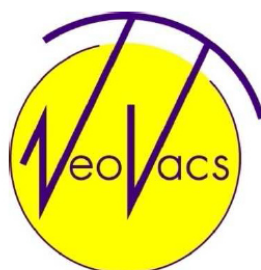




## **Research Report (Initial Coverage)**



**Innovative approach to treating incurable autoimmune diseases; short-term potentials possible with fast-track approval**

**Target price: EUR 2.90**

**Rating: BUY**

### **IMPORTANT NOTE:**

**Please take note of the disclaimer/risk warning, as well as the disclosure of potential conflicts of interest as required by section 34b of the Securities Trading Act (WpHG) from page 18**

## Neovacs S.A. \*5a,5b,11

### BUY

Price Target: 2.90

current price: 0.86  
17/6/2016 / FRA / closing price  
currency: EUR

### Key date:

ISIN: FR0004032746  
WKN: A1CVKR  
Ticker symbol: 0LW  
Number of shares<sup>3</sup>: 32,056  
Marketcap<sup>3</sup>: 27,664  
EnterpriseValue<sup>3</sup>: 22,651  
<sup>3</sup> in m / in EURm  
Freefloat: 64 %

Transparency Level:  
Freiverkehr  
Market Segment:  
Open Market  
Accounting Standard:  
IFRS

Financial year-end: 31/12

Designated Sponsor:  
ICF Bank AG

### Analyst:

Cosmin Filker  
filker@gbc-ag.de

Felix Gode, CFA  
gode@gbc-ag.de

\* catalogue of potential conflicts of interests on page 19

### Company Profile

Sector: Biotechnology

Focus:

Founded in: 1993

Headquarter: Paris

Executive Board: Miguel Sieler (CEO)



Neovacs is a biotechnology company, which specialises in a technology platform called "Kinoid" for active immunotherapy in the area of autoimmune and inflammatory diseases. On the basis of the company's own technology for the introduction of a polyclonal immune response (protected by six patent families until at least 2032). Neovacs focuses its development activities on active immunotherapy with IFN $\alpha$  kinoid, which is being developed for the medical indications SLE (systemic lupus erythematosus) and DM (dermatomyositis). Neovacs also conducts preclinical trials with IFN $\alpha$  kinoid for certain chronic viral infections, VEGF kinoid for age-related macular degeneration (AMD) and solid tumours, and IL-4 kinoids to treat allergies. The goal of the Kinoid approach is to give patients access to safe treatments which have a lasting positive impact on these chronic diseases.

P&L in EURm	2015	2016e	2017e	2018e	2019e	2020e	2021e	2022e	2023e
Sales	1.18	0.00	0.00	5.11	2.66	18.08	128.30	190.54	253.24
EBIT	-11.28	-7.26	-8.57	-11.77	-19.09	-5.48	81.25	124.09	167.06
Net Profit	-4.68	-7.36	-8.67	-11.87	-19.19	-5.58	81.15	123.99	116.84

in €									
Earnings per share	-0.15	-0.21	-0.21	-0.26	-0.36	-0.10	1.41	2.15	2.02

Ratios									
EV/Sales	19.18	n.def.	n.def.	4.44	8.52	1.25	0.18	0.12	0.09
EV/EBIT	neg.	neg.	neg.	neg.	neg.	neg.	0.28	0.18	0.14
P/E	neg.	neg.	neg.	neg.	neg.	neg.	0.34	0.22	0.24

### Financial Schedule


### \*\*last research published by GBC:

Date: publication / price target in € / rating


\*\* the research reports can be found on our website [www.gbc-ag.de](http://www.gbc-ag.de) or can be requested at GBC AG, Halderstr. 27, D86150 Augsburg

## EXECUTIVE SUMMARY

- Neovacs S.A., a biotechnology company based in France, focuses on the development of what are known as kinoids, which are used for the treatment of autoimmune and inflammatory diseases. Within the Kinoid platform, which was developed within the company, interferon alpha kinoid (IFN $\alpha$  kinoid) has progressed the furthest towards clinical approval for the two indications SLE (systemic lupus erythematosus) and DM (dermatomyositis). Further products based on Kinoid technology which could address autoimmune diseases are currently in preclinical development and represent possible upside potential.
- It is assumed that both autoimmune diseases DM and SLE are caused by the dysregulation of the cytokine IFN $\alpha$ . Neovacs' technology addresses IFN $\alpha$  with the aim of neutralising the overproduction of IFN $\alpha$ , thereby bringing the immune system back into balance. The Neovacs kinoid can be used to trigger a highly targeted immune response without the addition of foreign antibodies. High effectiveness and the absence of rejection reactions (with no loss of efficacy) have both been observed in previous studies. With regard to Belimumab (trade name Benlysta<sup>®</sup>), which is currently the only approved drug for the treatment of SLE, doubts have been cast about the additional benefit of this comparatively expensive active substance. Life-threatening side effects have also been observed.
- The Neovacs drug is currently being researched in a clinical study IIb (SLE) in 19 countries (Europe, Asia, Latin America and the USA) with 178 patents. We expect the first results to be available in the summer of 2017. In parallel, a licensing agreement has also been concluded with Chong Kun Dang (CKD) Pharmaceutical Corp. for the South Korean market. There is a high chance that SLE will be categorised as a rare disease (orphan disease) in South Korea, which would enable faster marketing approval and omit the lengthy periods of time and high costs associated with trial phase III. The indication DM may achieve global orphan disease status, which is characterised by a significantly lower prevalence, although we expect faster global marketing authorisation here. A clinical phase I/IIa trial is expected to start here in 2016.
- We expect marketing revenues to be generated for the first time in 2018 (SLE - South Korea). While we anticipate that the marketing approval for the indication DM will be granted in 2020, global marketing for the indication SLE is likely to start in the 2022 financial year. Initially, we have conservatively assumed a small market share. Fundamentally, the IFN $\alpha$  kinoid should generate a lot of attention and, therefore, high potential demand, particularly considering the lack of medication available for the incurable diseases SLE and DM.
- **Within the scope of the DCF valuation model, we calculated a fair value of €2.90 per share and, on the basis of the current price level of €0.86, have issued a BUY rating. We have taken the existing marketing risk of phase II products into account with a valuation allowance of 77.2%. During a meta-analysis, it was noted that 77.2% of drugs in phase II studies do not achieve market approval. Once clinical progress is recorded, we will reduce the risk discount correspondingly.**

