the MERECA study – was initiated in May 2015. We filed an IND application with the USFDA in late July 2016 to obtain approval to also treat renal cancer treatment patients in the U.S. with INTUVAX®, and we are anticipate receiving notification shortly.

The MERECA Study has been delayed by approximately 9 months, due to an extensive transfer of the production process to a larger GMP facility located in Germany, our efforts to develop a much simpler product that is easier for the hospitals to manage, and the protracted evaluation process of the applications to start the clinical trials in most of the European countries. The latter is due to that INTUVAX® is an entirely new type of advanced cell therapy, which therefore requires special evaluation and assessment by the public authorities.

We have recently received approval to commence the recruitment in seven of the eight planned countries in Europe and anticipate being able to commence the process for recruiting in the U.S. within a year, as soon as we have received our IND application approved. We are planning, after approval, to return with more information concerning the design and timelines for the study.

Furthermore, we also plan to conduct two melanoma studies in the United States and Sweden with INTUVAX® in combination with various different immune checkpoint inhibitors. The preliminary plan for these studies has not yet been finalised, therefore changes may be made, based on among other things the agencies' responses after the applications have been submitted.

Our focus is on the studies with INTUVAX®, however we also see great potential in our other two technology platforms: CD70 and the adenovirus vector. For these projects, Immunicum is conducting ongoing developmental collaboration with Professor Essand at Uppsala University.

In February, Uppsala University and Professor Essand received the green light for the launch of a clinical trial at Uppsala University Hospital with patients with neuroendocrine tumours (NET) using Immunicum's genetically modified adenovirus vector, and the first patient has already received treatment. Immunicum has licensed-out the vector exclusively for oncolytic treatment within NET. We are of course following this clinical trial with great interest since we own the intellectual property rights for all other indications. The study is expected be underway for a period of two years.

Right before the summer, a successful preferential rights share issue was implemented which injected SEK 128 million (before share issue costs). In order to increase the possibilities of broadening our shareholder base plus to further facilitate the Company's financing in the future, we have applied to have Immunicum's shares listed on the NASDAQ Stockholm Main Market List. In view of that the Nominating Committee has nominated three new board members – Steven Glazer, Charlotte Edenius and Kerstin Valinder Strinnholm – for election at the Annual General Meeting in October, a listing on the Main Market List would be able to occur at the soonest in early 2017. As part of the process to be listed on the Main Market List, Immunicum's shares have been approved for listing on NASDAQ OMX First North Premier.



Efforts to secure the future intellectual property rights continues, and during the financial year we have had several patents for INTUVAX® and CD70 approved in China, Japan and Europe, and just now in September 2016, also in the USA.

It is also encouraging to see the strong scientific interest that is out there for INTUVAX® and our clinical data. The most recent evidence of this is that in November we will be presenting data from our INTUVAX® - HCC I/II clinical study at the annual meeting in United States of the Society for Immunotherapy of Cancer (SITC), to be held at National Harbor in Maryland.

Immunicum's organisation has been strengthened in several respects over the course of the financial year. In March, the Company's Scientific Advisory Board was expanded with Anders Öhlén, M.D., Ph.D., and in July Peter Suenart, M.D., Ph.D., was recruited as Chief Medical Officer. The organisation has been further strengthened by recruiting new staff with a focus on the implementation of our comprehensive clinical programmes as well as via an increased focus on investor relations. At the Annual General Meeting in December 2015, Magnus Persson was elected as a new member of Immunicum's Board of Directors.

For my part, it has been incredibly exciting in my role as the CEO to take Immunicum from that development project that the Company was nine years ago to the well-developed publicly listed biopharmaceutical company that it presently is today.

Now Immunicum is entering a new phase, as it gears up for the intensification of clinical and commercial efforts that lie ahead for the Company. In conjunction with that, Dr. Carlos de Sousa has been recruited as the new CEO. He brings relevant extensive international business and clinical development experience, from both the pharmaceutical and biotech sector. With Carlos de Sousa at the helm, Immunicum is best equipped with the best preconditions to succeed in the work of our innovative treatment solutions the entire way up to the patient level, and thus create a profitable business for the Company's shareholders. Immunicum has a promising and exciting future ahead of it, to say the least!

*Jamal El-Mosleh*  
CEO



*"We received a green light In December to launch our fourth clinical trial with INTUVAX®."*

# The various stages with pharmaceutical drug development

*All development of pharmaceutical drugs begins with pre-clinical research that spans everything from the detection of an active compound or therapy, to the development and improvement of the concept, including tests in appropriate animal models. Experiments with animals are important so as to assess if the drug has any serious side effects, and to ensure that it has the desired medicinal effect.*

The experiments with animals are also subject to regulatory approval and control. Based on the results of this pre-clinical work, an application can be submitted to seek approval from the regulatory authorities for tests of the pharmaceutical in humans. When an application is filed with the relevant regulatory authorities - in Sweden this would be Läkemedelsverket, the Swedish Medical Products Agency - an evaluation of the entire scientific documentation provided by the applicant is conducted by independent medical experts who make

an assessment and determine whether or not a clinical trial with humans may be initiated to test the drug. If an approval to initiate a clinical trial is granted, the clinical trial must be conducted in three distinct phases, where each phase has its own well-defined purpose. With each successfully completed phase, the probability of eventual market approval increases, which also increases the intrinsic value of the project. A short description of the various phases of a clinical trial is presented below.<sup>1</sup>



1. Pharmaceutical Specialists in Sweden, FASS, Pharmaceutical Development, 2014.

## PHASES I/II

A drug candidate is usually tested in healthy volunteers, however in Immunicum's case the vaccine is tested on cancer patients, with the primary objective to research the safety.

## PHASE II

The drug candidate is tested in various different groups with the objective to determine the optimal dosage and the dosage schedule, as well as to study its efficacy.

## PHASE III

The drug candidate is tested in broad patient populations where the objective is to ensure statistically significant efficacy prior to marketing authorisation.

## PHASE IV

Even after approval, the pharmaceutical drug is subjected to additional further scrutiny in follow-up studies with patients undergoing treatment.

**The Phase I Study** is the first time a new compound is administered to humans. Ordinarily, the test subjects are a group of healthy volunteers, kept under constant medical surveillance. The purpose of the clinical trials is to determine whether the test subjects tolerate the drug and whether it behaves in the body in the way as indicated with the animal studies and other research. Phase I studies are also used preliminarily to try out what dosage is reasonable to be given to future patients: The clinical trial begins with the lowest dosage considered sufficient in order to determine the safety profile of therapy, and if everything goes according to plan, it may be increased as the clinical trial progresses. Since Immunicum's cancer immune primer, INTUVAX®, is tested in cancer patients and not in healthy volunteers, the Company has the opportunity to not only study any side effects (the primary purpose), but also study potential efficacy of the treatment (the secondary purpose). That is why Immunicum's first therapeutic cancer vaccine clinical trials are referred to under the designation Phase I/II Study.

**The Phase II Study** is normally the first time the drug is administered to patients with the disease. During the study, the dosage and other details are fine-tuned, and the effects of the drug on the disease and its symptoms are studied. The number of patients in a Phase II Study is still limited. If the patient group is of the appropriate size, a Phase II trial may give a clear indication of the efficacy of the new drug.

**The Phase III Study** is only initiated if the results of Phase II Study are promising enough to motivate further studies. In a Phase III Study, the new therapy is evaluated relative to an ineffective copy of the drug, most commonly referred to as a "placebo." The newly developed drug can also be evaluated relative to an already approved drug for the same indication. Drug combination studies, where the established therapy and the newly developed drug are combined, are also possible as a comparison to treatment using only the new therapy. The distribution of patients between the selected

therapies must be random, and neither the physicians nor the patients can know which of the treatments any particular patient is receiving. If both of these criteria are fulfilled, the study is called a "double blind randomised" clinical trial, which is considered the method that provides the best and most objective results. Since the trial constitutes a comparison between various therapy groups, the number of patients in this phase is considerably larger than in previous phases. The objective of a completed Phase III study is to be able to ascertain with statistical certainty whether the new drug has a better efficacy, or if it minimises side effects to a greater extent than existing treatment alternatives. If the new drug appears promising and is well tolerated by patients, further tests are carried out in order to verify the results. Only after this can a request for approval be submitted to a relevant regulatory authority – most commonly the European Medicines Agency (EMA) and/or the Food and Drug Administration (USFDA) in the U.S.

The duration of the clinical trials depends upon the indication to be treated. In a clinical trial where existing treatment alternatives have shown low efficacy, the duration of the trial may be reduced significantly. Following market approval, further studies – sometimes referred to as Phase IV clinical trials – are conducted in order to ensure that no unexpected side effects arise, for instance in unusual patient groups.

In order to speed up access to drugs that treat serious illnesses, both the Food and Drug Administration in the U.S. and the EMA, its European counterpart, have developed processes and methods for making these drugs available on the market as rapidly as feasible, for example a "Breakthrough Designation" (USFDA) and "PRIME" (EMA). These options are particularly relevant for drugs that are the first drug available for a particular illness or disease, or those which have advantages over existing treatments, for example either better efficacy or a reduction in the number of and/or less severe side effects.



# Immunicum's Technologies

## THE BACKGROUND

Traditional therapies for the treatment of cancer, such as surgery, radiation and chemotherapy, are often found to be insufficient for the treatment of patients, and as well, they usually cause severe adverse side effects. Cancer immune primers, which triggers an activation of the patient's own immune system by specifically attacking the cancerous cells, provide hope for new, effective treatments, and with fewer side effects. The immune system recognises and attacks what is foreign to the body, but the problem with cancer is that tumour cells are usually not treated as unknown invaders. This makes it extremely difficult for the immune system to effectively neutralise tumour cells, which is why several methods have been developed, mainly cell-based vaccines, to enhance the immune response against cancer.

It is now well established that the immune system has cells, particularly CD8+ cytotoxic T-lymphocytes (CTLs) that can recognise and can potentially kill tumour cells. Nevertheless, there is a major obstacle that needs to be resolved, as these T cells are not induced at all or are only weakly induced. One explanation for this may be that tumour antigens from dendritic cells (DCs), "natural immunopotentiators/adjuvants" are not sufficiently presented in order to elicit the T-cell immunity. Another reason may be that tumour-reactive T cells become tolerant of the tumours.

The dendritic cells play a very central role in specific immune responses and activate the systems which, among other things, helps the body to eliminate the virus infected or bacteria infected cells (the Nobel Prize in Medicine was awarded to the discoverer of the dendritic cell in 2011). The dendritic cells acquire and processes protein antigens in order to subsequently present these antigens to antigen-specific T cells. This leads to an activation and proliferation of the T cells whose function is then to attack cells that express this antigen. In the same manner, the immune system could similarly be trained to attack cancer transformed malignant cells.

Despite the fact that several clinical studies have been conducted which treated cancer patients with various types of therapeutic cancer immune primer, there is still no cancer immune primer that has shown a convincing and prolonged clinical effect. The Company's assessment is that this can be

explained by at least three different weaknesses in previously evaluated cancer vaccines:

1. The use of cancer-associated tumour antigens that are also present in normal healthy tissue. In order to protect the body against T cells that react against these antigens that are naturally present in the human body, the immune system makes sure that these cells are weakened or killed via what is referred to as "development of central tolerance."
2. Inadequate immune enhancer, known as adjuvant, which is an important component of a vaccine.
3. The tentative cancer vaccines have not been combined with anything that can slow down the immunosuppressive environment found in the tumour.

### Endogenous tumour antigen versus foreign body tumour antigens (neoantigen)

There are many indications that foreign body tumour antigens, consisting of peptides (small protein pieces) which are formed by the individual patient's tumour-specific mutations (specific changes in tumour cells' genetic code), known as neoantigen, will be the paradigm shift that is needed in order to provide cancer vaccines with patient-specific tumour antigens that are perceived as a "foreign body" and against which there is an opportunity to push forward an effective immune response.<sup>2</sup>

### Neoantigen-based vaccines

Neoantigen-based vaccines that are designed to target the immune response vis-à-vis the individual patient's tumour-specific neoantigen have breathed new life into the field of cancer vaccines. Immunotherapy with vaccines based on neoantigen, in which the patient's first neoantigen is characterised and then synthesised in vitro (in a test tube) is presently undergoing several clinical trials. On a purely practical level however, this production process includes many obstacles that will need to be overcome. In addition, this production is entirely patient dependent, i.e. can only be performed after the neoantigen for each individual patient has been characterised by a tissue sample from patient's own tumour.<sup>3</sup>

2. Robbins et al, 2013.

3. Fritsch et al, 2014.

### Intratumoural administration of the immunological adjuvant (immune enhancer)

One obvious way to get around the practical problems that the production of neoantigen in the test tube entails, is to use the patient's existing tumour (or metastasis of) as a direct neoantigen source by injecting an adjuvant directly into the patient's tumour, that means without first having to identify the patient's specific tumour mutations and then produce the corresponding neoantigen.

### Activated allogeneic dendritic cells as optimal immunopotentiators

Natural viral infection and vaccination with live viruses (as in smallpox vaccinations) leads to the development of specific cytotoxic CD8+ T cells that effectively kill the virus-infected cells. More and more pre-clinical data suggest that dendritic cells that are first infected by a virus lose their ability to present viral antigens to T cells, but instead begin to function as an immune enhancer by secreting numerous inflammatory substances leading to the recruitment and maturation of non-infected dendritic cells from the surrounding tissue/ blood stream.<sup>4</sup> These newly recruited dendritic cells eat up the virus-infected, dying, dendritic cells and tissue cells, in other words, they are thus "recharged" with viral antigen. Thanks to the inflammatory environment, the newly recruited dendritic cells will be protected from infection and will instead mature out so that they can begin to migrate to draining lymph nodes where they can activate the CD8+ T cells. Finally, the activated T cells migrate into the body where they specifically attack the virus-infected tissue cells.<sup>5</sup>

Immunicum-related studies have shown that human dendritic cells can be activated to produce long-lasting inflammatory substances that mimic the production that characterises the virus-infected dendritic cells, i.e. an inflammation that leads to the recruitment and activation of other dendritic cells, known as "bystander DCs."<sup>6</sup> Since Immunicum's dendritic cells also are allogeneic (from another individual) in relation to the patient, this difference in tissue type will lead to a rejection process which stimulates the recruitment and activation of "bystander DCs."<sup>7</sup>



4. Smed-Sørensen et al, 2011; Pang et al, 2013.

5. Smed-Sørensen et al, 2011; Pang et al, 2013.

6. Gustavsson et al, 2008.

7. Wallgren et al, 2005.

## PLATFORMS

Immunicum has three different platform technologies for the development of immunotherapies: COMBIG, CD70, and Ad5PTDf35 adenovirus vector. Both COMBIG and CD70 are based on findings showing that activated dendritic cells from individuals other than the patient function as an excellent immunopotentiator (adjuvant). The primary significant difference between the technologies is that COMBIG aims at activating the patient's tumour-specific T-cells intratumoural administration, while the CD70 platform aims at a powerful expansion/replication and the activation of the patient's tumour-specific T-cells in test tubes and then injecting them back into the patient. The latter method is generally referred to as adoptive immunotherapy, and is a relatively new way to treat cancer. The latter method is generally referred to as adoptive immunotherapy, and is a relatively new way to treat cancer. The difference between Immunicum's CD70 platform and the adoptive immunotherapies developed by other organisations is that tumour-specific T-cells that have been expanded using Immunicum's CD70 method exhibit a significantly improved survivability and survival rate as well as cancer killing efficacy in test tubes according to studies performed by the Company's collaborative partner Professor Magnus Essand's research group in Uppsala, which was published in an article entitled "Allogeneic lymphocyte-licensed DCs expand T-cells with improved anti-tumour activity and resistance to oxidative stress and immunosuppressive factors," published 6 March 2014 in the American journal Molecular Therapy – Methods & Clinical Development (published by Nature Publishing Group in cooperation with the American Society of Gene & Cell Therapy).

The Ad5PTDf35-adenoviral vector was acquired in late 2014 by Virex AB for the purpose of being incorporated in the SUBCUVAX® the concept for the production of relevant tumour antigens. The concept is currently being evaluated in preclinical studies with Professor Magnus Essand's research group at Uppsala University.

*There are four major advantages with INTUVAX®*

### The COMBIG Platform

Via the improvement of the basic technology which was developed by Immunicum in 2002, during 2010 a new platform was developed which the Company calls COMBIG ("COM-Bined toll-like receptor agonists and Interferon-Gamma"), which describes some of the factors used in the activation of Immunicum's allogeneic vaccine cells (important parts of the processing process are kept as trade secrets). Immunicum develops two main categories of therapeutic cancer immune primers based on this platform, SUBCUVAX® and INTUVAX®.

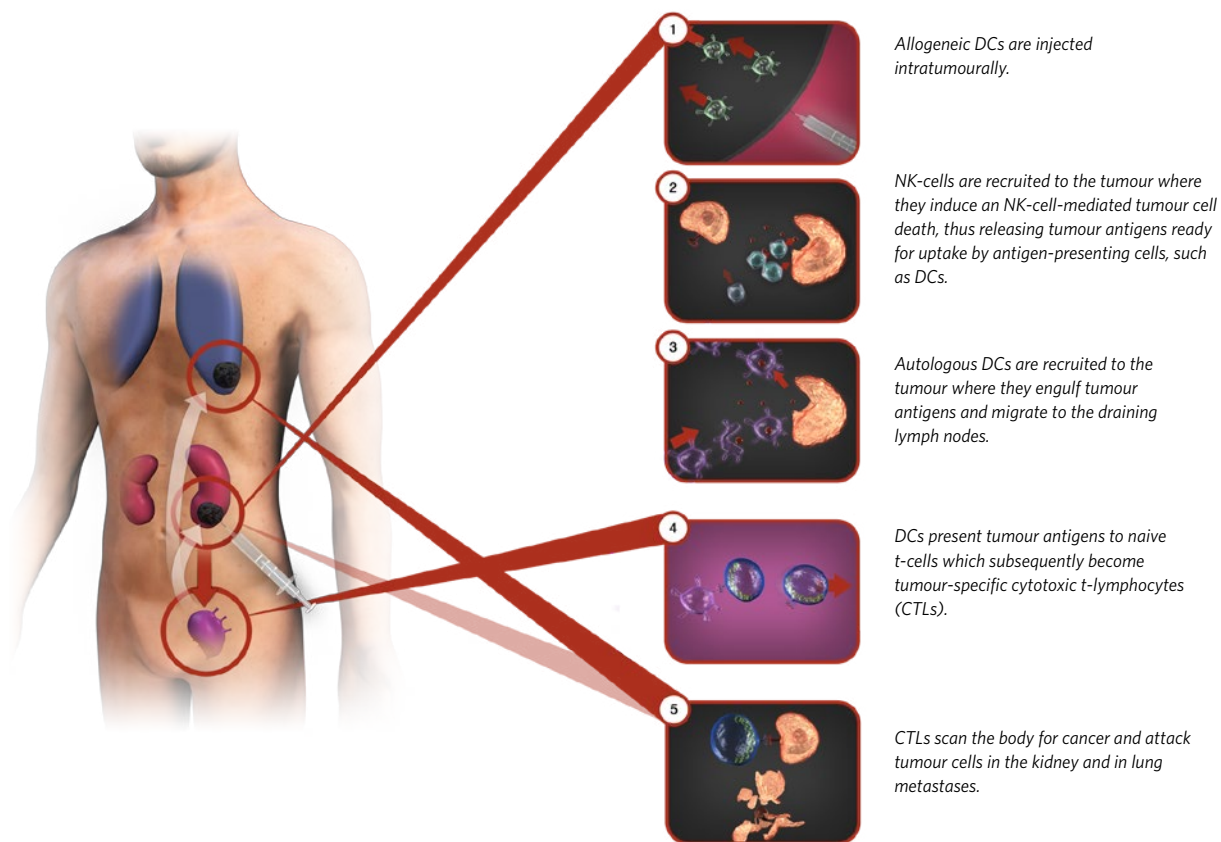
The major difference between the cancer immune primers is that SUBCUVAX® is combined with tumour antigens in test tubes and injected subcutaneously (under the skin), while INTUVAX® is injected intratumourally (within a tumour), without prior loading with tumour antigens, allowing this cancer immune primer to instead utilise the patient's own tumour as an antigen source. A great advantage of INTUVAX® is that the entire set-up and structure of the individual patient's unique tumour antigens, including mutated tumour antigens, is utilised for a personalised individually-adapted treatment.

### INTUVAX®

INTUVAX® has been developed in order to be able to take advantage of each patient's unique tumour antigens and to circumvent the need to combine the cells with tumour antigens in test tubes in order to create an effective cancer immune primer. Since INTUVAX® is administered directly into the tumours, the recruitment of the patient's own dendritic cells will be done inside the tumour, where there are already high levels of tumour specific antigens (these antigens are available to be taken up by the patient's dendritic cells, because INTUVAX® induces NK cell recruitment and activation which leads to NK cell-mediated cell death in the tumour at the injection site), and these can be swallowed by the recruited dendritic cells thus in this manner will become loaded with antigens. INTUVAX® is targeted against all solid tumours.

- 1 INTUVAX® is targeted against all solid tumours.
- 2 Cancer immune activators can be produced on a large scale.
- 3 The concept uses the patient's own antigens, including mutating tumour antigens, which aims to ensure that an optimal set of antigens is used for each of the patients in the activation of a tumour-specific immune response.
- 4 Immunicum is independent of antigens from third parties.

## Description of INTUVAX®'s mechanism of action and effect



The figure above shows that INTUVAX® creates an inflammation in the tumour, which then attracts NK cells (for release of autologous tumour antigens) and autologous DCs for uptake of autologous antigens. Thus, what Immunicum expects to accomplish by means of a standardised vaccine is to load the patients' own DCs with their own tumour antigens in vivo, and in this way also offer patients an individually-adapted treatment. This is something that makes INTUVAX® a unique cancer immune primer.

## CLINICAL TRIALS

### Clinical Strategies

Immunicum's strategy is to position INTUVAX® as the first choice of cancer immune primers that are to be combined with standard treatments that can dampen immune suppression for the effective and safe treatment of various types of cancer. The Company's clinical strategy aims at designing clinical trials in various indications where INTUVAX® is combined with different types of standard treatments. The ongoing and planned clinical studies are expected to be able to provide support for the assertion that INTUVAX®:

- is an effective cancer immune primer, in particular via measuring intratumoural infiltration of CD8+ T cells and the frequency of tumour specific CD8+ T cells in peripheral blood;
- has a clinical efficacy, primarily via measuring any extended overall survival and objective tumour response;
- will become the first choice of cancer immune primers that are to be combined with standard treatments that can dampen immune suppression, especially with various tyrosine kinase inhibitors and various immune checkpoint inhibitors, and
- is effective in several different cancer indications via that it is used in the treatment of patients with various types of cancer.

The Company believes that it is vital to concentrate its clinical trials to Europe and the United States, in order to prepare the way for a future licensee of INTUVAX®. In addition, clinical trials in Europe and the United States also constitute an important step in the facilitating of a future application for market approval in two of the world's largest and most important pharmaceutical markets.

### Clinical trials concerning treatment of RCC

On 31 March 2014, the concluding report for a Phase I/II study with the treatment of twelve (12) patients (including eleven evaluable) with metastatic Renal Cell Carcinoma (RCC) was released. The study clinical trial began in February 2012 and the last patient was treated in August 2013. No vaccine-related serious adverse events have been noted and the report presented a hitherto achieved median survival time for patients with poor prognosis in excess of the expected median survival time that prevails for established pharmaceuticals which are also often associated with difficult undesirable side effects. The data also show clear signs of tumour-specific immune activation. A presentation entitled "Intratumoural vaccination with activated allogeneic dendritic cells in patients with newly diagnosed metastatic renal cell carcinoma (mRCC)," consisting of the data from the Phase I/II study, was presented at one of the world's most important conferences for cancer research, ASCO (American Society of Clinical Oncology), which took place between 30 May - 3 June 2014.

Updated survival time data, as per September 2016, from the Phase I/II study, which was presented in a concluding report on 31 March 2014, showed that five of eleven evaluable patients were alive at that point in time. The median overall survival time for the patient group as a whole was, at that time, 40 months - compared to the expected median survival time of 15.2 months based on historical data of newly diagnosed patients being treated with the tyrosine kinase inhibitor Sutent (sunitinib).

For the group patients with the prognosis high risk (six patients), the median overall survival time was 32 months, compared to the expected nine months, and for patients with a prognosis intermediate risk (five patients), the median survival time was 45 months, compared to the expected 26 months.

In May 2015, an international Phase II study concerning the treatment of patients with metastatic renal cancer was initiated, which is called the MERECA study, named after acronym from METastatic RENal Cancer. The primary purpose of the MERECA study is to evaluate the median survival time in high risk patients and the proportion of patients with the prognosis intermediate risk who have survived for 18 months. The secondary objectives include, among other things, the proportion of patients exhibiting significant tumour reduction, progression free survival and evaluation of T cell infiltration in primary tumours, healthy kidney tissue and evaluable metastases.

The Company has submitted an Investigational New Drug (IND) application to the FDA in the latter part of July 2016, with the ambition to be able to start the recruitment process in 2016 for kidney cancer patients in the U.S.

### Clinical trials concerning treatment of HCC

In July 2013, Immunicum received approval to start a Phase I/II study for the treatment of patients with primary cancer of the liver, Hepatocellular Carcinoma (HCC), and the first patient was treated in October 2013. The study includes twelve patients and is being conducted at Sahlgrenska University Hospital at Gothenburg University. The primary objective is to investigate whether INTUVAX® is safe, however immunological response and possible extended overall survival will also be evaluated. The study includes patients who are no longer responding to their treatment. After an adjustment of the study protocol, one patient with extrahepatic bile duct cancer, which initially was believed to be cancer of the liver, was also included. Based on the favourable established safety profile and the promising survival time data reported with the treatment of liver cancer, in December 2015 the Company received approval from the Swedish Medical Products Agency and the Ethical Vetting Board to expand the study with six patients who are to receive INTUVAX® in combination with first-line treatments. As of 10 March 2016, the first patient in the extended part of the study had been treated with

INTUVAX® as the first-line treatment in combination with a standard treatment. The Company also provided a status update on 18 April 2016, reporting that:

- > Of the eleven evaluated liver cancer patients treated with INTUVAX®, nine have received full treatment with three doses of INTUVAX®.
- > Five of the nine fully-treated patients have surpassed their expected median survival time, while two out of three patients who are still alive have not yet surpassed their expected median survival time.
- > Analyses were performed that compared the frequency of CD8+ T cells in the blood which produce interferon-gamma, which is a sign that the T cells have a killing function, with the stimulation with two different tumour-associated antigens (antigens that can be expressed in primary liver tumours) before the first INTUVAX® dose one week after the third and final dose. Respective
- > Six of the nine fully-treated patients showed an increased frequency of these interferon-producing CD8+ T cells in the blood, reactive to at least one of the two tumour-associated antigens of liver cancer, one week after completing treatment with INTUVAX®. In five of the six patients, an increased frequency of CD8+ T cells persisted against at least one of two tumour-associated antigen upon re-analysis six weeks after the third INTUVAX® dose.
- > Four of six patients who have shown an increased incidence of these tumour-specific CD8+ T cells have surpassed their expected median survival time and the other two patients are still alive but have not yet surpassed their expected median survival.
- > Two of three patients who did not show an increased rate of tumour-specific CD8+ T cells died before they could exceed their expected median survival.

One patient with extrahepatic bile duct cancer who was also treated with three doses of INTUVAX® exhibited an increased frequency CD8+ T cells in the blood, reactive against the two different tumour-associated antigens (which may also be expressed in extrahepatic bile duct cancer) after the INTUVAX® therapy. Over the course of events, the patient received standard treatment with gemcitabine (G) which is known for inhibiting immunosuppressive cells in tumours in combination with cisplatin (C). This patient was still alive, at the latest reporting date in April 2016, approximately 26 months after receiving the first dose of the vaccine, compared with an expected average median survival time of 11.7 months in patients with extrahepatic bile duct cancer who are treated with G/C.<sup>8</sup>

8. Valle et al, N Engl J Med 2010; 362:1273.





### Clinical trials concerning the treatment of GIST

In September 2015, Immunicum and the Karolinska Institute submitted a joint application for authorisation to initiate a Phase I/II clinical trial for the investigation of INTUVAX® in combination with sunitinib with patients with incurable gastrointestinal stromal tumour (GIST).

The Swedish Medical Products Agency approved the application in December 2015, and the first patient has received treatment.

The study's primary objective is to determine the safety and the most important secondary objective is to investigate whether patients showing progression and resistance to existing treatment after INTUVAX® treatment show objective tumour response.

### Clinical trials concerning the treatment of melanoma

Immunicum is planning to carry out two additional Phase I/II clinical trials, one in Sweden and one in the U.S., with INTUVAX® in combination with immune checkpoint inhibitors with the treatment of malignant melanoma. The Company has retained U.S.-based Accelovance and Midwest Melanoma Partnership to conduct the clinical trials in the United States. Immunicum believes that immune checkpoint inhibitors, to an increasing degree will obtain marketing approval in various indications, to a more significant extent, and in this way the Company will have an opportunity to possibly confirm a synergistic effect in combination with a new product category that is likely to be an important part of the future standard treatment for cancer.

Finally, the Company believes that malignant melanoma is a particularly relevant indication to focus on for the investigation of important immunological parameters that are otherwise difficult to implement in other indications.

### Details about the Clinical Studies

#### INTUVAX-RCC

Indication	Renal Cell Cancer/Renal cancer	
Phase	I/II	II
Number of patients	12	90 (60 in the treatment group and 30 in the control group)
Location	Uppsala University Hospital at Uppsala University	Europe (some 20 sites) United States (a number of sites, in planning)
Number of INTUVAX® doses	2 (5, 10 million or 20 million vaccine cells/dose/group)	2 (10 million vaccine cells/dose)
Combination treatment	No, but half of the patients retrospectively receive adjunctive treatment with either Sutent (sunitinib) or Votrient (pazopanib)	Sutent (sunitinib)
Final Report	H1 Autum 2014 (concluded)	H2 2018
Aggregated data	<p>Massive/strong intratumoural infiltration of CD8+ T cells in 7 out of 12 primary tumours.</p> <p>Median survival (ongoing in September 2016) for the entire patient group of over 40 men, compared with the expected 15.2 months with standard treatments.</p> <p>Median survival (ongoing in September 2016) for patients with poor prognosis (6 patients) of over 32 men, compared with the expected 9 months with standard treatments.</p>	<p>Initial data in January 2016 shows clear signs of tumour-specific immune activation.</p> <p>It is too early to evaluate the efficacy data.</p>

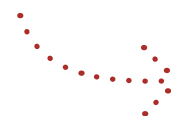


## ESTABLISHED LARGE-SCALE AND COST EFFECTIVE PRODUCTION PROCESS

Since INTUVAX®'s proposed mechanism of action is partly based on an allogeneic concept, this provides the basis and possibilities for scalable production. The raw materials are provided by healthy volunteers, similar to an ordinary blood donation, and provide the vast majority of treatments per production batch. The production method has a short turnover time from start to finish, is personnel intensive and is established in routine instrument, which facilitates the transfer of the process to multiple production units. Previously, the production took place only at the Cancer Centrum Karolinska, but production has also been established at Eufets GmbH in Germany, which offers the opportunity to produce scaled-up quantities.

Immunicum works with collaborative partners in order to develop production and logistics processes with a focus on scaling up and cost efficiency, while maintaining quality. Today's concept has been developed to accommodate standard

treatment procedures, and therefore the number of handling and care steps in hospitals is continuously reduced. Simplifying the procedures will also increase the number of hospitals that can handle INTUVAX®. That INTUVAX® can be stored "off-the-shelf," makes it possible the storage at a central warehouse or directly at hospitals, which also provides freedom and latitude in the design of future supply chains. Ongoing process development also includes patent-pending methods for further scaling-up and increasing the cost-efficiency of the manufacturing process for INTUVAX®.



### Details about the Clinical Studies

	INTUVAX-HCC	INTUVAX-GIST
<b>Indication</b>	Hepatocellular carcinoma/cancer of the liver	Gastrointestinal stromal tumours/GIST
<b>Phase</b>	I/II	I/II
<b>Number of patients</b>	18 (12 in second-line therapy and 6 in first-line therapy/primary treatment)	Up to 12
<b>Location</b>	Sahlgrenska University Hospital at the University of Gothenburg	Karolinska Institutet medical university in Solna
<b>Number of INTUVAX® doses</b>	3 (10 million vaccine cells/dose and 20 million vaccine cells/dose).	2 or 3 doses (10 million vaccine cells/dose)
<b>Combination treatment</b>	The first 12 patients, no combination therapy. The last 6 patients, Nexavar (sorafenib) or chemoembolization.	Sutent (sunitinib) or Stivarga (regorafenib)
<b>Final Report</b>	H2 2017	H1 2018
<b>Aggregated data</b>	<p>Second-line treatment (per update in April 2016):</p> <ul style="list-style-type: none"> <li>- 11 HCC patients treated</li> <li>- 9 fully-treated patients</li> <li>- 5 patients exceeded their expected median survival time</li> <li>- 2 out of 3 patients who had not yet passed their expected median survival time, are still alive</li> <li>- a patient with bile duct cancer is also treated with INTUVAX® in combination with chemotherapy and showed a significantly prolonged survival (in March) compared with what was expected</li> </ul> <p>Immunological data in April 2016 point to an up-regulation of CD8+ T cells in the blood which clearly correlates with prolonged survival</p>	-

## SUBCUVAX®

During organ transplantation, the accompanying dendritic cells from the donor are what causes the inflammatory process that leads to the recipient's specific immune system seeking to reject the transplanted organ after the fact, something which Immunicum takes advantage for the development of its cancer immune primers. By also using the rejection process as immunopotentiators for immunisation against concurrently injected tumour antigens, significant antitumour responses have been able to be detected in cancer models in rats.

The following is a description of SUBCUVAX®'s expected mechanism of action (also refer to the diagram on the opposite page). Dendritic cells from healthy donors (allogeneic DCs) are loaded with tumour-specific antigens in vitro and treated with activating factors. Since the vaccine cells can be loaded with different antigens, it is possible to individually-adapt the cancer immune primers for therapeutic treatment of all types of cancers. Immunicum takes advantage of the fact that DCs can be activated to produce high levels of NK, NKT and T-cell recruiting chemokines in a sustained fashion over an extended period of time.<sup>9</sup>

If the injected DCs are allogeneic, the interaction between these injected DCs and recruited lymphocytes will further create a highly inflammatory milieu (corresponding to an allogeneic mixed leucocyte reaction (MLR)) at the vaccination site, containing several inflammatory mediators that are capable of recruiting the patients' own monocytes and subsequently also capable of maturing these into highly activated DCs.<sup>10</sup> The patients' recruited DCs will then engulf the invading allogeneic vaccine cells and in this way become loaded with tumour-specific antigens.