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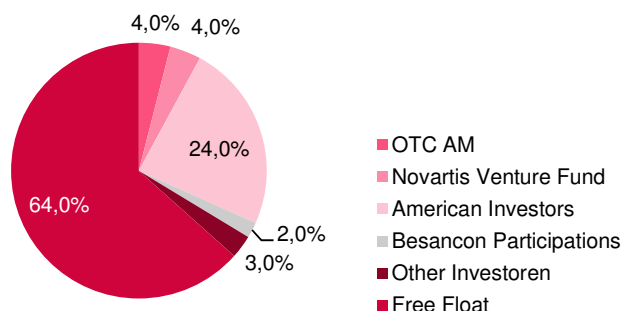
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## COMPANY

### Shareholder Structure

Shareholder	in %
OTC AM	4%
Novartis Venture Fund	4%
American Investors	24%
Besancon Participations	2%
Other Investors	3%
Free Float	64%







Source: Neovacs S.A.; GBC AG



### History of the company

Year	Event
1993	Foundation of Neovacs
2003	<ul style="list-style-type: none"> <li>- Preclinical development of the first anti-TNF therapeutic vaccine begins.</li> <li>- Truffle Capital becomes the major shareholder of Neovacs.</li> </ul>
2007	Neovacs concludes a "Series A" funding agreement with Truffle Capital, Novartis Venture Fund and OTC AM. Truffle Capital remains a major shareholder of the company.
2008	The TNF kinoid is tested on patients for the first time in a clinical I/II trial.
2010	<ul style="list-style-type: none"> <li>- Primary listing of Neovacs on NYSE Alternext in Paris</li> <li>- The IFN<math>\alpha</math> kinoid IFN-K-001 is studied in a clinical trial phase I/II among patients with SLE (systemic lupus erythematosus).</li> </ul>
2011	<ul style="list-style-type: none"> <li>- During further rounds of financing (private placements within the scope of capital increases), total proceeds amount to €9.9 million in the 2011 financial year.</li> <li>- Presentation of the results of the clinical trial I/II of IFN<math>\alpha</math> in lupus patients. Good tolerability and a high immunological response are observed.</li> </ul>
2013	<ul style="list-style-type: none"> <li>- A total of €7.2 million is collected over the full year 2013 as part of further capital increases.</li> <li>- Miguel Sieler, a former board member of Bayer France, is appointed as the new CEO of Neovacs S.A.</li> <li>- New agreement with Kepler Cheuvreux regarding an equity line of credit</li> </ul>
2014	<ul style="list-style-type: none"> <li>- Entry into a strategic partnership with Pharmedartis for delivery of interferon alpha (IFN<math>\alpha</math>) for trial phase IIb in lupus patients</li> <li>- Expansion of equity line of credit with Kepler Cheuvreux up to €20.0 million</li> <li>- The end point is not achieved in the clinical trial phase IIb for the TNF kinoid in rheumatoid arthritis.</li> </ul>
2015	<ul style="list-style-type: none"> <li>- New product focus on the clinical development of IFN<math>\alpha</math></li> <li>- Cooperation with Stellar Biotechnologies, Inc. for the production of KLH (keyhole limpet hemocyanin), one of the main components for Neovacs' Kinoid technology</li> <li>- Expansion of IFN<math>\alpha</math> kinoid programme to include the therapeutic indication DM (dermatomyositis)</li> <li>- US investors subscribe a capital increase of €7.5 million.</li> <li>- Start of phase IIb trial of IFN<math>\alpha</math> kinoids for lupus</li> <li>- Strategic distribution partnership agreement with CKD Pharmaceutical Corp. for the South Korean market</li> </ul>
2016	<ul style="list-style-type: none"> <li>- Authorities grant approval for the phase IIb trial in South Korea</li> <li>- Equity line of credit in the amount of €5.0 million is agreed within the scope of the French public programme "Investments for the Future".</li> <li>- FDA grants approval for the phase IIb trial (SLE) in the US.</li> <li>- Joint venture agreement between Neovacs and Stellar Biotechnologies for the foundation of Neostell (ensuring KLH production)</li> <li>- Capital increase through the issue of 9.46 million new shares at a price of €0.85 per share (gross proceeds: €8.05 million)</li> </ul>