Thus, the inflammation that the allogeneic DCs induce is used to recruit, activate, and load the patients' own (autologous) DCs with tumour antigens in vivo (in human) instead of artificially in vitro, which would otherwise be necessary. This "natural" activation is expected to optimally prepare the patients' own DCs for migration to the draining lymph nodes where they can trigger the immune system against tumour antigens.

Immunicum currently conducts preclinical studies for SUBCUVAX® in conjunction with the Ad5PTDf35-adenovirus vector in joint collaboration with Professor Magnus Essand's research team at Uppsala University in order to explore the possibility of using the vector for the production of appropriate tumour antigens in the SUBCUVAX® concept.

## *Preclinical studies using the SUBCUVAX® concept*

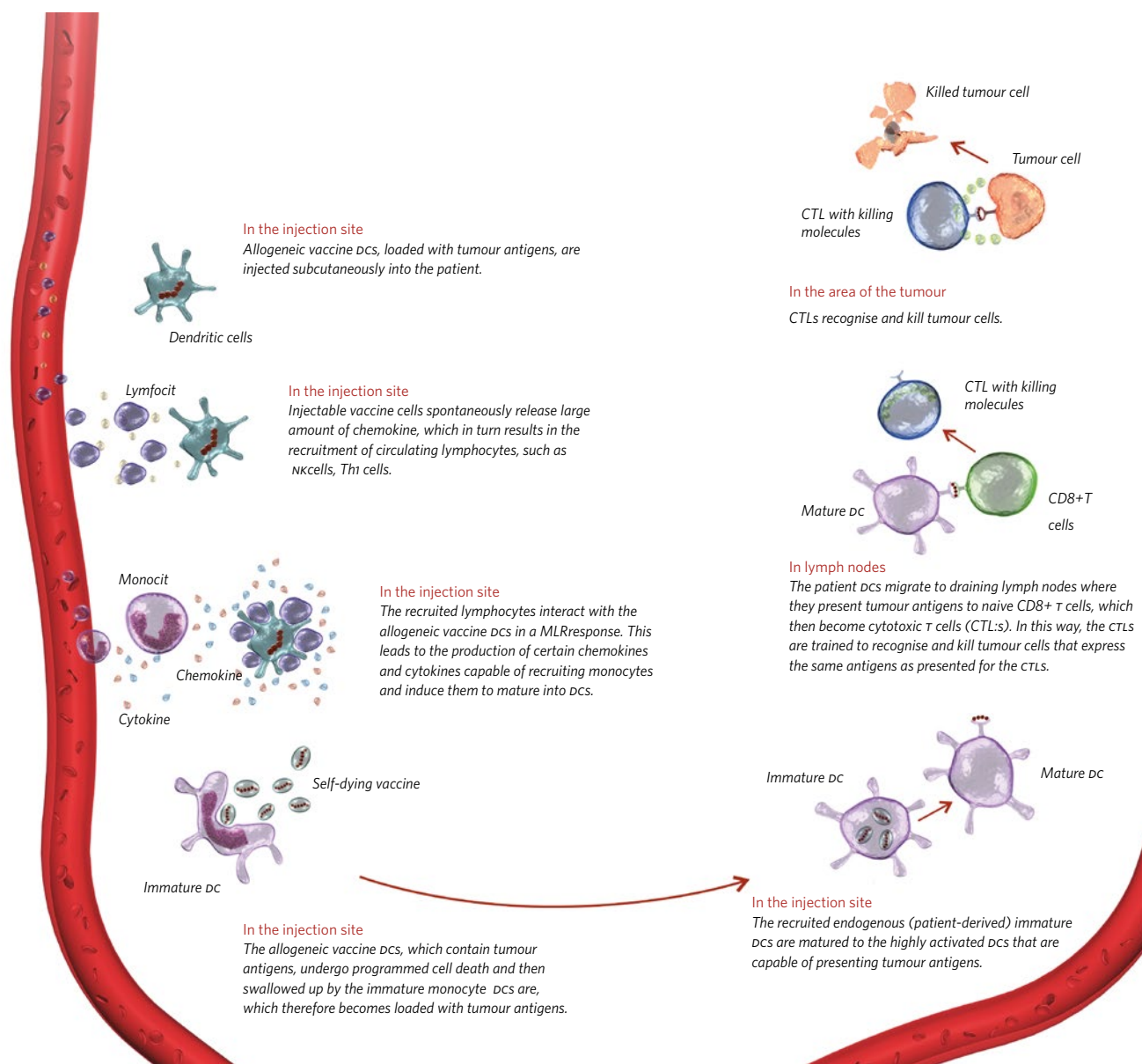
The concept of using activated allogeneic dendritic cells that are loaded with tumour antigen as a cancer vaccine has been evaluated in preclinical studies and the results are promising. The initial studies were performed in vitro (in test tubes) with allogeneic DCs and formed the foundation for Immunicum's first patent application in 2002. Data from the clinical trial was published in the Scandinavian Journal of Immunology, and shows that DCs mixed with immune cells from another individual will induce an immune response which leads to the production of inflammatory substances that can recruit and activate DCs of the "recipient" in a test tube. The patent covers the use of both allogeneic dendritic cells and allogeneic monocytes as vaccine cells.

Following the successful in vitro-studies, Immunicum moved on to perform studies in animal models. Rats were injected subcutaneously (under the skin) with a breast cancer cell line and were vaccinated in both prophylactic and therapeutic settings. Activated allogeneic monocytes or monocyte-derived allogeneic dendritic cells were loaded with apoptotic tumour cells and subsequently used as vaccine cells. Prophylactic vaccinations reduced tumour take from 80 percent in non-vaccinated rats to 20 percent in vaccinated rats. This immunity was long-lasting since re-challenge of tumour rejecting rats with tumour cells six weeks later failed to induce any tumour growth. In therapeutic setting all rats developed tumours, but tumour growth was significantly reduced in rats given tumour-loaded and activated allogeneic monocytes ( $p < 0.05$ ) or monocyte-derived DCs ( $p < 0.001$ ). Data was published in the scientific journal Cancer Immunology and Immunotherapy. In order to advance SUBCUVAX® to clinical trials, Immunicum is seeking a collaboration partner who can contribute with appropriate tumour antigens. Preclinical studies with the vector for the development of SUBCUVAX® is ongoing in joint collaboration with Uppsala University and Professor Magnus Essand's research, for the purpose of examining the possibilities of using the vector for the production of appropriate tumour antigen in SUBCUVAX® and whether the concept shows potential as an effective treatment. Professor Essand's research team is carrying out a Phase I/II clinical trials with the vector for oncolytic treatment of neuroendocrine tumours. Immunicum does not own the intellectual property rights to this indication, however it does to all subsequent indications, and is following the developments with great interest because this has the potential to confirm the vector as usable also for oncolytic treatment.

9. Gustafsson, et al, Cancer Research, 2008 and Gustafsson, et al, Scand J Immunology, 2011.

10. Wallgren, et al, Scand J Immunol, 2005.

## Description of the SUBCUVAX® mechanism of action



## The CD70 platform

It is now well established that the immune system has cells, in particular CD8+ cytotoxic T lymphocytes (CTLs), which can recognise and potentially kill tumour cells. There is nevertheless a problem that must be resolved, as these T cells are either not induced at all or only weakly. There are different ways to use immunotherapy in order to increase the effectiveness of the T cells for the purpose of combating cancer. One example is adaptive immunotherapy, a treatment strategy that entails that T cells which originate from the cancer patient themselves are activated and expanded in vitro and then re-introduced into the patient for the purpose of killing the tumour cells.

With adaptive immune therapy against cancer, there are some considerations that need to be taken into account. During the expansion in test tubes, the T cells will usually need to be stimulated several times in order to achieve clinically relevant levels of tumour specific CTLs. This process means that the cells are less active and more sensitive to factors in the tumour's microenvironment, which means that they can cause themselves to die. Therefore a common observation is that expanded CTLs that are generated in test tubes with good antitumour activity in vitro are less effective in triggering tumour regression in humans (in vivo). A consequence of this is that it is necessary to provide a protocol for in vitro expansion of tumour-specific T cells, which can increase their chances of survival in vivo.

The concept with CD70 involves a method for in vitro expansion of antigen-specific CTLs that are appropriate and suitable to give to cancer patients. In summary, the method is used in order to prolong the survival of expanded and returned tumour-specific T cells. As mentioned above, the problem today is that expanded CTLs do not live long enough to develop an effective anti-tumour response, and the research has been focused on increasing the duration of the life of the CTLs. This research has led to the realisation that antigen-specific stimulation of T cells with DCs that express the co-stimulatory molecule CD70 leads to prolonged survival of activated T cells, particularly CTLs. However the current problem is that it is very difficult to produce human DCs that express significant levels of with CD70, thus Immunicum has succeeded via using a patented method for which there are also a number of pending patent applications.

The Company has successfully conducted several in vitro experiments during the years 2009 - 2011. Immunicum's CD70-concept has been compared with inter alia the "Rapid Expansion Protocol" (REP) which, according to an article in the Journal of Immunology Methods, is regarded as "best practice." Immunicum's in vitro experiments show, according

to the article, that with CD70 work equally well to expand the number of tumour-specific T cells as the REP protocol, and additionally that the cells seem to have greatly increased survivability when they come into a "hostile" tumour environment that is rich in immunosuppressive factors.

Today, the development with the CD70-concept continues in joint collaboration with Professor Magnus Essand's research group at the Department of Immunology, Genetics and Pathology, Rudbeck Laboratory, Uppsala University.

In a publication entitled *"Allogeneic lymphocyte-licensed DCs expand T cell with improved anti-tumour activity and resistance to oxidative stress and immunosuppressive factors"*, published March 6, 2014 in the American journal Molecular Therapy Methods & Clinical Development (published by Nature Publishing group in cooperation with the American Society of Gene & Cell Therapy) Professor Essand's research team has compared Immunicum's patent pending expansion protocol designated as with CD70-CD3 with established expansion protocols.

The article how T cells which have been expanded with Immunicum's protocol, compared with the established protocols, show a better survivability capacity, better ability to kill off tumour cells in the test tube, and better capability to begin to expand once again upon contact with tumour cells when the cells are subjected to immunosuppressive factors that reflect the "hostile" tumour environment.

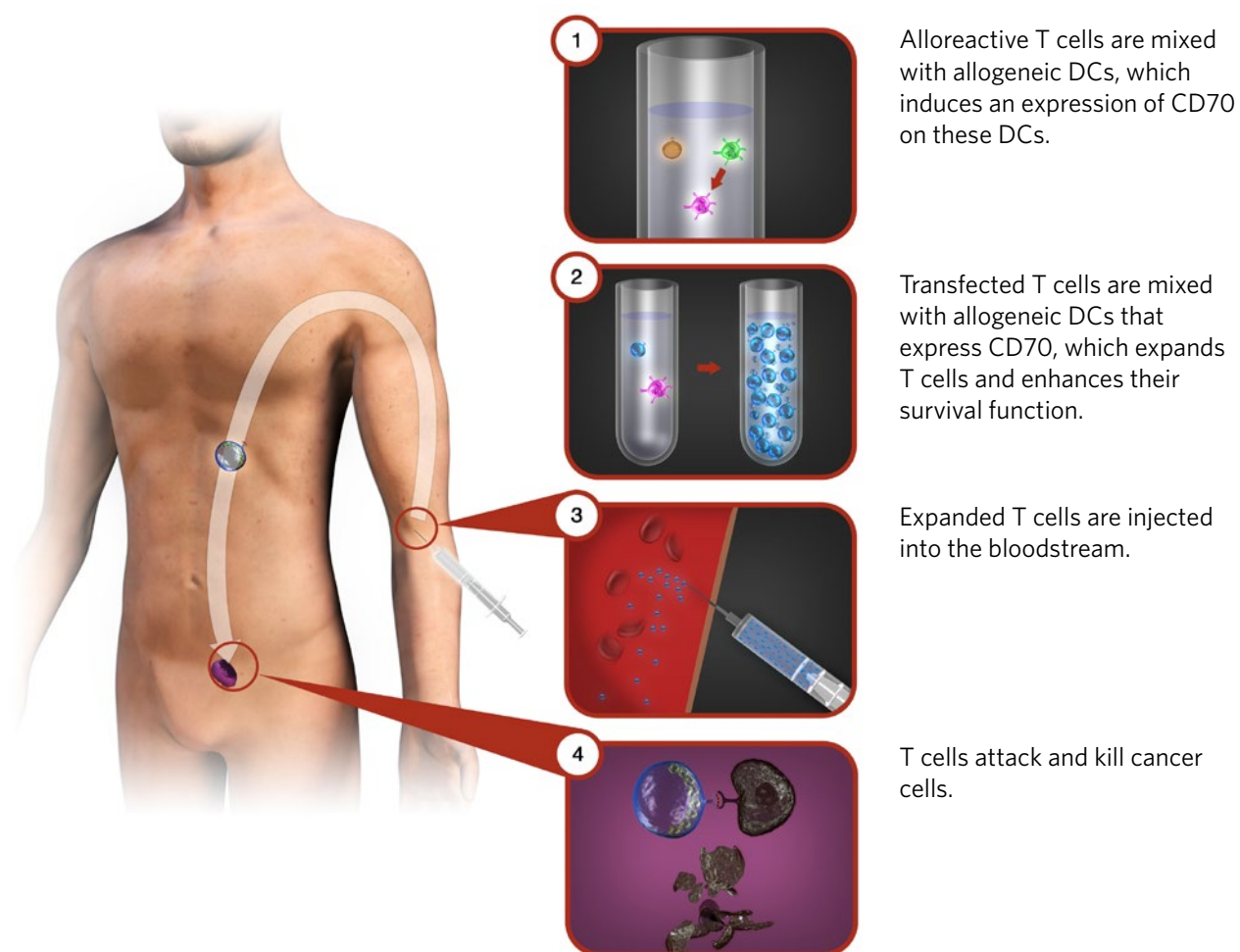
## Ad5PTDf35-adenovirus vector

The Ad5PTDf35-adenoviral vector was acquired in late 2014 by Virex AB for the purpose of being incorporated in the SUBCUVAX® the concept for the production of relevant tumour antigens. The concept is currently being evaluated in preclinical studies with Professor Magnus Essand's research group at Uppsala University.

However, the adenovirus vector can potentially be used for the production of virus particles which only replicate themselves in cancer cells and thereby causes the cancer cells to die, known as oncolytic treatment. VirEx AB has received an exclusive license from Immunicum for the development of oncolytic treatment in neuroendocrine tumours and a clinical trial within this indication has begun. Immunicum does not own the intellectual property rights to the project for the oncolytic treatment of neuroendocrine tumours, it does however to all other indications. The Company is therefore following the development of the clinical trials within the field of neuroendocrine tumours with great interest.

11. J Immunol Methods. 2009 June 30; 345(1-2): 90-99.

*Description of the CD70-concept's mode of action*



# Market Overview

## THE GLOBAL MARKET

In a 2014 report from the World Health Organization (WHO), cancer is described as one of the gravest threats to public health. The number of new cancer cases is expected to increase by over 40 percent by 2025, equivalent to about 20 million new cases annually worldwide. The total economic burden of cancer in 2010 was estimated at USD 1.6 trillion, more than 2 percent of global GDP.<sup>12</sup> The research makes constant progress, whilst at the same time it is clear that more and more people will suffer from cancer as the average life expectancy increases. Cancer remains a disease and state of ill health associated with high mortality, and five-year survival is low for most indications. It is hoped that future anti-cancer therapies, particularly immunotherapies, will change therapeutic landscape and make cancer a chronic, treatable state of ill health.

According to IMS Health, the total market for cancer therapies amounted in 2014 to around USD 100 billion, representing a growth of about 10 percent from 2013. The average annual growth over the previous five years was estimated at 6.5 percent. Future growth is estimated to be 6-8 percent per year until 2018.<sup>13</sup>

The expected growth is based on a growing demand from patients in combination with the launch of new medicines. In 2014, ten new medicines were launched, five of which were immune oncological.

According to a new forecast from the Swedish National Public Health Agency and the Swedish Cancer Society, 100,000 Swedish people a year will suffer from cancer in 2040, which is nearly double the number of cases today.<sup>14</sup>

## IMMUNE ONCOLOGY

Immune Oncology is a rapidly growing area of cancer research and treatment. In 2013, immunotherapy against cancer was named the scientific breakthrough of the year by the prestigious journal, Science – and since then significant strides have

occurred with the research. According to MarketsandMarkets, the market for immune therapies is expected to grow at an annual growth rate of 13 percent, and by 2020 to amount to USD 74 billion.<sup>15</sup> The growth is expected to be driven by an increased incidence of various types of cancer, a focus on targeted therapies with fewer side effects, and expedited processes for drug approval. Among the factors that hinder growth, mainly the high cost of new cancer therapies seen.<sup>16</sup> Unlike more traditional cancer therapies, immune-oncology is designed to activate the body's own immune system to fight cancer. The immune system is very effective in attacking foreign invaders such as bacteria and viruses, and can combat all types of diseases, including cancer. However since cancer tumours are composed of the body's own cells, the immune system has a more difficult time to identify them as harmful. Also, tumour cells have different strategies in order to avoid that the immune system perceives them as harmful, so-called immunosuppression.

### Positioning and competition

Immunotherapies are designed to attack cancer in one of two different ways: either by activating the immune system (therapeutic cancer vaccines, CAR T-cells, etc.), or by combating immunosuppression (immune checkpoint inhibitors, tyrosine kinase inhibitors, chemotherapy, etc.). The Company's goal is to position INTUVAX® as the drug that will be chosen for activating the immune system in combination with different types of category-2 drugs that combat immunosuppression. In this way, many of today's standard treatments (such as tyrosine kinase inhibitors and various types of chemotherapy), as well as many potential future standard treatments for cancer (such as various immune checkpoint inhibitors), will form potential combination therapies rather than competing treatments.

Adaptive therapy with CAR T cells constitute a competing treatment method for cancer immune activation, which has been found in a number of clinical trials to be able to lead to complete regression of previously incurable patients. This

12. World Cancer Report 2014, International Agency for Research on Cancer, 2014.

13. Developments in Cancer Treatments, Market Dynamics, Patient Access and Value, Global Oncology Trend Report 2015, IMS Institute for Healthcare Informatics, 2015.

14. A new forecast shows: Dramatic increase in cancer victims by 2040, Public Health Agency of Sweden/National Institute of Public and the Swedish Cancer Society, 2016.

15. Immunotherapy Drugs Market by Type of Drug (Monoclonal Antibodies, Interferon-Alpha, Interleukins, Vaccines, (Therapeutic Vaccines and Preventive Vaccines), Checkpoint Inhibitors), Epidemiology, Regulatory and Pipeline Analysis – Global Forecast to 2020, 2015.

16. Immunotherapy Drugs Market by Type of Drug, (Monoclonal Antibodies, Interferon-Alpha, Interleukins, Vaccines, (Therapeutic Vaccines and Preventive Vaccines), Checkpoint Inhibitors), Epidemiology, Regulatory and Pipeline Analysis – Global Forecast to 2020, 2015.





type of treatment does see success, however but usually against various types of blood cancer, and not for solid tumours. This is due to that solid tumours have an inherent immunosuppression, which the “fatigued” CAR T cells are presently not able to survive. Therefore adaptive therapy with CAR T cells is not considered a major competitor to INTUVAX® in the current situation.

Therapeutic cancer vaccines, which also aim to activate the immune system to fight against cancer and therefore constitute a clearer competitor than category 2 drugs that combat immunosuppression, have so far failed to show sufficient clinical efficacy in order to obtain approval for release to the market (with the exception of Provenge, which received marketing approval in 2010 but whose owners Dendreon then went bankrupt and the company was then acquired by Valeant in 2015). Immunicum’s assessment is that competing cancer immune activators have failed so far to show adequate clinical efficacy, primarily because they have not had the right set of adjuvants (immune enhancers) in combination with the right set of tumour antigens (the patient’s own mutagenised/neo-antigens). It is also the Company’s assessment that the unique profile of INTUVAX®, based on allogeneic dendritic cells, can serve as an optimal adjuvant, and that intratumoural injection of INTUVAX® cells utilising the patient’s own tumour as an antigen source (with access to each patient’s unique mutagenised tumour antigens) may create good conditions for optimal cancer immune activation.

Over the years, Immunicum has presented its data received from treatment with INTUVAX® at a number of venues including at the American Society of Clinical Oncology in 2015, at a Symposium on Breakthroughs in Clinical & Translational Immunology together with Professor Steven Rosenberg, plans to make an additional presentation at the Society for Immunotherapy of Cancer’s meeting SITC 2016 in November.

## CANCER INDICATIONS

With Immunicum’s cancer immune activator INTUVAX® it is possible to treat all solid tumours which are accessible via intratumoural injection. The Company has chosen to initially

invest in metastatic renal cancer treatment and has initiated a Phase II study (MERECA). A further two clinical Phase I/II studies have been initiated, including one relating to liver cancer and one focusing on gastrointestinal stromal cell tumours (GIST). In addition, the Company plans to initiate two additional Phase I/II clinical trials concerning the treatment of melanoma in combination with so-called immune checkpoint inhibitors. The overall potential market is quite considerable. Examples of tumours that are considered suitable for treatment are those found in the kidney, liver, breast, lung, prostate, pancreas and thyroid. Lung cancer is the most common form of cancer, with about 1.8 million new cases each year. Breast cancer is the second most common, with about 1.7 million new cases per year. Even prostate cancer (1.1 million/year) and liver cancer (approximately 0.78 million/year) are common.<sup>17</sup> WHO expects that liver cancer will be the world’s most common cancer indication in 2020, due to hepatitis B, which is widespread, especially in Asia, often causing liver cancer and which is expected to increase.

## THE RENAL CELL CANCER MARKET

According to GLOBOCAN, in 2012 an estimated 338,000 new cases of renal cell cancer treatment are diagnosed each year globally, which represents about 2 percent of all cancer cases.<sup>18</sup> Transparency Market Research estimates that the global market for renal cancer treatment was worth USD 2.6 billion in 2013 and predicts that it will grow at an average annual growth rate of 6.6 percent to reach USD 4.5 billion by 2020.<sup>19</sup> The growth rate is attributed primarily factors such as obesity and smoking, which leads to an unhealthy lifetime and thereby increase the risk of kidney cancer. In pace with the patent rights expiring, commercialisation of new therapies and drugs is considered to constitute the majority of the expected market growth.

The global renal cancer treatment market in 2014 consisted primarily of eight products, so-called targeted therapies: (tyrosine kinase inhibitors) - Avastin (bevacizumab), Sutent (sunitinib), Nexavar (sorafenib), Afinitor (everolimus), Votrient (pazopanib), Torisel (temsirolimus), Inlyta (axitinib) and Proleukin (Aldesleukin).<sup>20</sup> Despite the fact that new drugs

17. GLOBOCAN, WHO, 2014.



have taken large market shares (Sutent had sales in 2015 in the amount of USD 1.1 billion for three different indications, with RCC as the main indication) they often constitute costly forms of therapies that provide limited efficacy and are accompanied with severe negative side effects.<sup>21</sup> The products cause significant side effects, but many patients are left with no other alternative than these therapies that can provide some degree of relief from the disease. The Company believes, therefore, that the market has a relatively large unmet need due to the limited efficacy and safety profiles of the products currently on the market. There is considerable scope for new entrants to capture market share and considerable potential for products such as INTUVAX®, which is based on new technology with potentially less or no side effects. The annual cost of current treatments is in the range of USD 38,000 to USD 124,000, however a new participant in the market who can offer a treatment with superior advantage, can charge more according to Global Data. Nor should cancer immune primers be regarded as only a substitute for conventional therapies, but rather should be viewed as a potential complement. Generally, targeted therapies are considered to have reached their potential as “stand-alone” products, where Sutent has shown median survival of 26.4 months.<sup>22</sup>

Prior to when targeted therapies were approved, IL-12 was used as treatment with mixed results. Due to the severe side effects however, the treatment has only been used for a small number of patients, and today IL-12 has been removed as recommended treatment in the current guidelines. The three principal competing products in Phase III that have been identified are the two immunotherapies (AGS-003 by Argos Therapeutics and Nivolumab + Ipilimumab by Bristol-Myers Squibb), plus a targeted therapy (Cabozantinib by Exelixis). In addition, in 2015 the U.S. Food and Drug Administration (USFDA) gave approval to immune-based cancer treatments in the form of Bristol-Myers Squibb's Opdivo antibody for the treatment of patients previously receiving another treatment, referred to as a second-line treatment. In 2016, Opdivo has also received the corresponding approval by the European supervisory authority, European Medicines Agency (EMA). According to the Company's considered assessment however, none of these treatments have adequate efficacy sufficient to replace the current primary treatment alternatives, referred to as first line treatment. Bristol-Myers Squibb's products are thought to be potential combination drugs.

Immunicum primarily wants to compete on better efficacy, but INTUVAX® also has potential advantages because of its ability to lessen the patient's side effects as well to improve the patient's overall well-being during treatment and thereby increase the possibility of returning to normal everyday life. Thus, the treatment can also add value and produce savings when looked at other perspectives: for the society as a whole, for public health and medical care services, for insurance companies and for the patient's social environment. The absence of serious side effects is one of the points that was the main focus of the evaluation in the Phase I/II study that ended 31 March 2014. In the Phase II study, which began in May 2015, the primary objective is to study the median survival in high risk patients, and the survival rate at 18 months for patients with intermediate risk prognosis who have been treated with INTUVAX® in combination with sunitinib.

## THE MARKET FOR LIVER CANCER TREATMENTS

Liver cancer is the sixth most commonly diagnosed cancer in the world, with about 0.78 million new cases each year. Datamonitor Healthcare estimates that the global market for renal cancer treatment amounted to USD 515 million in 2013 in the United States, Japan, France, Germany, Italy, Spain and UK, and predicts that the market will grow by 172 per cent to reach USD 1.4 billion in 2019.<sup>23</sup> The disease is especially common in Asia and globally is the third most deadly form of cancer. The limited spread of liver cancer in the West presents the opportunity for novel treatment alternatives to obtain Orphan Drug Designation (ODD) status in strategic markets (such as the U.S., Europe and Japan), while great potential also exists in other markets. More than half of the world's liver cancer patients are found in China, where approximately 400,000 patients are diagnosed every year. The incidence in the world's largest drug markets (the U.S., France, Germany, Italy, Spain, UK and Japan) is 105,000 new cases of individuals falling ill per year.<sup>24</sup>

Of all the forms of liver cancer, 85 percent is of type HCC (Hepatocellular carcinoma) and this is the indication in which Immunicum is conducting a Phase I/II study. The disease is often asymptomatic and few appropriate biomarkers are available. That is why a large proportion of the patients progress (approx. 50 percent in Europe and the U.S., and 73 percent in Japan) progress so far that few realistic treatment alternatives remain. Globally, only 20-30 percent of patients are diagnosed early enough to be treated surgically. Surgery and preferably transplantation of a new liver is usually the first treatment alternative when chemotherapy and other standard treatments prove ineffective for HCC because of adverse side effects on the healthy part of the liver and other organs. Even after surgical treatment the recurrence rate is quite high, surpassing 70 percent after 5 years.<sup>25</sup>

Limiting factors for the market potential include better diagnostics, which would allow more patients to be treated with

18. Ferlay J, Soerjomataram I, Ervik M, et. al. GLOBOCAN 2012 v1.0.

19. Kidney Cancer Drugs Market - Global Industry Analysis, Size, Share, Growth, Trends and Forecast 2014-2020, 2015.

20. Transparency Market Data, Kidney Cancer Drugs Market - Global Industry Analysis, Pipeline Analysis, Size, Share, Growth, Trends and Forecast 2014-2020, 2015.

21. GlobalData: Renal Cell Carcinoma (RCC) Therapeutics - Pipeline Assessment and Market Forecasts to 2017, 2011.

22. Pfizer, Annual Report 2015 and J. Clin., Overall survival and updated results for sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. Oncol. 27 (22): 3584-90. August 2009

23. Datamonitor Healthcare: Hepatocellular cancer market to nearly treble in size by 2019, 2013.

24. Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1.0.

surgery at an early stage. Even an expanded vaccination program for hepatitis is mentioned as a competing treatment alternative, since viral infections of the hepatitis A and B type are the primary reason for the significant prevalence in Asia. Still, neither of these factors is expected to significantly influence the patient population in the immediate future.

The competitive landscape for liver cancer resembles that for renal cell carcinoma. Since 2006, one new medicine with proven clinical effect has entered the market, Nexavar (sorafenib, Bayer Healthcare). Nexavar (sorafenib) is active against receptors and enzymes that are important for tumour cell growth, and is used in cases where surgical treatment is not possible. Even though Nexavar has a limited impact on survival (approx. 12 weeks), the lack of alternatives makes it useful. Nexavar sales in 2012 were approx. USD 1 billion for two approved indications (including renal cell carcinoma).

In addition to being a treatment for growing patient populations, new therapies are expected to make a contribution by having higher efficacy and less severe side effects. One target for new therapies is to reduce the number of recurrences post surgery, or to delay recurrence. Nexavar is being evaluated for administration to patients directly, post surgery. The new therapies that have reached late clinical phase for liver cancer are mostly drugs that are aimed at specific molecular targets, similar to the function of Nexavar. However, a significant need for more effective alternatives still remains.<sup>25</sup>

## GIST - GASTROINTESTINAL STROMAL TUMOURS

A gastrointestinal stromal tumour (GIST) is a tumour arising from mesenchymal cells in the gastrointestinal tract. GISTs do occur in the gastrointestinal tract, but are most common in the stomach, followed by the small intestine. GlobalData estimated the global market for this cancer indication to USD 920 million with an expected annual growth rate of 2 percent to reach USD 1.1 billion 2017. The reason for the low growth is mainly explained by the expiry of the patent rights for Glivec (imatinib) in 2014 which, in conjunction with the Sutent (sunitinib) has been the treatments that have been available where the first choice of surgery has not worked.<sup>27</sup> GIST is a relatively rare disease, which means that only a few experts have deeper knowledge of how the disease should be evaluated and treated. Surgery is the primary treatment for localised GIST through which more than half (1/2) of the patients are cured. For non-operable patients, there are effective drugs where Glivec is the first choice. More than 60 percent exhibit a response to treatment within a few months, but 10-15 percent do not benefit from the treatment. Treatment with Glivec continues as long as a significant deterioration is

not observed, i.e. usually for very long treatment periods. Treatment with Glivec is probably not curative, but the objective is that the tumour will stop growing and subsequently slowly shrivel. If treatment is discontinued, the tumour receives vitality again. For those patients who do not respond to Glivec or falter during treatment, despite an escalation of dosage, it is possible to receive treatment with Sutent (sunitinib), a tyrosine kinase inhibitor. Stivarga (regorafenib) is now registered for those patients who do not respond to sunitinib and is thus considered to be third-line therapy. Other tyrosine kinase inhibitors, such as Nexavar (sorafenib), Votrient (pazopanib) and Sprycel (dasatinib) have not been registered as an approved medication for GIST, but have been tested in clinical trials. Conventional cancer treatment with cytotoxic therapy, chemotherapy, or radiation treatment has very little effect with GIST.<sup>28</sup>

## MALIGNANT MELANOMA

According to the World Health Organization (WHO), the number of skin cancer cases is increasing and the present expectation, according to information on WHO's website, is that the number of new cancer cases worldwide each year will amount to between 2 and 3 million, of which about 132,000 are expected to be malignant. According to the Skin Cancer Foundation (pursuant to data on WHO's website), one in three detected cases of cancer are skin cancers.<sup>29</sup> The increasing number of skin cancer cases are believed to be due to that people are exposing themselves to UV radiation to an increasing degree, combined with a thinner ozone layer in Earth's atmosphere.

According to the research firm GBI Research, the size of the global market for malignant melanoma amounted to approximately USD 1.3 billion in 2013, and is expected to grow to USD 3.6 billion by 2020.<sup>30</sup> This anticipated growth approaching year 2020 corresponds to an average annual growth rate of 15.4 percent. The primary reason behind the strong growth is also the same factors for cancer drugs in general, a greater need for medications and that they are more readily available.

Since 2011, no fewer than nine new drugs were released to the market: Sylatron (peginterferon alfa-2b), Yervoy (ipilimumab), Opdivo (nivolumab), Keytruda (pembrolizumab), Zelboraf (vemurafenib), Tafinlar (dabrafenib), Imlytic (talimogene laherparepvec), Cotellic (cobimetinib) and Mekinist (trametinib). Others that are approaching the market include Polynomas Seviprotimut-L and AstraZeneca Selumetinib, for instance. It follows that competition within the indication is expected to become increasingly fierce. However it is Immunicon's assessment that the Company's drugs will primarily be used in combination with other drugs and that the Company is strategically well-positioned for a market with a growing proportion of the immune oncological drugs.

25. Stakeholder Opinions: Hepatocellular Cancer, Datamonitor 2010.

26. Stakeholder Opinions: Hepatocellular Cancer, Datamonitor 2010.

27. Gastrointestinal Stromal Tumors (GIST) Therapeutics - Pipeline Assessment and Market Forecasts to 2017, 2011.

28. Hagberg, H, Internetmedicin, Gastrointestinal stromacellstumör (GIST), 2016.

29. WHO, Ultraviolet radiation, FAQ, Skin Cancers, www.who.int, 2016.

30. Melanoma Therapeutics Market to 2020 - Rising Prevalence and Evolving Treatment Algorithms to Drive Market Growth, BGI Research, September 2014.

# Organisation

## THE COMPANY'S BOARD OF DIRECTORS



### AGNETA EDBERG

**CHAIR OF THE BOARD (COB),  
MEMBER OF THE AUDIT COMMITTEE**

**HOLDS 36,250 SHARES**

*Alumna of the the Stockholm School of  
Economics, Biomedicinsk Analytiker  
Born in 1956*

Agneta Edberg has served as Chair of the Board of Directors (COB) of Immunicum AB since 2010.