## Product pipeline

Product	pre-clinical	phase I	phase II	phase III
<b>IFN<math>\alpha</math>-Kinoid in SLE</b> (Europe, Latin America, Asia, USA)				
<b>IFN<math>\alpha</math>-Kinoid in DM</b> (EU)				
<b>IFN<math>\alpha</math>-Kinoid in diabetes type 1</b>				
<b>VEGF-Kinoid in AMD</b>				
<b>VEGF-Kinoid in solid tumors</b>				
<b>IL-4/IL-13 Kinoid in allergies</b>				

Source: Neovacs S.A.; GBC AG

Neovacs' proprietary Kinoid technology platform provides the basis for the heterogeneous product pipeline. The IFN $\alpha$  kinoid (interferon alpha kinoid) has progressed the furthest towards clinical approval for the two indications SLE (systemic lupus erythematosus) and DM (dermatomyositis) and is consequently Neovacs' most important product. Due to the mode of action of IFN $\alpha$  kinoid (IFN $\alpha$ -K), other autoimmune disease studies can also be addressed. For example, a study into type 1 diabetes is currently in the preclinical phase.

The VEGF (Vascular Endothelial Growth Factor) kinoid was developed for the treatment of solid tumours and AMD (age-related macular degeneration) on the same technological basis. As this is currently still in the preclinical stage, we will attach only secondary importance to this product and range of indications in the context of this study, and will, therefore, only deal with these perspectives as an additional upside potential.

## Indication systemic lupus erythematosus (SLE)

SLE is a systemic inflammatory rheumatic autoimmune disease which is heterogeneous and non-specific and is associated with a range of symptoms. For reasons which are currently still unknown, the body's immune system attacks various organs of the body, such as the skin, joints, kidneys, liver, heart, etc. The dysregulation of the immune system is typical of autoimmune diseases and causes an increased number of antibodies (ANA: antinuclear antibodies) which permanently damage the body's cells. Due to the systemic nature of the disease, it manifests itself in different forms, which range from mild skin rashes to multiple organ failure.

Butterfly-shaped redness on the cheeks and nose are typical for SLE patients, who also suffer from a concomitant sensitivity to UV radiation. Most patients also experience inflammation of joints, tendons and muscles. The frequent involvement of the kidneys (nephritis lupus) is a serious side effect which, if left untreated, can lead to a loss of kidney function and even to dialysis dependency.

#### Symptoms of SLE

Joint pain	85%
Non-specific symptoms	84%
Changes to the skin	81%
Kidney findings	77%
Arthritis	63%
Raynaud's syndrome	58%
Disease of the central nervous system	54%
Mucosal changes	54%
Gastrointestinal problems	47%

Source: Hettenkofer, Hans-Jürgen: *Rheumatologie*; GBC AG

#### Current treatment approach for SLE

A form of therapy comprehensively addressing the disease mechanism does not currently exist. In fact, existing SLE treatments, which are usually long-lasting, focus on the treatment of symptoms with the objective of reducing the immune activity to limit the progression of SLE. The drug therapy is divided into different groups of substances, in order of severity of the SLE disease.

##### Nonsteroidal anti-inflammatory drugs (NSAIDs)

This group of drugs has analgesic and anti-inflammatory effects. A prominent representative of this group is acetylsalicylic acid (aspirin). This demonstrates that NSAIDs are usually administered to patients with mild SLE, who are primarily affected by joint pain and fever.

In the case of long-term treatment with NSAIDs, there are potential side effects such as increased bleeding, changes in the gastric mucosa and gastric ulcers. There is also a risk of kidney damage, which is why the long-term treatment of lupus nephritis using NSAIDs is avoided.

##### Antimalarials

In the case of a more rapid progression of SLE, where treatment with NSAID drugs is no longer sufficient, antimalarials (chloroquine, hydroxychloroquine) can be administered to reduce disease activity and avoid relapses. SLE patients benefit in particular from improved skin symptoms and decreased joint pain.

##### Corticosteroids

Acute flare-ups are usually treated using corticosteroids (coll.: cortisone). This hormone, which is produced by the body in the adrenal gland, has a rapid inhibitory effect on the immune system, which is why it is used in many chronic inflammatory diseases. In the case of acute SLE disease activity, high cortisone doses are administered intravenously in the context of what is known as pulse therapy. The treatment tends to be short, primarily due to the many associated side effects (susceptibility to infection, weight gain, moon face, etc.).

##### Immunosuppressants

If SLE is accompanied by organ involvement or is of a high severity, drugs to inhibit immune activity are usually administered. This aims to stop the immune response against the body's own structures caused by the disease. In some cases, serious side effects such as increased susceptibility to infections, allergic reactions, nausea, and liver and kidney damage may occur. Treatment with immunosuppressive drugs, therefore, always takes place under controlled conditions.

### **Monoclonal antibodies**

In 2011, Belimumab (tradename Benlysta<sup>®</sup>) was the first medicinal product used specifically for the treatment of SLE to be approved in 50 years. This biological drug is a monoclonal antibody which is administered as an adjunctive therapy in severe cases and when SLE is very active and cannot be managed with a standard course of therapy. The goal is to reduce disease activity.

The additional benefit of treatment with this relatively expensive active agent is, however, in doubt and has not been demonstrated in practical terms (source: Institute for Quality and Efficiency in Health Care). Side effects were also observed by the producer (GSK), including severe or life-threatening hypersensitivity and infusion reactions. The administration of Benlysta<sup>®</sup> is, therefore, performed under close clinical monitoring.