**Chairwoman of the Board of Directors:** Ambulanssjukvården i Storstockholm Aktiebolag, Likvor AB, Idogen AB

**Member of the Board:** Temperature Sensitive Solutions Systems Sweden AB, Valvet Förvaltning AB, Probac AB, A Edberg Consulting AB, TSS Holding AB, Svenska Läkemedelsförsäkringen AB.

Has held a number of different managerial positions and responsibilities within Pfizer AB, Pharmacia AB, Orion AB, Cederroth International AB and Johnson & Johnson.



### BENGT FURBERG

**MEMBER OF THE BOARD, CHAIRMAN  
OF THE SCIENTIFIC ADVISORY BOARD**

**HOLDS 3,000 SHARES**

*Associate Professor of Clinical Physiology  
Born in 1941*

Bengt Furberg has been a member of Immunicum AB's Board of Directors since 2008.

**Member of the Board:** Solutio AB, Hamlet Pharma AB, Redwood Pharma AB, BrainCool AB

Is an expert in the field of clinical trials and has written numerous books and scientific articles on the subject. Has been the Medical Director, a member of the management team as well as the Medical Committee and Security Committee in GlaxoWellcome.



### MARTIN LINDSTRÖM

**BOARD MEMBER, CHAIRMAN OF THE  
AUDIT COMMITTEE**

**HOLDS 2,760,000 SHARES, OF WHICH  
2,750,000 ARE HELD VIA CLOSELY-  
RELATED PARTIES**

*Master of Civil Engineering, Roads and  
Watter, B.Sc. Born in 1980*

Martin Lindström has been a member of Immunicum AB's Board of Directors since 2008.

**Member of the Board:** SHH Invest nr 16 AB, SHH Invest nr 21 AB

**Alternate member of the Board of Directors, and the Managing Director:** Loggen Invest AB, Loggen Fastighetsutveckling AB

**Alternate member of the Board of Directors:** Loggen Fastighets AB, Lars Lindström Förvaltning i Kalmar AB  
Represents the owner, Loggen Invest AB.



**MAGNUS PERSSON**

**MEMBER OF THE BOARD  
NO SHAREHOLDINGS**

*Medical Physician, Professor and Associate Professor of Physiology at the Karolinska Institute in Stockholm*

*Born in 1960*

Magnus Persson has been a member of Immunicum AB's Board of Directors since 2015.

**Chairman of the Board of Directors:** Karolinska Institutet Innovations AB, Karolinska Institutet University Press AB, Karolinska Institutet Information AB, Cantargia AB, SLS Invest AB, Galecto Biotech AB, HIP Health Innovation Platform AB

**Member of the Board:** Cerecor Inc. MPi AS, Albumedix AS, Karolinska Institutet Support AB, Karolinska Institutet Housing AB, Karolinska Institutet Science Park AB, KCIF Fund Management AB, Själbådan AB, Gyros Protein Technologies Holding AB

**External Managing Director:** Karolinska Institutet Holding AB

Has 15 years experience as a partner within Venture Capital. Has led development teams in Phase II and III programmes in the pharmaceutical industry.



**MAGNUS NILSSON**

**BOARD MEMBER, MEMBER OF THE  
AUDIT COMMITTEE  
NO SHAREHOLDINGS**

*Doctorate of Medical Sciences from  
Uppsala University  
Born in 1956*

Magnus Nilsson has been a member of Immunicum AB's Board of Directors since 2014.

**Chairman of the Board of Directors:** Vivoline Medical AB

**Member of the Board:** Dignitana AB, Magnus HL Nilsson Management Consulting AB

**External Managing Director:** Xvivo Perfusion Aktiebolag  
He has previously been CEO of Vitrolife AB for approx. 9 years. Has been the project manager of preclinical and clinical development at Karo Bio AB and Pharmacia & Upjohn AB.

## SCIENTIFIC ADVISORY BOARD

CHAIR: BENGT FURBERG



**ROLF KIESSLING**  
**BOARD MEMBER**  
**NO SHAREHOLDINGS**

*Professor of Experimental Oncology,  
Karolinska Institutet  
Born in 1948*

Rolf Kiessling has been a Professor of Experimental Oncology at the Karolinska Institute since 1995, and has a part-time position as Chief Physician at the Radiumhemmet, a non-surgical cancer treatment and radiotherapy research institution at Karolinska Hospital. Professor Kiessling has published more than 200 publications in peer reviewed journals, and has extensive and broad scientific expertise in the field of experimental and clinical immunology. An early milestone in his career was when he discovered and named the NK cell in the middle of the 1970s, a discovery that earned him the "Anders Jahre Medical Award for Young Researchers" in 1985 and the "Erik Fehrströms Prize" in 1989. More recently, his research group has focused on the field of immunotherapy against cancer and the group conducts Investigator Initiated Studies in cancer patients as well as conducting basic research in preclinical animal models.



**ROGER HENRIKSSON**  
**BOARD MEMBER**  
**NO SHAREHOLDINGS**

*Professor of Experimental Oncology  
Born in 1953*

Roger Henriksson has been a Professor of Experimental Oncology and senior physician in the field of medical oncology and radiotherapy since 1994. He has also served as medical adviser to AstraZeneca (globally) part-time since 2000. Professor Henriksson has published over 270 articles in peer-reviewed journals relating to all phases and stages of drug development. Among his current scientific assignments, the following can be mentioned: Director of the Department of Radiation Sciences, Umeå University, Chairman of the National Planning Group CNS-tumours, Member of the Cancer Society's Scientific Advisory Board, Member of the Swedish Lung Cancer Study Group.



**CURT FURBERG**  
**BOARD MEMBER**  
**NO SHAREHOLDINGS**

*Professor of Public Health  
Born in 1936*

Furberg is an internationally renowned cardiovascular researcher and epidemiologist with specialist expertise in clinical trials and public health. He is one of the authors of the book about methodology with clinical trial, "Fundamentals of Clinical Trials". He has also co-authored a recently published book, "Data Monitoring in Clinical Trials: A Case Studies Approach", and has published extensively, with over 400 papers and articles to his name. His strong commitment to evidence-based medicine and his lengthy background in public health provides a solid foundation for his views in issues surrounding the evaluation of medicines and patient safety. He has been a member of the USFDA's Drug Safety and Risk Management Advisory Committee, and has appeared as a witness before U.S. congressional committee hearings.



**ANDERS ÖHLÉN**  
**BOARD MEMBER**  
**NO SHAREHOLDINGS**

*M.D., Ph.D  
Born in 1953*

Anders Öhlén has extensive experience in the senior management in pharmaceutical research and development and medical issues from Kabi Pharmacia (now a part of Pfizer), Astra, Aventis and Bristol-Myers Squibb. He has worked in various therapeutic areas and has been involved in all aspects of a product's lifecycle management during his 30 years of work in the healthcare and pharmaceutical industries. During 2010-2016, he was the Managing Director of Svenska Läkemedelsförsäkringen/Swedish Pharmaceutical Insurance.

## MANAGEMENT



### JAMAL EL-MOSLEH

**CEO**

**HOLDS 393,000 SHARES**

*Master of Engineering, Industrial Economics, Innovation and Entrepreneurship born in 1981*

Jamal El-Mosleh has been the CEO of Immunicum AB since in 2007.

Professor Kiessling been a management consultant and project manager of a start-up in the field of life science.



### LISE-LOTTE HALLBÄCK

**CHIEF FINANCIAL OFFICER (CFO)**

**HOLDS 5,000 SHARES, OF WHICH 1,250 ARE HELD VIA CLOSELY-RELATED PARTIES**

*Bachelor of Science in Business Administration and Economics*

*Born in 1966*

Lise-Lotte Hallbäck has been the CFO of Immunicum AB since 2015.

Previously, has been an authorised public accountant, a management consultant, and a financial manager. Has extensive experience in accounting, tax and legal issues primarily relating to companies active internationally.



### ALEX KARLSSON-PARRA

**CHIEF SCIENTIFIC OFFICER (CSO)**

**HOLDS 612,726 SHARES, OF WHICH 281,363 ARE HELD VIA CLOSELY-RELATED PARTIES**

*Adjunct Professor, Chief of Clinical Immunology, University Hospital, Uppsala  
Born 1950*

Alex Karlsson-Parra is one of Immunicum AB's founders.

Karlsson-Parra has over 30 years experience in transplantation immunology and former chairman of a Swedish group of experts of Clinical Immunology, and was awarded the Athena Prize in 2014, Swedish healthcare's largest prize.



### PETER SUENAERT

**CHIEF MEDICAL OFFICER (CMO)**

**NO SHAREHOLDINGS**

*M.D., Ph.D  
Born in 1968*

Peter Suenart has been the CMO of Immunicum AB since July 2016.

Has 14 years of experience in preclinical and clinical development of a variety of anti-cancer and immune-oncological drugs. Has held senior positions at Glenmark Pharmaceuticals R&D, Danone Research, Vaccines, GlaxoSmithKline and Amgen.



# The Immunicum share, share capital and ownership structure

## THE IMMUNICUM SHARE

The shares have been trading on NASDAQ First North under the ticker symbol IMMU, with the ISIN code SE0005003654 since 22 April 2013. As of 4 May 2016, the Company's shares have been listed on the First North Premier segment.

## NUMBER OF SHARES

The number of shares in the Company as of 30 June 2016 amounts to 24,270,869 (20,030,000). At that time there was a preferential rights share issue underway and an oversubscription of new shares relating to 1,687,672 shares. With the registration in full in July 2016 of the shares from the new share issue, the total number of shares will amount to 25,958,541.

## CHANGES IN CAPITAL (FROM 2010)

YEAR	EVENT	CHANGE IN THE NUMBER OF SHARES	TOTAL NUMBER OF SHARES	CHANGE IN SHARE CAPITAL (SEK)	TOTAL SHARE CAPITAL (SEK)	QUOTA VALUE (IN SEK, AMOUNTS ROUNDED OFF)
2010	New share issue	1,326	6,629	33,150	165,725	25.00
2012	New share issue	600	7,229	15,000	180,725	25.00
2012	Share split 1000:1	7,221,771	7,229,000	-	180,725	0.025
2012	Bonus issue/stock dividend	12,771,000	20,000,000	319,275	500,000	0.025
2013	Reverse share split (consolidation) 2:1	-10,000,000	10,000,000	-	500,000	0.05
2013	New share issue	2,675,000	12,675,000	133,750	633,750	0.05
2013	New share issue	1,100,000	13,775,000	55,000	688,750	0.05
2014	New share issue	3,500,000	17,275,000	175,000	863,750	0.05
2014	New share issue	2,755,000	20,030,000	137,750	1,001,500	0.05
2016	Subscription warrants	130,000	20,160,000	6,500	1,008,000	0.05
2016	New share issue	5,040,000	25,200,000	252,000	1,260,000	0.05
2016	New share issue	758,541	25,958,541	37,927,05	1,297,927,05	0.05



## THE ISSUANCE OF NEW SHARES IN 2016

The subscription period for the 2012/2016 warrants programme concluded on 31 March 2016. A total of 130,000 new shares were subscribed for, of a total of 600,000 potential shares. The subscription price was SEK 24 per share. Via this new share issue, Immunicum was provided with SEK 3.1 million (before share issue costs). The share capital increased by SEK 6,500.

On 18 May 2016, an Extraordinary Meeting of Shareholders resolved to implement a new share issue with preferential rights for existing shareholders in the total amount of 5,040,000 shares at a subscription price of SEK 22 per share. The Extraordinary Meeting of Shareholders also authorised the Board of Directors to conduct a private placement (in

the event the preferential rights issue is fully subscribed) of a maximum of 910,000 shares at the identical subscription price. The subscription period ended on 14 June 2016. The final result showed that a total of 4,110,869 shares were subscribed for based on subscription rights, representing approximately 82% of the preferential rights share issue. In addition, applications were received for the subscription of shares without subscription rights for a total of 1,687,672 shares, representing approximately 33% of the preferential rights share issue. The degree of over-subscription was approximately 15%. Via the issuance of these new shares, Immunicum was received a capital injection of SEK 127.6 million (before share issue costs). The share capital will increase by SEK 289,927.

## MAJOR SHAREHOLDERS (TEN LARGEST AS PER 29/07/2016)

SHAREHOLDER	NUMBER OF SHARES	SHARE OF CAPITAL/VOTES
Holger Blomstrand Byggnads AB	2,975,386	11.50%
Loggen Invest AB	2,750,000	10.60%
Försäkringsaktiebolaget, Avanza Pension	2,031,712	7.80%
Swedbank Robur Fonder AB	1,562,500	6.00%
Nordnet Pensionsförsäkring AB	649,912	2.50%
Alex Karlsson-Parra, incl. related parties	612,726	2.40%
Bengt Andersson	557,939	2.10%
Jamal El-Mosleh	393,000	1.50%
Mats Dahlgren	380,000	1.50%
UBS Switzerland AG	362,644	1.40%
<b>Total, for the ten largest shareholders</b>	<b>12,275,819</b>	<b>47.30%</b>
Other shareholders	13,682,722	52.70%
<b>TOTAL</b>	<b>25,958,541</b>	<b>100.00%</b>

# Annual Statutory Administration Report

The Board of Directors and the Chief Executive Officer of Immunicum AB (556629-1786) hereby submit the Annual Report for the 01/07/2015 – 30/06/2016 financial year.

## General description of the business activities

Immunicum is a biomedical company that develops cancer immunotherapies based on three different proprietary platform technologies: COMBIG, CD70 and Ad5PTDf35-adenovirus vector. The Company was founded in 2002 as a spin-off from the Sahlgrenska University Hospital at the University of Gothenburg. Since Immunicum's products are based on platform technologies, the Company can develop treatments against many different cancer indications. Immunicum's project portfolio currently consists of five different projects, three of which are in clinical trials.

The Company is a public limited liability company registered in Sweden, with its registered offices in Gothenburg. Its address is Grafiska vägen 2, SE-412 63 Gothenburg.

On 29 September 2016, the Board of Directors approved this Annual Report for release and publication.

## Financial overview

### Financial results

The operating loss amounted to MSEK -43.6 (MSEK -36.4)  
The net loss amounted to MSEK -43.9 (MSEK -35.6)

Operating expenses were MSEK 43.6 (MSEK 36.6). The growth in expenses is primarily due to increased costs for clinical trials and increases costs for personnel.

### Financial position and liquidity

Cash flow used in operating activities amounted to SEK -40.2 million (-40.1 million). The Company's cash and cash equivalents, including short-term investments, amounted to SEK 129.4 million (68.2 million) at the close of the financial year. Existing funds are assessed to be able to adequately cover the Company's capital requirements over the next 12 months.

Shareholders' equity at close of period amounted to SEK 139.2 million (64.6 million) and the equity ratio was 90% (91%). Shareholders' equity per share amounted to SEK 5.36 (3.23)

In light of that the ongoing and future new clinical studies will entail in significant costs, the Company is expected to continue to show a negative cash flow. This need for capital may be addressed by a number of different options.

## Significant events during the 2015/2016 financial year

- > On 9 November, the European Patent Office (EPO) provided notification that it intends to grant a patent based on the application pertaining to Immunicum's cancer immune activator, INTUVAX®. On 20 November, the Japanese Patent Office (JPO) announced that it intends to grant a corresponding patent application concerning INTUVAX®.
- > At the Annual General Meeting held in December, Magnus Persson was elected as a board member of Immunicum, where he replaces Sven Andréasson who had declined to stand for re-election.
- > On December 16, the Swedish Medical Products Agency (MPA) and the Ethical Vetting Board gave the green light to launch the Company's fourth clinical trials, with the cancer immune activator INTUVAX®. The clinical trial will be conducted on 12 patients with gastrointestinal stromal tumours (GIST) at the Karolinska University Hospital in Stockholm.
- > On 16 December, the Swedish Medical Products Agency and the Ethical Vetting Board also gave its approval that the Phase I/II clinical trials concerning liver cancer may be expanded by up to six patients, who will receive INTUVAX® in combination with first-line treatments.
- > Immunicum's Scientific Advisory Board was further strengthened on 3 March with Anders Öhlén, who has extensive experience in the senior management level within pharmaceutical development from Kabi Pharmacia, Astra, Aventis and Bristol-Myers Squibb, among other concerns.
- > Updated data from the Phase I/II study with INTUVAX® in the treatment of primary liver cancer was submitted at three instances during the year. In the most recent update on 18 April, data was presented showing that the treatment with INTUVAX® increases the frequency of tumour specific CD8+ T cells in the majority of full-treated liver cancer patients, and that this increase directly correlates with prolonged survival.
- > On 22 April, the State Intellectual Property Office (SIPO) of the People's Republic of China reported that it intends to grant Immunicum's patent application concerning INTUVAX®.

- > On 2 May Immunicum announced that the Company has applied for listing of the Company's shares on NASDAQ Stockholm's Main Market List. As part of the process, Immunicum's shares have been approved for listing on NASDAQ OMX First North Premier.
- > On 17 May, a cooperation agreement was reached with Accelovance for clinical development services in order to advance INTUVAX® in the U.S. for the treatment of kidney cancer and melanoma.
- > Updated follow-up and survival data from the Phase I/II studies with INTUVAX® concerning the treatment of metastatic kidney cancer was submitted on three instances. In the latest update on 13 June, it was found that the results show an ongoing and extended median survival rate that has more than doubled for the patient group overall, and presently the ongoing extended median survival of rate patients with a poor prognosis has more than tripled.
- > In June, Immunicum's concluded its preferential rights share issue with the utilisation of the over-subscription issue. Immunicum thus raised approximately SEK 128 million (before share issue costs).
- > On 23 June, the Company announced its preliminary plan for the implementation of two separate clinical trials with INTUVAX® concerning the treatment of advanced melanoma in combination with immune checkpoint inhibitors, a first-line treatment, and the other in a second-line treatment, in the U.S. and Sweden respectively.

#### Significant events after the closing of the financial year

- > Peter Suenart, MD, Ph.D., was recruited in July to become Immunicum's first Chief Medical Officer (CMO).
- > On 22 July, Immunicum submitted an Investigational New Drug (IND) application with the Food and Drug Administration (USFDA) in the United States. The application concerns an authorisation to treat kidney cancer patients in the U.S. with Immunicum's cancer immune activators, INTUVAX®, in the Company's ongoing Phase II study, known as the MERECA study (MEtastatic REnal cell CARcinoma).
- > On 26 July, it was announced that the Chinese State Intellectual Property Office (SIPO) intends to grant approval

to the patent application pertaining to Immunicum's CD70 technology.

- > On 27 September, it was announced that Carlos de Sousa was appointed to succeed Jamal El-Mosleh as the Company's CEO.

#### Research and Development

The focus of product development is to validate the various effects of the vaccine concept in humans. Immunicum also carries out work to optimise the production process. Immunicum has entered into a research collaboration with Professor Magnus Essand at Uppsala University Hospital around the CD70 platform and vector technology.

#### Significant risks and uncertainty factors

##### *Immunicum is a development company without historical revenue*

Immunicum has not yet, either on its own or via partners, introduced any cancer immune primers or any other medicinal product to the market. Therefore the Company has not engaged in the sale of any pharmaceutical products, nor does it generate any sales revenue. The Company's assessment is that it will continue to be reporting a loss for the next few years. Immunicum's product candidates are presently in either a clinical or preclinical phase, which means that continued research and development, as well as granted authorisations from public agencies and positive outcomes in preclinical and clinical studies, is required before product candidates will be able to reach the market. If the present product candidates' introduction on the market is delayed, are made more expensive, or never occur, it could have a significant negative impact on the Company's business operations, financial results and financial position.

##### *Risks related to possible future income*

Immunicum's future earnings will be dependent upon that Immunicum is able to enter into agreements for the licensing of the Company's product candidates and/or technology platforms. The possibility of entering into such contracts is dependent upon, inter alia, the credibility of Immunicum as a potential business partner, the quality of the Company's product candidates, and the robustness of the Company's intellectual property rights. There is a risk that such contracts may not be entered into, or can be entered into only on terms and conditions that are unprofitable or unfavourable to the Company. Potential cooperative partners can, as a precondition to

entering into contracts, impose a requirement that additional supplemental clinical trials be conducted on Immunicum's products, which may involve delays and increase costs for the Company. Furthermore, a significant share of Immunicum's potential earnings is expected to consist of what is referred to as milestone payments, in other words, one-time payments from partners which will be paid if and when certain specified objectives or targets have been attained. If Immunicum fails to enter into agreements for the licensing of products on terms and conditions that are favourable to the Company, if such agreements lead to delays and/or increase costs, or if payments to be made pursuant to such agreements are delayed or are not received at all, this could have a significant negative impact on the Company's business operations, financial results and financial position.

#### ***Needs for additional financing***

Immunicum has reported operating losses since the Company was started and the cash flow is expected to remain negative until the time when Immunicum can generate ongoing revenues. Immunicum will continue in the future to have a need of additional capital in order to carry out further research and development. The amount and timing of Immunicum's future capital needs depends upon a number of factors, such as the cost of its business operations and the preconditions for the entering into agreements which make the potential receipt of revenues possible. The availability of and the preconditions for raising additional capital is affected by a number of factors such as general market conditions and the overall access to capital or external financing. Even disruptions and uncertainty in the credit and capital markets may restrict access to additional capital. Access to capital may also be dependent upon on the outcome of the clinical trials and preclinical development including nonclinical studies that the Company implements, along with other factors related to the operations of the Company. If Immunicum chooses to acquire additional financing via the issuance of new shares or equity instruments, the shareholders who do not participate in such new share emissions may be negatively affected by dilution of their holdings. In the event debt financing, if this is available for the Company, terms and conditions may be established which limits the Company's freedom of action in various respects. There is a risk that new capital cannot be obtained when the need arises, that it cannot be acquired on preferential terms, or that it cannot be acquired at all. If Immunicum cannot obtain financing, the Company may be forced to seriously restrict its research and development activities or in the worst case, suspend its operations, which would most likely have a significant negative impact on the Company's business operations, financial results and financial position.

#### ***Dependence on collaborative partners***

Immunicum is a research and development Company with a limited organisation of its own, and is therefore highly dependent upon cooperation with external partners to conduct its business operations. Furthermore, the Company is dependent on being able to initiate or intensify the cooperation in

the future, in particular with regard to the development of product candidates, clinical trials, the supply needed material, and production. The Company's collaborations with external companies may develop in a negative direction, and Immunicum might not be able to enter into new agreements or may only be able to enter into agreements on terms and conditions that are unprofitable or unfavourable to the Company. The companies that perform preclinical or clinical studies may not be able to maintain the clinical and regulatory quality that is required for a future regulatory approval or may not be able to fulfil their commitments. Agreements with partners may also require the approval from governmental agencies, which in and of itself entails a risk for delays in clinical trials and potential consequential market launches of product candidates. Should any of these risks occur it could have a significant negative impact on the Company's business operations, financial results and financial position.

#### ***Depending on the key persons and qualified personnel***

Immunicum's business operations are highly dependent upon a number of key individuals, some of whom hold senior management positions and/or are shareholders of the Company. If any of these key people would leave the Company, this could delay or complicate the Company's continued research and development, and cause an obstacle to the continuation of the business operations. Furthermore, the Company is dependent on its ability to attract and retain qualified personnel with relevant training and experience. There is fierce competition for experienced staff within the field of activities the Company is involved in, and many of the Immunicum's competitors have significantly greater financial resources than the Company, which can lead to a situation where the requisite staff cannot be recruited, or can only be recruited on terms and conditions that are unprofitable or unfavourable to the Company. If Immunicum cannot recruit and retain key persons and other qualified personnel to the extent and under the terms and conditions that are required, it could have a significant negative impact on the Company's operations, financial results and financial position.

#### ***Dependence on the compensation system***

The Company and its potential partners' possibilities to successfully commercialise products and the potential for possible future sales, will depend on the existence and the level of compensation for the products from insurance companies, governmental authorities and other payers of medical products and services. Changes in the existing body of legislation and regulations, political decisions or changed practices and rules among public authorities or agencies, insurance companies and other decision-makers can lead to the situation where the compensation for Immunicum's future products becomes be lower than expected or fails to materialise at all, which could have a significant negative impact on the Company's business operations, financial results and financial position.

### **Research and Development**

The preclinical development and clinical studies that the Company pursues are based on the platform technologies COMBIG®, CD70 and Ad5PTDf35-adenovirus vector. No product based on these platform technologies has yet to be approved for release on the market. Before a medicinal product can be put on the market, the safety and efficacy concerning the treatment of humans must be assured for each individual indication, which is proven by preclinical investigations carried out with animals and with clinical trials in humans. The results of such investigations and clinical trials can be unforeseen and even undesired, and thus considerable uncertainty is associated with the Company's projected costs related to such studies. Unforeseen outcomes from the investigations and clinical trials may also lead to that the concepts and studies must be reconsidered and revised, which means that new additional studies may need to be performed at a significant cost, or that the studies are discontinued and completely shut down. This can in turn lead to that the planned launches of product candidates to the market may be delayed or withdrawn altogether, due to, for instance, if the governmental agencies or other decision makers make the product candidates do not satisfy established standards. A delayed or failure to launch the Company's product candidates could have a significant negative impact on the Company's business operations, financial results and financial position.

Furthermore, successful previous studies do not necessarily mean that subsequent studies will obtain the desired results. Pre-clinical experiments are based on a limited number of studies and can, after further examination, be revised or discredited or invalidated, due to regulatory decisions or further preclinical investigations or clinical trials at later stages. The outcomes from preclinical investigations may not be consistent with the results obtained in clinical trials, and the results from preliminary clinical trials do not always correspond with the results found in more extensive and subsequent clinical trials.

If Immunicum can not prove to a sufficient extent via clinical studies that a product candidate is safe and effective, and thus enabling it to be commercialised, that could have a significant negative impact on the Company's business operations, financial results and financial position.

### **Liability for side-effects, etc.**

Patients participating in the clinical studies with Immunicum's product candidates may be affected by adverse reactions. The consequences of such potential adverse side effects may delay or stop the continued product development and/or restrict or prevent the commercial use of the product, or lead to liability for compensation for damages or other claims, including claims based on product liability, directed against the Company. The possibility exists that future claims may exceed the amount of insurance coverage the Company has taken out. If such claims were to be made or liability be asserted, it could have a significant negative impact on the

Company's business operations, financial results and financial position. Side effects can also have the effect that the Company's reputation is damaged, which in turn may affect the Company's position in relation to the public authorities, its suppliers and cooperative partners, as well as the risk of undermining confidence in the Company's technologies and product candidates. Such circumstances could have a significant negative impact on the Company's business operations, financial results and financial position.

### **Competition**

Immunicum operates in a competitive industry, and many companies, universities and research institutions are engaged in research and development of pharmaceutical products, including those who can, or may in the future, compete with the Company's product candidates. The Company's future competitive potential is partly dependent upon that the Company's product candidates obtain effective intellectual property protection and via such protection they can be maintained. Furthermore, Immunicum operates in a market where many of the Company's competitors have greater financial resources than the Company has access to. In addition, the Company may be exposed to competition from copies of medicines or from generics that are launched in pace with the patent expiring. If the Company is not able to effectively compete in the market, it could have a significant negative impact on the Company's business operations, financial results and financial position.

### **Complex and evolving regulatory requirements**

In order to be allowed to market any future pharmaceutical products, it is required that the Company, its cooperative partners and/or subcontractors will obtain the relevant permits and authorisations from the public authorities, such as the Swedish Medical Products Agency and Ethical Vetting Board, as well as the European Medicines Agency (EMA), and in the U.S. the Food and Drug Administration (USFDA). Such rules, which relate among other issues to preclinical investigations and clinical trials as well as the commercialisation and the marketing of the drug candidates in Immunicum's project portfolio, can change over time. Changes in legislation, regulations, rules or administrative practices relating to cancer immune primers and other medicines may increase Immunicum's expenses, or hinder the development of Immunicum's product candidates, which could then have a significant negative impact on the Company's business operations, financial results and financial position.

### **Immunicum's intellectual property rights, know-how, trade secrets and confidentiality**

Immunicum's future success will largely depend on its ability to obtain and maintain the protection of intellectual property rights, mainly patent protection, in the USA, EU, Asia and other countries, for the intellectual property rights relating to the Company's product candidates. The preconditions for patenting and patent protection of inventions in the field of biotechnology, cancer immune primers and other medicinal



products is generally difficult to assess and includes complex legal and scientific assessments. There is a risk that the Immunicum cannot obtain patents for its products or its technology. In addition, patents have a limited lifetime.

There is a risk that the existing and potential future portfolio of patents and other intellectual property rights held by the Company will not constitute sufficiently adequate commercial protection. There is also a risk that the Company's existing and possible future patent portfolio will not be able to be maintained or be burdened by the obligation for the Company to pay license fees or similar fees to third parties. The technologies Immunicum uses in its research, or that which is included in the product candidates Immunicum develops and intends to commercialise, may infringe on patents owned or controlled by another party. Third parties may also infringe a patent that is owned or controlled by Immunicum. Furthermore, a third party may have applied for a patent covering the same product or technology as the Company's. If Immunicum is forced to conduct legal proceedings in order to have established who has the rights to particular patent, this can result in significant expenses and expenditures of time that will be needed for such legal proceedings, and it cannot be ruled out that the Company may not prevail in such legal proceedings, which could lead to that the protection of any or all of the Company's products ceases, or even that Immunicum will be forced to pay significant amounts in compensation for damages.

Immunicum is also dependent on know-how and business secrets/trade secrets, and the Company strives to protect such information, including via confidentiality agreements with its employees, consultants and cooperative partners. However it is not possible to fully protect oneself against unauthorised dissemination of information, which creates the risk that competitors may receive copies of/information about such information and can take advantage of the know-how that has been developed or is held by Immunicum. Furthermore, the dissemination of trade secrets or commercial secrets affects the Company's prospects of having the patent(s) for inventions being granted.

If events related to of the above risks would occur, it would be able to have a significant negative impact on the Company's business operations, its profits, and its financial position.

#### **Claims and legal disputes**

As a consequence of normal business operations, Immunicum can become involved in legal disputes and litigation. Legal disputes and litigation can be time-consuming, disrupt the on-going business operations, relate to significant amounts or fundamentally important issues, and result in significant costs which can lead to a substantial negative impact on the Company's business operations, its profits, and its financial position.

#### ***Changes in the pharmaceutical industry can result in that the Company's products become obsolete***

The pharmaceutical industry is characterised by rapid changes in technology, new technological achievements, and continual improvement of industrial know-how. Immunicum's possible successes will thus largely depend on the Company's ability to adapt to such external factors, diversify its project portfolio and develop new and competitively-priced products that meet the requirements of the ever-changing market. Nor can it be excluded that future technological achievements may cause the Company's currently planned products (or products planned for the future) to lose their commercial value. If the Company is not able to adapt to technical developments, this could have a significant negative impact on the Company's business operations, its profits, and its financial position.

#### **The recommendation of the Board of Directors for the appropriation of the Company's profits/losses**

##### **AMOUNTS IN SEK**

The following funds are available to the Annual General Meeting for its disposition:

Share premium reserve	252,535,222
Retained earnings	-70,730,294
Net profit/loss for the year	-43,922,885
<b>TOTAL</b>	<b>137,882,043</b>

The Board of Directors proposes that the funds are appropriated so that:

is carried forward to the following accounting period	137,882,043
<b>TOTAL</b>	<b>137,882,043</b>

For information on the Company's financial performance and financial position in general, please refer to the following Profit & Loss Statement and Balance Sheet with accompanying Notes.



# Financial Summary

AMOUNTS IN SEK

SUMMARY PROFIT & LOSS STATEMENT	2015/2016	2014/2015	2013/2014	2012/2013	2011/2012
Miscellaneous operating income	-	160,000	560,000	1,473	5,134
Operating expenses	-43,642,748	-36,563,839	-17,211,957	-6,974,772	-4,310,500
<b>Operating profit/loss</b>	<b>-43,642,748</b>	<b>-36,403,839</b>	<b>-16,651,957</b>	<b>-6,973,299</b>	<b>-4,305,366</b>
Net financial income/expense	-280,137	789,216	476,921	85,325	64,475
<b>Total profit/loss, before taxes</b>	<b>-43,922,885</b>	<b>-35,614,623</b>	<b>-16,175,036</b>	<b>-6,887,974</b>	<b>-4,240,891</b>
Income taxes	-	-	-	-	-
<b>Profit/loss for the period</b>	<b>-43,922,885</b>	<b>-35,614,623</b>	<b>-16,175,036</b>	<b>-6,887,974</b>	<b>-4,240,891</b>

SUMMARY BALANCE SHEET	30/06/2016	30/06/2015	30/06/2014	30/06/2013	30/06/2012
Subscribed capital unpaid	16,687,902	-	-	-	-
Tangible assets	180,793	263,507	347,313	95,184	57,206
Financial assets	1,000	1,000	1,000	1,000	1,000
Current receivables	7,927,590	2,604,317	1,346,131	992,214	270,035
Investments	9,493,383	35,426,626	-	-	-
Cash and cash equivalents	119,948,858	32,738,441	107,840,568	25,607,241	5,750,558
<b>Assets</b>	<b>154,239,526</b>	<b>71,033,891</b>	<b>109,535,012</b>	<b>26,695,640</b>	<b>6,078,799</b>
Shareholders' Equity	139,179,970	64,626,697	100,241,320	24,604,113	4,431,491
Long-term liabilities	850,000	850,000	850,000	850,000	850,000
Current liabilities	14,209,556	5,557,194	8,443,692	1,241,527	797,309
<b>Total shareholders' equity and liabilities</b>	<b>154,239,526</b>	<b>71,033,891</b>	<b>109,535,012</b>	<b>26,695,640</b>	<b>6,078,800</b>

SUMMARY CASH FLOW STATEMENT	2015/2016	2014/2015	2013/2014	2012/2013	2011/2012
Cash flow from operating activities	-40,228,602	-40,102,127	-9,280,851	-7,146,028	-4,845,068
Cash flow from investment activities	25,650,763	-35,000,000	-298,065	-57,886	-57,579
Cash flow from financing activities	101,788,256	-	91,812,243	27,060,597	6,336,000
Change in cash and cash equivalents	87,210,417	-75,102,127	82,233,327	19,856,683	1,433,353
Cash and cash equivalents at the beginning of the period	32,738,441	107,840,568	25,607,241	5,750,558	4,317,205
<b>Cash and cash equivalents at the end of the period</b>	<b>119,948,858</b>	<b>32,738,441</b>	<b>107,840,568</b>	<b>25,607,241</b>	<b>5,750,558</b>