### **Indication range dermatomyositis (DM)**

Like SLE, dermatomyositis (DM) is an autoimmune disease which causes inflammation of the skin (dermato) and the striated muscles (myositis). DM is an inflammatory rheumatic disease. In the case of DM, the trigger is also high autoimmune activity whereby, for example, the immune system attacks the small vessels (capillaries) in the muscle and skin. The resulting damage to the capillaries causes circulatory problems, which lead to a breakdown of muscle tissue and to dermatological inflammation.

Like SLE, dermatomyositis is not generally curable and treatment is limited to relieving symptoms and reducing disease activity. There is currently no approved medicinal product which is specifically tailored to the treatment of DM. Depending on the severity of the disease, the basic therapy includes the administration of corticosteroids, highly potent NSAIDs and immunosuppressive agents, which may be associated with significant side effects in some cases.

### **IFN $\alpha$ as an immune regulator in SLE and DM**

Cytokines, i.e. small water-soluble proteins which regulate the growth and differentiation of cells, are responsible for helping to balance the immune system and, therefore, play an important role, especially in the case of immunological diseases like SLE and DM. Cytokines support local communication between immune cells and can control the activation of inflammatory cells and the regulation of the natural immune system.

An important cytokine is interferon alpha (IFN $\alpha$ ), which is produced by the dendritic cells of the immune system in response to pathogens and tumour cells, which in turn stimulates the body's defences. It has been noted on numerous occasions that the interferon family (INF), especially IFN $\alpha$ , plays an important role in chronic diseases such as SLE and DM. Excessive levels of IFN $\alpha$  lead to an over-reaction and, therefore, the dysregulation of the immune system. This assumption is backed up by scientific studies that found a direct link between IFN $\alpha$  and SLE (source: Timothy B. Niewold et al. Interferon Alpha in Systemic Lupus Erythematosus). It has also been demonstrated that a high IFN $\alpha$  concentration is accompanied by high disease activity.

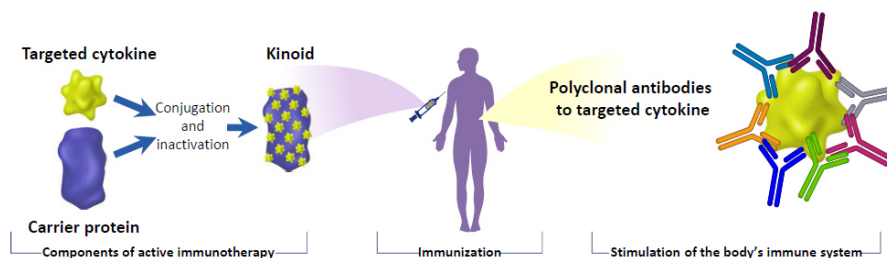
IFN $\alpha$  can be divided into 13 different types, which may have a certain homogeneity among each other, but need to be addressed together as part of a regulatory therapy.



## Neovacs' kinoid technology

The kinoid technology developed by Neovacs addresses the overproduction of cytokine IFN $\alpha$  with the goal of neutralising it and thereby bringing the immune system back into balance. An IFN $\alpha$  molecule is chemically inactivated while maintaining its immunogenicity and is then combined with a carrier protein (KLH). The carrier protein is the highly effective and well-known KLH (keyhole limpet hemocyanin), a high molecular weight protein complex derived from the Californian keyhole limpet. This carrier protein induces a strong immune response, thereby stimulating the immune system to produce polyclonal cytokine antibodies.

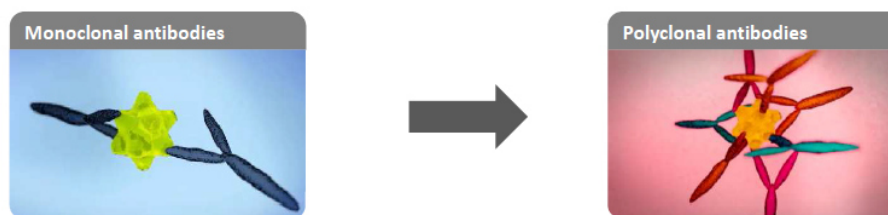
### Effect of Neovacs' IFN $\alpha$ -K (Interferon Alpha Kinoid)



Source: Präsentation der Neovacs S.A.

The polyclonal property of the antibody stimulated in this way allows several (possibly all) epitopes (area of the surface where specific bonding is possible) to block IFN $\alpha$ , thereby generally reducing its overproduction and thus the cause of SLE and DM. The Neovacs kinoid can be used to trigger an immune response with a high degree of accuracy, whereby all 13 different types are addressed and neutralised by IFN $\alpha$ . This was demonstrated in an ex vivo study, where the strong neutralisation of all IFN $\alpha$  subtypes was observed. In contrast to the currently approved therapeutic approach with monoclonal antibodies, this covers a larger area of IFN $\alpha$ :

### Monoclonal vs. Polyclonal Antibodies



Source: Neovacs-Presentation

Compared to the monoclonal therapy currently approved for the treatment of SLE, the Neovacs technology generates an immune response without the addition of other antibodies, which means that there is no rejection reaction and no loss of activity. Over time, a loss of activity was observed on several occasions when treating with foreign monoclonal antibodies. This is due to the fact that the monoclonal antibody contains foreign proteins which are detected and deactivated by the immune system. No loss of efficacy was observed during Neovacs' IFN $\alpha$ -K therapy. In fact, prolonged biological activity was actually observed during the clinical studies. Anti-IFN $\alpha$  antibodies were even found in patients four years after the end of one phase I/IIa trial (IFN-K-001).

## Clinical trials of IFN $\alpha$ kinoid in SLE and DM

Study	Therapeutic indication	End point	Beginning of Study	Ende of Study	Number of patients
IFN-K-001 (Phase I/IIa)	SLE	Primary: safety and tolerability Secondary: immune response to IFN $\alpha$ -K	04.2010	11.2011	28
IFN-K-002 (Phase IIb)	SLE	Clinical and biological effectiveness (nine months of treatment)	09.2015	Study is ongoing	178
Phase I/IIa	DM	End point not yet communicated	1st half 2016		approx. 15

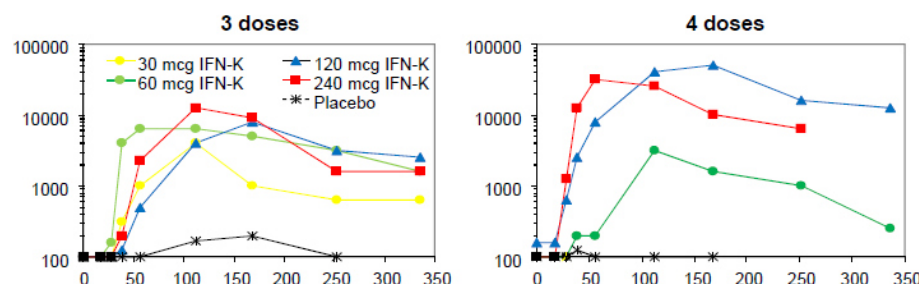
Quelle: Neovacs S.A.; GBC AG

After the clinical trial phase I/IIa for the indication SLE was successfully completed in 2011, a total of 178 patients are currently being treated with the Neovacs drug in a clinical study IIb (IFN-K-002). This involves a multicentre, double-blinded, placebo-controlled and randomised study, which is being conducted in 19 countries in Europe, Asia, Latin America and, since April 2016, in the USA. The aim of this study is to demonstrate the biological and clinical efficacy of the IFN $\alpha$  kinoid. The initial results are expected in mid-2017 after the planned 18-month course of study. At the same time, the company has been granted permission to conduct a phase IIb study in South Korea. The company also plans to acquire "orphan drug" status for the South Korean market, thereby avoiding a significantly costly and long-winded study phase III. Neovacs concluded an exclusive licensing agreement with Seoul-based Chong Kun Dang (CKD) Pharmaceutical Corp. at the end of 2015. Five clinical centres are currently involved in the ongoing phase IIb trial in South Korea.

In parallel, the clinical development of the IFN $\alpha$  kinoid was extended to include DM (dermatomyositis) during the first half of 2016. Fifteen patients in France and other European countries will initially be included in a phase I/IIa study for this autoimmune disease, which is also caused by the excess production of IFN $\alpha$ -cytokine.

The efficacy of IFN $\alpha$ -K is currently measured on the basis of the results of the clinical trial I/IIa (IFN-K-001). According to the results presented in November 2011, 100% of SLE patients enrolled in the study showed an immune response and thus formed IFN $\alpha$  antibodies. This effect was particularly observable at high doses (120mcg per dose and 240mcg per dose), with a very good safety profile overall.

### Formation of Anti-IFN $\alpha$ (Antibodies) within the IFN-K-001-study



Source: Neovacs-Presentation

The high dose-dependent increase in anti-IFN $\alpha$  is operative evidence of the Neovacs product's effectiveness. Overall, a correlation between a higher number of anti-IFN $\alpha$  and lower disease activity was noted. In addition, there was a significant reduction of those genes associated with the SLE disease.

Moreover, the public presentation of Neovacs at the Lupus Congress in Vienna (November 2015) was remarkable. Four years (now five years) after the end of their treatment,

evidence of antibodies and the continued absence of typical lupus symptoms were observed in six patients who were treated with the highest dose. In particular, the annual lupus flare-ups have not yet returned. These patients did not have any infectious diseases during these years and did not need to be treated medically for lupus.

## The company's executive bodies

### CEO

#### Miguel Sieler (CEO)



- Held international positions at Bayer for over 32 years
- CEO of Bayer Korea until 1994, then CEO of the Bayer Group in France until 1998
- Member of the Board of Nexity S.A.
- Master of Law, University of Tübingen, graduate degree from Institut d'Etudes Politiques de Paris, France

### Management

#### Bernard Fanget (Vice President Drug Development)



- With Neovacs since 2005
- Before joining Neovacs, Bernard Fanget acted as Senior Vice President of Pharmaceutical Development at Flamel Technologies.
- Previously, he served as Corporate Vice President, Global Industrialisation at Sanofi Pasteur.
- Bernard Fanget has a degree in Biochemistry from the University of Lyon.

#### Olivier Dhellin (Director Drug Development)



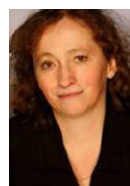
- With Neovacs since 2005
- His career includes positions at Anosys and research activities at the Gustave Roussy Institute (molecular biology and genetics).
- Worked as a post-doctoral researcher at the Pasteur Institute in the field of molecular pharmacology
- He previously worked as resident doctor in various hospital departments.
- Degree in Pharmacy and PhD in Virology

#### Therese Croughs (Chief Medical Officer)



- With Neovacs since 2015
- Previously, Therese Croughs worked as Chief Medical Officer at the French biotech company Cytheris.
- Worked as Director at BU Lauriad & NCE, following several years at Novo Nordisk as an international medical consultant for the European clinical approval of r-FVIIa (recombinant factor)
- Degree in Medical Studies from the Catholic University of Louvain, Brussels

#### Geraldine Grouard-Vogel (Chief Scientific Officer)



- With Neovacs since 2005
- Worked in the field of bacterial vaccine development at Sanofi Pasteur. Geraldine Grouard-Vogel also worked at the Walter Reed Army Institute in Seattle.
- Has a degree in Pharmacy from the University of Angers (France) and a PhD in Immunology from Schering-Plough, Lyon (France)
- She is the author of numerous scientific publications in journals.