KEY RATIOS	30/06/2016	30/06/2015	30/06/2014	30/06/2013	30/06/2012
Liquidity ratio (%)	967%	1,273%	1,293%	2,142%	755%
Equity ratio (%)	90%	91%	92%	92%	73%
Dividends	-	-	-	-	-

## Definition of Financial Terms

**Liquidity ratio:** Liquidity ratio: Current assets divided by current liabilities

**Equity ratio:** Equity ratio: Shareholders' equity as a percentage of total assets

# Statement of Comprehensive Income, Summary

AMOUNTS IN SEK	Note	01/07/2015 - 30/06/2016	01/07/2014 - 30/06/2015
Miscellaneous operating income		-	160,000
		-	160,000
<b>OPERATING EXPENSES</b>			
Other external costs	3, 4, 5	-33,377,951	-30,638,046
Personnel costs	5	-9,965,352	-5,776,020
Depreciation of tangible fixed assets	6	-82,714	-83,806
Other operating expenses		-216,731	-65,967
<b>Operating profit/loss</b>		<b>-43,642,748</b>	<b>-36,403,839</b>
<b>INCOME FROM FINANCIAL ITEMS</b>			
Interest income and similar items	7	19,677	813,037
Interest expense and similar items	8	-299,814	-23,821
<b>Profit/loss after financial items</b>		<b>-43,922,885</b>	<b>-35,614,623</b>
<b>TOTAL PROFIT/LOSS BEFORE TAXES</b>		<b>-43,922,885</b>	<b>-35,614,623</b>
Income tax expense on the year's net income	9	-	-
<b>PROFIT/LOSS FOR THE PERIOD</b>		<b>-43,922,885</b>	<b>-35,614,623</b>
The statement of total comprehensive income is consistent with the financial results for the period.			
Earnings per share, before and after dilution	10	-2.18	-1.78

# Summary Balance Sheet

AMOUNTS IN SEK	Note	30/06/2016	30/06/2015
<b>ASSETS</b>			
Subscribed capital unpaid		16,687,902	-
<b>FIXED ASSETS</b>			
<b>Tangible assets</b>			
Equipment	11	180,793	263,507
<b>Total tangible assets</b>		<b>180,793</b>	<b>263,507</b>
<b>Financial assets</b>			
Other securities held as fixed assets	12	1,000	1,000
<b>Total financial assets</b>		<b>1,000</b>	<b>1,000</b>
<b>TOTAL FIXED ASSETS</b>		<b>181,793</b>	<b>264,507</b>
<b>CURRENT ASSETS</b>			
<b>Current receivables</b>			
Tax credits and related receivables		101,285	-
Other receivables		3,640,900	1,232,222
Prepaid expenses and accrued income	13	4,185,405	1,372,095
<b>Total current receivables</b>		<b>7,927,590</b>	<b>2,604,317</b>
<b>Investments</b>	14	<b>9,493,383</b>	<b>35,426,626</b>
<b>Cash and bank balances</b>	15	<b>119,948,858</b>	<b>32,738,441</b>
<b>TOTAL CURRENT ASSETS</b>		<b>137,369,831</b>	<b>70,769,384</b>
<b>TOTAL ASSETS</b>		<b>154,239,526</b>	<b>71,033,891</b>



## Balance Sheet, cont'd

AMOUNTS IN SEK	Note	30/06/2016	30/06/2015
<b>TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES</b>			
<b>SHAREHOLDERS' EQUITY</b>			
<b>Restricted equity</b>			
Share capital		1,213,543	1,001,500
New share issues in progress		84,384	-
<b>Total restricted equity</b>		<b>1,297,927</b>	<b>1,001,500</b>
<b>Unrestricted equity</b>			
Share premium reserve		252,535,222	134,355,491
Retained earnings		-70,730,294	-35,115,671
Profit/loss for the period		-43,922,885	-35,614,623
<b>Total unrestricted equity</b>		<b>137,882,043</b>	<b>63,625,197</b>
<b>TOTAL SHAREHOLDER EQUITY</b>		<b>139,179,970</b>	<b>64,626,697</b>
<b>LIABILITIES</b>			
<b>Long-term liabilities</b>			
Other long-term liabilities	16	850,000	850,000
<b>Total long-term liabilities</b>		<b>850,000</b>	<b>850,000</b>
<b>Current liabilities</b>			
Accounts payable		5,043,606	2,453,352
Other liabilities		199,826	103,919
Accrued expenses and deferred income	17	8,966,124	2,999,923
<b>Total current liabilities</b>		<b>14,209,556</b>	<b>5,557,194</b>
<b>TOTAL LIABILITIES</b>		<b>15,059,556</b>	<b>6,407,194</b>
<b>TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES</b>		<b>154,239,526</b>	<b>71,033,891</b>
Pledged assets	15	565,537	465,478
Contingent liabilities		None	None

# Report on Changes in Shareholders' Equity, Summary

AMOUNTS IN SEK	Share capital	Share premium reserve	Retained earnings	Net profit/loss for the year	Total
Opening shareholders' equity 01/07/2014	1,001,500	134,355,491	-18,940,635	-16,175,036	100,241,320
Transfer of prior years' profit/loss			-16,175,036	16,175,036	
Profit/loss for the period				-35,614,623	-35,614,623
Shareholders' equity 30/06/2015	1,001,500	134,355,491	-35,115,671	-35,614,623	64,626,697
Opening shareholders' equity 01/07/2015	1,001,500	134,355,491	-35,115,671	-35,614,623	64,626,697
The issuance of new shares	212,043	93,347,075			93,559,118
Costs attributable to the new share issues		-12,211,744			-12,211,744
New share issues in progress	84,384	37,044,400			37,128,784
Transfer of prior years' profit/loss			-35,614,623	35,614,623	
Profit/loss for the period				-43,922,885	-43,922,885
Shareholders' equity 30/06/2016	1,297,927	252,535,222	-70,730,294	-43,922,885	139,179,970

# Summary Cash Flow Statement

AMOUNTS IN SEK	01/07/2015 – 30/06/2016	01/07/2014 – 30/06/2015
<b>OPERATING ACTIVITIES</b>		
Operating profit/loss before financial items	-43,642,748	-36,403,839
Depreciation, amortisation and other non-cash items	82,714	83,806
Interest income received	19,677	386,411
Interest expense paid	-17,334	-23,821
<b>Cash flow from operating activities before changes in working capital</b>	<b>-43,557,691</b>	<b>-35,957,443</b>
Increase/decrease in other current term receivables	-5,323,273	-1,258,186
Increase/decrease in accounts payable	2,590,254	1,430,468
Increase/decrease in other short-term liabilities	6,062,108	-4,316,966
<b>Changes in working capital</b>	<b>3,329,089</b>	<b>-4,144,684</b>
<b>CASH FLOW FROM OPERATING ACTIVITIES</b>	<b>-40,228,602</b>	<b>-40,102,127</b>
<b>INVESTMENT ACTIVITIES</b>		
Acquisition of short term investments	-	-35,000,000
Sale of investments	25,650,763	-
<b>CASH FLOW FROM INVESTMENT ACTIVITIES</b>	<b>25,650,763</b>	<b>-35,000,000</b>
<b>FINANCING ACTIVITIES</b>		
The issuance of new shares	114,000,000	-
Share issue costs	-12,211,744	-
<b>CASH FLOW FROM FINANCING ACTIVITIES</b>	<b>101,788,256</b>	<b>-</b>
Cash flow for the year	87,210,417	-75,102,127
Cash and cash equivalents at the beginning of the period	32,738,441	107,840,568
<b>CASH AND CASH EQUIVALENTS AT THE END OF THE PERIOD</b>	<b>119,948,858</b>	<b>32,738,441</b>

# Notes

All amounts are in SEK, unless specified otherwise. Figures in parentheses refer to the previous year.

## NOTE 1 – ACCOUNTING POLICIES AND VALUATION PRINCIPLES

The annual report and accompanying financial statements have been prepared in accordance with the Swedish Annual Accounts Act and pursuant to the Recommendation of Swedish Financial Reporting Board, RFR 2 Accounting for Legal Entities. RFR 2 states that in its annual accounts the parent company must apply International Financial Reporting Standards (IFRS) as adopted by the EU, to the extent possible within the framework of the Swedish Annual Accounts Act and the Act on Safeguarding of Pension Commitments, and taking the relationship between accounting and taxation into regard. The Recommendation stipulates which exceptions and additions are required in relation to IFRS.

### Translation of foreign currency

Transactions in foreign currency are translated at the exchange rates applicable on the transaction date.

Receivables and liabilities in foreign currencies have been translated at the closing day rate. Exchange gains and losses on operating receivables and liabilities are included in operating profit/loss. Gains and losses on financial receivables and liabilities are reported as financial items.

### Recognition of revenue

Subsidies received are posted as revenue as well as under Miscellaneous Operating Income.

### Expenditures for research and development

The Company's expenditures on research and development are expensed as they arise.

### Leasing

All leasing agreements are reported as operational leasing agreements, which means that the leasing fees are distributed on a linear basis over the term of the lease.

### Taxes

Deferred tax assets relating to unutilised losses carried forward and deductible temporary differences are recognised only to the extent that it is probable that these will be able to be utilised against future taxable profits. As there is some uncertainty concerning when the Company's deductible deficiencies (tax loss carryforwards) may be able to be used for offsetting against taxable profits, deferred tax assets relating to deductible deficiencies are not recognised at any value.

### Tangible fixed assets

Tangible fixed assets are valued at their acquisition value with a deduction for accumulated depreciation. Tangible fixed assets are amortised on a linear basis over their expected useful life.

*Planned depreciation is taken as follows:*

Equipment	5 years
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### Financial instruments

A financial instrument is any form of contract that gives rise to a financial asset, a financial liability, or an equity instrument in another company. For Immunicum, this includes the cash and cash equivalents, short-term investments, other receivables, accounts payables, other outstanding debts and loans payable. Cash and cash equivalents consist of bank deposits. Short-term investments consist of investments in mutual funds.

### Accounting for financial instruments

A financial asset or a financial liability is recognised in the balance sheet when the Company becomes a party in accordance with the contractual provisions of the instrument. Liabilities are recognised once the

counterparty has presented them and there is a contractual obligation to pay, even if an invoice has not yet been received. Accounts payable are recognised when the invoice has been received. A financial asset is removed from the balance sheet when the contractual rights have been settled, have expired/lapsed, or the Company has lost control over them. The same applies for a part of a financial asset. A financial liability is removed from the balance sheet when the obligation in the contract is fulfilled or it becomes extinguished in another way. The same applies for a part of a financial liability. Acquisitions and sales of financial assets are recognised on the "trade date," i.e. the date the Company entered into the transaction, committing to purchase or sell the asset.

#### ***Classification and measurement of financial instruments***

The classification depends on the purpose(s) behind the acquisition of the financial instrument.

#### **OTHER RECEIVABLES**

Receivables are reported as current assets except for items with a due date of more than 12 months after the close of the reporting period, which are classified as fixed assets. Accounts receivable are recognised at the amount expected to be paid to the Company after deduction for any doubtful receivables as individually assessed.

#### **INVESTMENTS**

Securities acquired with intention of being held short term are initially recognised at acquisition cost and in subsequent valuations in accordance with the lowest cost principle at the lower of acquisition cost or market value. With valuation at the lowest cost principle, short-term investments are deemed to be a part of portfolio of securities and the valuation principle is applied to the portfolio as a whole.

#### **LOAN LIABILITIES AND AMOUNTS PAYABLE TO SUPPLIERS**

Loan liabilities and amounts payable to suppliers are initially recognised at acquisition value after deduction of transaction costs. If the carrying amount differs from the amount to be repaid at maturity, the difference is amortised as an interest expense over the term of the loan using the instrument's effective interest rate. In this way, the carrying amount and the amount to be repaid on the maturity date corresponds.

#### ***Offsetting of a financial asset and a financial liability***

A financial asset and a financial liability are offset and recognised with a net amount in the balance sheet only when a legally enforceable right exists and when a settlement with a net amount is regarded to occur or when a contemporaneous sale of the asset and settlement of the liability it relates to occurs.

## **NOTE 2 - FINANCIAL RISKS**

### **Foreign exchange exposure**

Immunicum's foreign exchange exposure increases in pace with as the development projects progress in the value chain and the costs for services in connection with clinical trials increases. These services are partially carried out outside of Sweden and paid for in foreign currency. The Company has not made use of currency hedging so far, but will evaluate the need of such as its business develops further and expands.

### **Interest rate exposure**

Immunicum's exposure to market risk for changes in interest rates relates to bank deposits and investments in interest-bearing securities.

### **Liquidity risk**

Liquidity risks are limited via liquidity planning and placement of funds in financial instruments with high liquidity.



## NOTE 3 – OPERATING LEASES

AMOUNTS IN SEK	01/07/2015 – 30/06/2016	01/07/2014 – 30/06/2015
The Company's leasing contracts relate in their entirety to the rental of office premises where its business operations are conducted. Leasing costs for the year concerning the rental of offices amounted to	628,800	628,800
<b>Future lease payments with respect to non-cancellable lease agreements amount to the following</b>		
Within one year	628,800	628,800
Later than one year, but within five years	1,048,000	1,676,800
Later than five years	-	-
<b>Total</b>	<b>1,676,800</b>	<b>2,305,600</b>

## NOTE 4 – REMUNERATION TO THE AUDITORS

AMOUNTS IN SEK	01/07/2015 – 30/06/2016	01/07/2014 – 30/06/2015
<b>ÖHRLINGS PRICEWATERHOUSECOOPERS</b>		
Audit assignment	160,000	155,000
Auditing activities over and above the audit assignment	90,000	125,000
Tax consulting	35,500	-
<b>Total</b>	<b>285,500</b>	<b>280,000</b>

What is meant by audit auditing assignment refers to review of the Annual Report and financial accounts plus the management by the Board of Directors and the CEO. Auditing activities over and above the auditing assignment relate i.a. to the review of the interim reports.

## NOTE 5 – INFORMATION ABOUT THE NUMBER OF EMPLOYEES, SALARIES, OTHER REMUNERATION AND SOCIAL INSURANCE EXPENSES

AMOUNTS IN SEK	01/07/2015 – 30/06/2016	01/07/2014 – 30/06/2015
<b>Number of employees (annualised average)</b>		
Men	3	3
Women	4	2
<b>Total</b>	<b>7</b>	<b>5</b>
<b>Gender breakdown of Members of the Board and senior management</b>		
Board Members	5	5
of which, men	4	4
CEO, and others in senior management	4	4
of which, men	2	4
<b>Salaries, other remuneration and social insurance expenses</b>		
Salaries and other remuneration	6,436,960	4,045,553
Social insurance expenses	2,698,000	1,928,929
(of which, pension costs)	(1,035,720)	(863,249)
<b>Total</b>	<b>9,134,960</b>	<b>5,974,482</b>
<b>(of which, pension costs)</b>	<b>(1,035,720)</b>	<b>(863,249)</b>

## NOTE 5 - CONT'D

AMOUNTS IN SEK	01/07/2015 – 30/06/2016	01/07/2014 – 30/06/2015
<b>Salaries and other remuneration distributed between Board Members, senior management, and other employees</b>		
Board Members and senior management	4,416,201	3,261,881
Other employees	2,020,759	783,672
<b>Total</b>	<b>6,436,960</b>	<b>4,045,553</b>
<b>Remuneration and other benefits provided to Board Members</b>		
Agneta E, COB	270,000	150,000
Sven Andréasson (Board Member until the 2015 AGM)	-	75,000
Bengt Furberg	75,000	75,000
Martin Lindström	75,000	75,000
Magnus Nilsson	75,000	75,000
Magnus Persson (Board Member until the 2015 AGM)	75,000	-
<b>The CEO's remuneration and employment benefits</b>		
Salary	1,085,300	1,010,460
Bonuses	100,000	74,250
Pension costs	403,628	375,203
<b>Remuneration and employment benefits to other senior management (three individuals)</b>		
Salaries	2,572,566	1,617,546
Bonuses	88,335	109,625
Pension costs	532,783	448,367

### **Pensions**

The Company has only defined contribution pension plans. The Company does not have any other pension commitments.

### **Remuneration to the Members of the Board of Directors and individuals in senior management in the Company**

The Board Fees (directors' emoluments) to the board members Agneta Edberg, Magnus Nilsson, Magnus Persson and Sven Andréasson have been paid to their respective companies. During the financial year, consulting fees were paid to the board member Bengt Furberg was paid SEK 45,000 (159,000) and consulting fees were paid to Per-Olof Gunnesson in the amount of SEK 161,700 (563,250) for his work as the Company's CFO. The determination of the amounts for both of these contributions to the Company have occurred on commercial terms.

### **Severance pay**

For the Company's CEO and CFO, the mutual period of notice is six months. For others in senior management, the mutual period of notice is three months. No agreements have been entered into with regards to severance pay.

### **Bonuses**

In addition to a fixed monthly salary, the CEO and others in senior management receive variable compensation conditioned on the achievement of specific performance goals. The variable part for the CEO may amount to the equivalent of a maximum of three times the ordinary monthly salary, and for others in senior management a maximum of one monthly salary.

### **Preparation and decision-making process**

The remuneration paid to the Chief Executive Officer is a matter decided by the Board of Directors, but the preparatory work for this decision is undertaken by the Chair of the Board. Remuneration to others in senior management is determined by the Chief Executive Officer in consultation with the COB, based on external labour market data and amounts.