**Nathalie Thomas-Pujol (Head of Regulatory Affairs)**



- With Neovacs since 2014
- 20 years of experience in the field of drug approval and the clinical approval process
- President of Regulatory Affairs EMEA at Cephalon/Teva
- 15 years of experience in research at Sanofi-Aventis
- PhD in Pharmacy from the University of Rouen (France) and PhD in Toxicology from the University of Paris VII (France)

**Scientific Advisory Board**

**Prof. Jacques Banchereau, PhD**

- Director in the field of Immunology at The Jackson Laboratory for Genomics Medicine, UConn Health Center
- Baylor Institute of Immunological Research, Dallas, USA

**Prof. Miriam Merad, MD, PhD**

- Professor of Oncology and Medicine at the Tisch Cancer Institute, New York
- Director of the Human Immunomonitoring Center at the Tisch Cancer Institute, New York
- Dr Merad is one of the first organisers of the famous Keystone Conference for "dendritic cell biology"

**Dr Virginia Pascual**

- Director at the Centre for Inflammatory and Autoimmune Diseases
- Director at the Centre for Personalised Medicine
- Lecturer in Paediatrics at the University of Texas Southwestern Medical Center, USA
- Lecturer in Pediatrics at the Mount Sinai School of Medicine, New York, USA
- Lecturer in Biomedical Studies at Baylor University, Waco, USA

**Prof. Betty Diamond, MD**

- Researcher and Chairperson of the Center for Autoimmune Diseases and Musculoskeletal Disorders at The Feinstein Institute for Medical Research
- Professor of Molecular Medicine and Medicine at the Hofstra North Shore-LIJ School of Medicine, Manhasset, USA

**Prof. Napoleone Ferrara, MD**

- Professor of Ophthalmology and Pathology
- Director of Basic Sciences at UC San Diego Health System, La Jolla, USA

**Prof. Bernard Lauwerys, MD, PhD**

- Activities in the field of Rheumatology at Cliniques Universitaires Saint Luc & Université Catholique de Louvain, Brussels, Belgium

**Prof. Laurence Zitvogel, MD**

- Research Director at INSERM U1015, Gustave Roussy Cancer Centre
- Works at the Centre of Clinical Investigations in Biotherapies of Cancer (CICBT) 507, Villejuif, France

## MARKET AND MARKET ENVIRONMENT

The market potential analysed below as the basis for the sales potential of the Neovacs product includes the two indications SLE (systemic lupus erythematosus) and DM (dermatomyositis) currently being addressed. In line with the broad regional coverage within the clinical approval process, we have taken a largely global approach when determining the specific market potential. In the field of SLE, we have studied the global potential of the major pharmaceutical markets (Europe, USA, China, Japan and South Korea). We initially determined the market potential for the treatment of DM on the basis of potential in Europe and USA, in the same way as in the study pipeline.

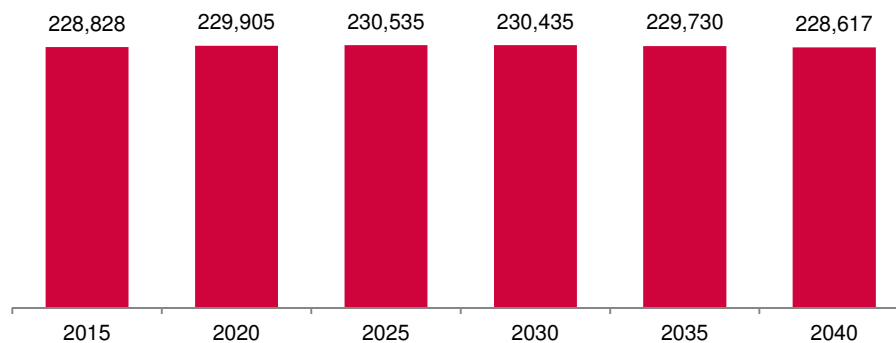
### Indication systemic lupus erythematosus (SLE)

The essential and initial factor for determining the market potential for the treatment of SLE is the prevalence (existing number of patients) and incidence (number of new cases) of the disease. SLE is a relatively rare disease, which, although accompanied by a low risk of occurrence, has a high number of patients and is, therefore, characterised by high demand for treatment.

#### *SLE in Europe*

For example, the incidence, i.e. the annual number of SLE diagnoses, in Germany is only 6-8 per 100,000 inhabitants (source: German Society for Rheumatology e.V.). According to statistics, however, 31,000 people in Germany alone are diagnosed with SLE, which means a prevalence of approximately 37.8 per 100,000 inhabitants. Overall, there is a relatively high population of people who have been diagnosed with SLE in Germany alone. Due to a lack of cross-regional data, we have applied the statistics calculated for Germany when determining the total number of patients in Europe. Some of the SLE statistics gathered for the UK, France, Sweden and Norway show significant differences to the figures for Germany, which can be primarily attributed to the fact that the statistics were gathered further in the past. More recent statistics take the more sensitive diagnostic methods into account, resulting in a higher annual incidence. In addition, the rise in life expectancy of patients with SLE, which will increase over time, is associated with a higher prevalence of the disease (Europe: 45 per 100,000 inhabitants).