## NOTE 6 - DEPRECIATION OF TANGIBLE ASSETS

AMOUNTS IN SEK	01/07/2015 - 30/06/2016	01/07/2014 - 30/06/2015
Equipment	82,714	83,806
<b>Total</b>	<b>82,714</b>	<b>83,806</b>

## NOTE 7 - INTEREST INCOME AND SIMILAR ITEMS

AMOUNTS IN SEK	01/07/2015 - 30/06/2016	01/07/2014 - 30/06/2015
Gains upon the liquidation of short-term investments	-	426,626
Interest income	19,677	386,411
<b>Total</b>	<b>19,677</b>	<b>813,037</b>

## NOTE 8 - INTEREST EXPENSE AND SIMILAR ITEMS

AMOUNTS IN SEK	01/07/2015 - 30/06/2016	01/07/2014 - 30/06/2015
Losses realised upon the liquidation of short-term investments	-249,237	-
Write-downs relating to short-term investments	-33,243	-
Interest expenses	-17,334	-23,821
<b>Total</b>	<b>-299,814</b>	<b>-23,821</b>

## NOTE 9 - INCOME TAX EXPENSE ON THE YEAR'S NET INCOME

AMOUNTS IN SEK	01/07/2015 - 30/06/2016	01/07/2014 - 30/06/2015
Current taxes	-	-
Deferred taxes	-	-
<b>Recognised tax expense on the year's net income</b>	<b>-</b>	<b>-</b>

### The difference between recognised tax expense and an estimated tax expense based on the current tax rate:

Total profit/loss, before taxes	-43,922,885	-35,614,623
Difference between reported tax expense and an estimated tax expense based on the current applicable tax rate	9,663,035	7,835,217
Tax effect of non-deductible expenses	-14,517	-2,755
Tax effect of non-taxable income	124	145
Tax effect of a deductible deficiency for which no deferred tax assets have been taken into account	-9,648,642	-7,832,607
<b>Tax expense</b>	<b>-</b>	<b>-</b>

The current tax rate is 22% (22%)

Unutilised deductible deficiency for which no deferred tax asset has been recognised	131,988,149	75,918,942
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## NOTE 10 - EARNINGS PER SHARE

AMOUNTS IN SEK	01/07/2015 - 30/06/2016	01/07/2014 - 30/06/2015
<b>Earnings per share, before dilution</b>		
Net profit/loss for the year	-43,922,885	-35,614,623
Average number of shares outstanding	20,169,695	20,030,000
<b>Earnings per share, before dilution, SEK</b>	<b>-2.18</b>	<b>-1.78</b>
<b>Earnings per share, after dilution</b>		
Net profit/loss for the year	-43,922,885	-35,614,623
Average number of shares outstanding	20,169,695	20,030,000
<b>Earnings per share, after dilution, SEK</b>	<b>-2.18</b>	<b>-1.78</b>

Earnings per share before dilution is based on the financial results for the year and the weighted average of the number of shares outstanding.

Earnings per share after dilution is based on the financial results for the year and the weighted average of the number of shares outstanding plus the dilutive effect of potential shares. This dilution effect has not been taken into account when a conversion would decrease the loss per share.

## NOTE 11 - EQUIPMENT

AMOUNTS IN SEK	30/06/2016	30/06/2015
Acquisition values brought forward	426,605	426,605
Acquisitions during the year	-	-
<b>Opening acquisition values</b>	<b>426,605</b>	<b>426,605</b>
Depreciation brought forward	-163,098	-79,292
Depreciation for the year according to plan	-82,714	-83,806
<b>Closing accumulated depreciation</b>	<b>-245,812</b>	<b>-163,098</b>
<b>CLOSING BOOK VALUE</b>	<b>180,793</b>	<b>263,507</b>

## NOTE 12 - OTHER LONG-TERM SECURITIES HELD AS FIXED ASSETS

AMOUNTS IN SEK	30/06/2016	30/06/2015
Holdings of shares of LFF Service AB	1,000	1,000
	<b>1,000</b>	<b>1,000</b>

## NOTE 13 - PREPAID EXPENSES AND ACCRUED INCOME

AMOUNTS IN SEK	30/06/2016	30/06/2015
Prepaid expenses relating to preclinical development/clinical trials	3,521,884	788,902
Prepaid insurance premiums	333,184	135,621
Prepaid rents	188,423	188,100
Accrued interest income	8,634	51,690
Other prepaid expenses	133,280	207,782
<b>Total</b>	<b>4,185,405</b>	<b>1,372,095</b>

## NOTE 14 - INVESTMENTS

The Company has placed funds in the Handelsbanken Multi Asset L (low risk) Fund. This fund invests in Swedish fixed income funds, Nordic and global equity funds, hedge funds and commodity funds.

## NOTE 15 - CASH AND BANK BALANCES

The Company has a contractual credit limit for Business Card amounting to SEK 300,000 (200,000). The Company has provided security for this credit and for a bank guarantee of SEK 314,400 (314,400) via a general pledge of bank deposits in the amount of SEK 565,537 (465,478).

## NOTE 16 - OTHER NON-CURRENT LIABILITIES

The Company has previously received financing in the form of conditional credits from Region Västra Götaland amounting to SEK 850,000. These terms of repayment for these loans are 5 per cent of potential future income, with the addition of interest at the reference rate set by the Swedish National Bank for the calendar half-year in question, plus an additional two percentage points.

## NOTE 17 - ACCRUED EXPENSES AND DEFERRED INCOME

AMOUNTS IN SEK	30/06/2016	30/06/2015
Deferred new share issue costs	5,042,730	-
Accrued expenses relating to preclinical development/clinical trials	1,958,350	2,093,678
Accrued personnel-related costs	1,447,771	538,128
Other accrued expenses	517,273	368,117
<b>Total</b>	<b>8,966,124</b>	<b>2,999,923</b>



# Signatures

GOTHENBURG, 29 SEPTEMBER 2016

Agneta Edberg

CHAIR OF THE BOARD (COB)

Bengt Furberg

MEMBER OF THE BOARD

Martin Lindström

MEMBER OF THE BOARD OF  
DIRECTORS

Magnus Nilsson

MEMBER OF THE BOARD OF  
DIRECTORS

Magnus Persson

MEMBER OF THE BOARD OF  
DIRECTORS

Jamal El-Mosleh

CEO

Our Auditor's Report has been submitted on 29 September 2016

Öhrlings PricewaterhouseCoopers AB

Birgitta Granquist

*Auktoriserad Revisor/Authorised Public Accountant,  
Auditor in Charge*

# Auditor's Report

TO THE ANNUAL MEETING OF THE SHAREHOLDERS OF IMMUNICUM AB, COMPANY  
REGISTRATION NUMBER (CRN) 556629-1786

## Report on the annual accounts

We have audited the annual accounts of Immunicum AB (publ) for the 1 July 2015 – 30 June 2016 financial year. The annual accounts of the company are included in the printed version of this document on pages 38-57.

### *The responsibilities of the Board of Directors and the Chief Executive Officer for the annual accounts*

The Board of Directors and the Chief Executive Officer are responsible for the preparation and a fair presentation of these annual accounts in accordance with the Annual Accounts Act, and for such internal control as the Board of Directors and the Chief Executive Officer determine is necessary to enable the preparation of annual accounts that are free from material misstatement, whether due to irregularities or error.

### *The Auditor's responsibility*

Our responsibility is to express an opinion on these annual accounts based on our audit. We conducted our audit in accordance with the International Standards on Auditing and generally accepted auditing standards in Sweden. Those standards require that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the annual accounts are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the annual accounts. The procedures selected are dependent upon the auditor's judgment, including the assessment of the risks of material misstatement in the annual accounts, whether due to irregularities or error. In making those risk assessments, the auditor considers the internal controls relevant to the company's preparation and fair presentation of the annual accounts, in order to design audit procedures that are appropriate under the particular circumstances, but not for the purpose of expressing an opinion on the effectiveness of the company's internal control. An audit also includes evaluating the appropriateness of the accounting policies used and the reasonableness of the accounting estimates made by the Board of Directors and the Chief Executive Officer, as well as evaluating the overall presentation of the annual accounts.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

### *Opinion*

According to our assessment, the Annual Report and accompanying financial statements have been prepared in accordance with the Annual Accounts Act and present fairly, in all material respects, the financial position of Immunicum AB as of 30 June 2016 and its financial performance and its cash flows for the year then ended in accordance with the Annual Accounts Act. The statutory administration report is consistent with the other parts of the annual accounts.

We therefore recommend that the Annual General Meeting of shareholders adopt the Profit & Loss Statement and Balance Sheet.

## Report on other legal and regulatory requirements

In addition to our audit of the Annual Report and accompanying financial statements, we have examined the proposed appropriations of the company's profit or loss and the administration of the Board of Directors and the Chief Executive Officer of Immunicum AB for the 1 July 2015 – 30 June 2016 financial year.

### *The Responsibilities of the Board of Directors and the Chief Executive Officer*

The Board of Directors is responsible for the proposal for appropriations of the company's profit or loss, and the Board of Directors and the Chief Executive Officer are responsible for administration under the Companies Act.

### *The Auditor's responsibility*

Our responsibility is to express an opinion with reasonable assurance on the proposed appropriations of the company's profits or losses, and on the administration of the company, based on our audit. We have conducted the audit in accordance with generally accepted auditing standards in Sweden.

As a basis for our opinion on the Board of Directors' proposal for the appropriations of the company's profits or losses, we examined whether the proposal is in accordance with the Companies Act.

As a basis for our opinion concerning discharge from liability, in addition to our audit of the annual accounts, we examined the significant decisions, actions taken and circumstances of the company in order to determine whether any member of the Board of Directors or the Chief Executive Officer has a liability for compensation to the company. We also examined whether any member of the Board of Directors or the Chief Executive Officer has in any other manner acted in contravention of the Companies Act or the Annual Accounts Act, or the company's Articles of Association.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

#### *Opinion*

We recommend to the Annual General Meeting of shareholders that the loss be appropriated in accordance with the proposal in the statutory administration report and that the Members of the Board of Directors and the Chief Executive Officer be granted a discharge of liability for the financial year.

Gothenburg, 29 September 2016

*Öhrlings PricewaterhouseCoopers AB*

Birgitta Granquist

*Auktoriserad Revisor/Authorised Public Accountant*

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## Articles of Association

### § 1 Company

The name of the company is IMMUNICUM AB (publ). The company is a public company (publ).

### § 2 Registered office

The Board of Directors is to have its registered office in the municipality of Gothenburg, Västra Götaland County.

### § 3 Business purposes

The Company is to engage in research, development, marketing and sale of pharmaceutical drugs and other medicinal products, and to engage in related activities.

### § 4 Share capital

The Company's share capital is to be not less than SEK 500,000 and SEK maximum 2,000,000.

### § 5 Number of shares

The number of shares will be a minimum of 10,000,000 shares and a maximum of 40,000,000 shares.

### § 6 The Board of Directors

The Board of Directors is to consist of not less than three and not more than eight members, with zero to three alternate members. The Members of the Board of Directors are to be elected annually at the Annual General Meeting for a term ending at the conclusion of the next Annual General Meeting.

### § 7 Auditors

For the purpose of examining the Company's Annual Report and accompanying financial accounts, as well as the Board of Directors' and the Chief Executive Officer's management of the Company, an Auditor is to be appointed at the Annual General Meeting for the period until the conclusion of the next Annual General Meeting.

### § 8 Notice

Notice for the General Meeting of Shareholders is to take place by placing an announcement in the Post och Inrikes Tidningar (the Swedish Official Gazette), plus via that the notice for the Meeting is posted on the Company's website. At the same time as the notice for the Meeting occurs, the Company is to inform the general public that the notice for the Meeting has occurred, via placing an announcement in Dagens Industri. Notice of convening the Annual General Meeting (AGM) and Extraordinary General Meeting of Shareholders (EGM) at which issues relating to amendments to the Articles of Association are to be dealt with must be issued not earlier than six weeks and not later than four weeks before the Meeting. Notice of convening other than an Extraordinary General Meeting of Shareholders is to be issued not earlier than six weeks and not later than three weeks prior to the Meeting.

### § 9 Notice of intention to attend the Annual General Meeting

Such shareholders who are listed in the share register, as prescribed in Chapter 7, §28, 3. of the Swedish Companies Act, and who have notified the Company not later than the date specified in the notice for the Meeting, shall have the right to participate in the Meeting. This day may not be on Sunday, any other public holiday, Saturday, Midsummer Eve, Christmas Eve or New Year's Eve, and may not fall earlier than the fifth weekday prior to the Meeting.

### § 10 Matters taken up at the Annual General Meetings

At the Annual General Meeting, the following matters are to be dealt with:

1. Election of a chairperson to chair the meeting.
2. Preparation and approval of the voting list.
3. Presentation and approval of the agenda.
4. Appointment of one or two persons to verify the minutes.
5. Determination of whether the AGM has been duly convened.
6. Presentation of the Annual Report and the Auditor's Report, and where relevant the consolidated financial statements and Auditor's report for the group.

### 7. Decisions concerning

- a) the adoption of the Profit & Loss Statement and the Balance Sheet, and where relevant the Consolidated Profit & Loss and Consolidated Balance Sheet.
  - b) the appropriation of the Company's profit or loss in accordance with the adopted Balance Sheet.
  - c) discharge from liability vis-à-vis the Company for the Members of the Board of Directors and the Chief Executive Officer.
8. Determination of remuneration and other fees for the Members of the Board of Directors and to the Auditor.
  9. Election of members to the Board of Directors and appointment of Auditor(s) and any alternate auditors.
  10. Other matters that are to be dealt with at the Annual General Meeting pursuant to the Swedish Companies Act or the Company's Articles of Association.

### § 11 Financial Year

The financial year of the Company is to be 1 July – 30 June.

### § 12 Central Securities Depository Clause

The Company's shares are to be registered with a CSD register in accordance with the Swedish Financial Instruments Accounts Act (SFS 1998:1479).

# *Annual General Meeting and Publication Dates\**

26 October 2016

**IMMUNICUM AB's ANNUAL  
GENERAL MEETING**

18 November 2016

**INTERIM REPORT Q1**

17 February 2017

**INTERIM REPORT Q2**

19 March 2017

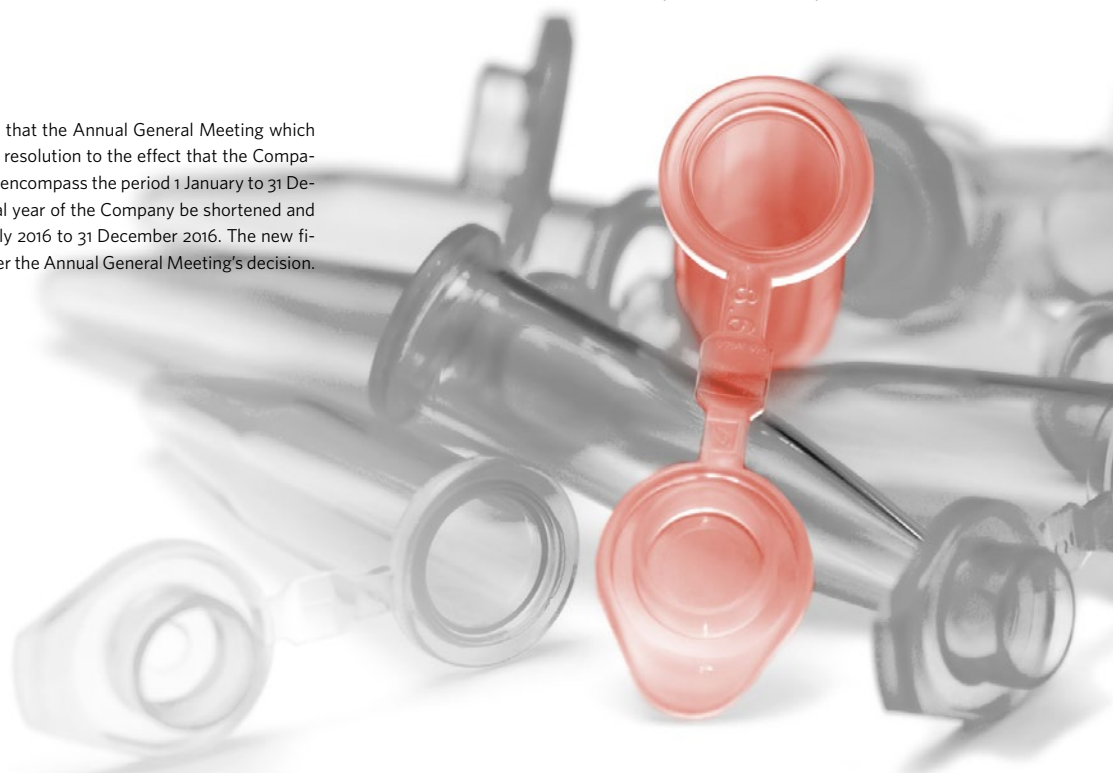
**INTERIM REPORT Q3**

18 August 2017

**YEAR-END REPORT 16/17**

*The reports will be available on the [www.immunicum.com](http://www.immunicum.com) website as of the date of release.*

The Board of Directors has proposed that the Annual General Meeting which will be held 26 October 2016 adopt a resolution to the effect that the Company's financial year will be modified to encompass the period 1 January to 31 December, and that the present financial year of the Company be shortened and thus encompass the period from 1 July 2016 to 31 December 2016. The new financial calendar will be published after the Annual General Meeting's decision.





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