#### **GBC-forecast on SLE-prevalence in Europe**



Source: Deutsche Gesellschaft für Rheumatologie e.V.; worldbank.org; GBC AG

Starting from the determined SLE frequency, taking the expected population growth in Europe into account, we have calculated 192,215 incidences of SLE in Europe for 2015. There are only expected to be minor changes in the coming years, whereby we have not

taken into account any advances in the treatment of SLE or an associated increase in life expectancy.

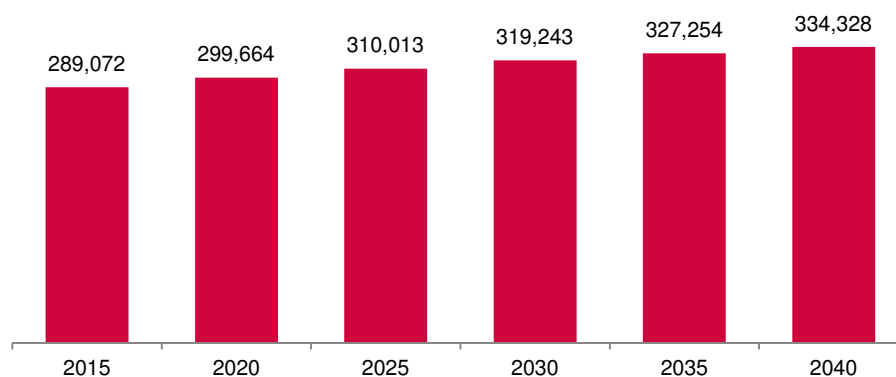
Our extrapolation is conclusive in this respect, as no risk factors are currently known for the development of SLE. While it is assumed that certain environmental factors, such as sun exposure, certain medications and infections, can be a possible trigger for the onset of SLE, genetic predisposition is considered to be the most significant factor.

As SLE predominantly occurs in women (ratio female to male: 9:1) and is more severe among people of African or Asian descent (2 to 3 times higher risk of disease; source: Understanding the Epidemiology and Progression of Systemic Lupus Erythematosus), the population composition is crucial for the number of SLE diagnoses.

### ***SLE in the USA***

Due to a higher proportion of people of colour, which is associated with significantly higher SLE disease rates than amongst Caucasian populations, SLE prevalence is higher in the USA than in Europe. On the basis of various studies conducted in the USA (see, for example, the Michigan Study and Georgia Study), a high SLE prevalence of between 64.6 - 92.1 per 100,000 inhabitants has been determined, which is significantly higher than the value calculated for Germany. Based on a current value of 90 per 100,000 inhabitants, this means that, in the USA alone, almost 300,000 people have been diagnosed with SLE. In the case of a statistically determined incidence of 5.5 - 5.6 per 100,000 inhabitants, the following SLE population has been calculated for the USA on the basis of the population projections:

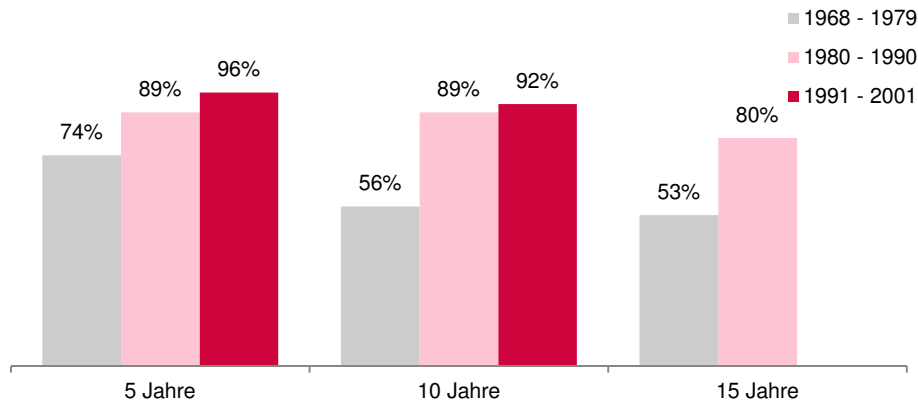
#### **GBC-forecast on SLE-prevalence in USA**



Source: medscape.com.; worldbank.org; GBC AG

A significant factor is the increasing life expectancy for patients previously diagnosed with the disease (more sensitive diagnostic methods, better understanding of the disease and improved treatment methods). According to a study conducted in the USA, the five-year survival rate has improved over the past few decades from 74% (1968-1979) to 89% (1980-1990) and finally to 96% (1991-2001). The significantly higher survival rate means that, at constant incidence rates, there will be an increase in the prevalence of this condition requiring ongoing treatment:

### Survival Rate of SLE-disease

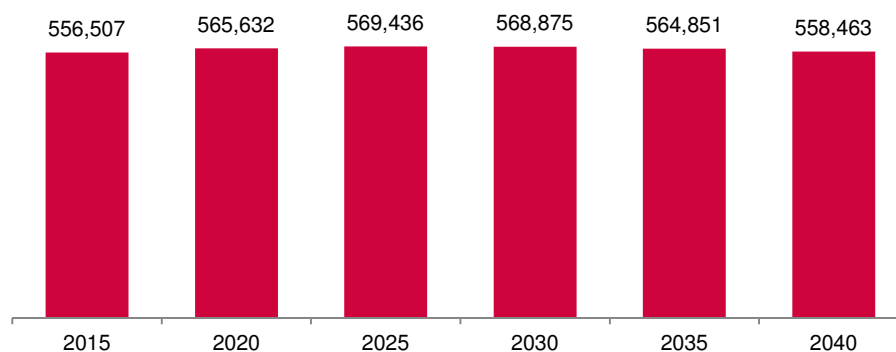


Source: Life expectancy of women with lupus nephritis now approaches that of the general population; GBC AG

### SLE in Asia

Various studies have shown that the prevalence of SLE depends on the ethnic composition of the population. A particularly high frequency was found among indigenous populations, such as the Aborigines and Native Americans. Asian immigrants in the USA, for example, also have a higher risk of the disease, while studies conducted in Asia showed a prevalence similar to that in Europe (Source: J. Thumboo and Hwee-Lin Wee: Systemic lupus erythematosus in Asia: is it more common and more severe?). The results of the Asian studies indicate a high range with a prevalence of 3.2 - 70.4 per 100,000 inhabitants. Overall, we have identified the following SLE total amounts in the countries we have categorised as relevant:

### GBC-forecast of SLE-prevalence in China, South-Korea and Japan



Source: worldbank.org; Shim JS et al; Julian Thumboo et al; GBC AG

To determine the market potential of the Neovacs products to be marketed globally, we have restricted ourselves to the largest Asian pharmaceutical markets in China, Japan and South Korea. In the studies conducted in China, the likelihood of SLE was 26.0 - 70.4 per 100,000 inhabitants. In Japan, this is significantly lower at 3.7 - 20.9 per 100,000 inhabitants. In South Korea, the first region where the Neovacs product has already been granted a licence, the SLE prevalence is 31.5 per 100,000 inhabitants. Given a population of 50.6 million, only around 16,000 people are likely to be diagnosed with SLE in South Korea. The upper limit for an orphan disease status in South Korea is 20,000, which means, that faster marketing approval excluding the phase III study is possible in this country.



### ***SLE treatment costs***

Although SLE is associated with a relatively low prevalence, the absolute numbers of patients diagnosed with the disease show high medical demand. At the same time, SLE is accompanied by a high burden on society, both due to the direct cost of treatment and indirect socio-economic and personal factors. In addition to the long duration of the disease (see survival rate for SLE disease), the severity of the course of the disease is a crucial issue in this regard. According to studies conducted in Europe and the USA, up to half of SLE patients are unable to continue working in the first few years after diagnosis (source: Lacie Scofield et al.). As the duration of the disease increases, the proportion of disabled patients also rises to 15% (5 years); 36% (10 years); 51% (15 years) and 63% (20 years) (source: Yelin et al.).

If the direct treatment costs are combined with these indirect socioeconomic costs, this results in an annual cost of €17,750 per SLE patient, according to data from German Federal Health Monitoring. In Germany, this amounts to a total cost associated with SLE of €500 million (for 31,000 patients).

Meaningful data is also available for the USA. With a total annual cost amounting to USD 29,232 per SLE patient (source: Health Care Utilization and Costs of Systemic Lupus Erythematosus in Medicaid; Hong J. Kan et al.), the annual total costs associated with SLE amount to USD 7.3 billion.

These two figures alone demonstrate the high saving potential within the context of SLE. Assuming that the study develops positively, rapid market approval and a quick decision regarding the potential reimbursement of costs for Neovacs products are, therefore, to be expected.

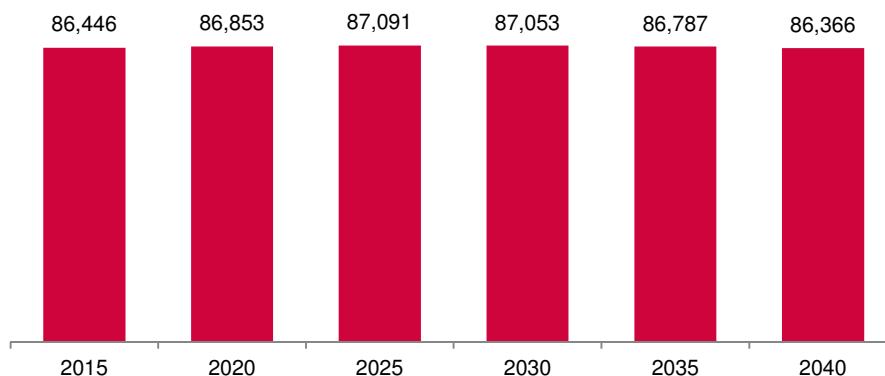
### **Therapeutic indication dermatomyositis (DM)**

The inflammatory muscle disease dermatomyositis (DM), which is currently incurable, is significantly rarer than systemic lupus erythematosus (SLE) and has the status of an orphan disease, even in the major pharmaceutical markets. This status, which is due to the relatively low prevalence of the disease, is associated with significantly easier and, therefore, faster market approval (fast-track procedure). In the case of orphan drugs, a request for market approval can typically be made after phase IIb, skipping the costly and time-intensive final phase III.

#### ***DM in Europe***

Dermatomyositis is accordingly classified as a rare disease in the EU. With a prevalence of 17 per 100,000 inhabitants, which means that around 87,000 people suffer from DM in Europe, the disease is significantly below the European orphan status limit of 50 per 100,000 or a maximum of 230,000 patients. As in the case of SLE, the causes of this disease are not fully understood, and no risk factors are known. Assuming a genetic predisposition, which is currently the only known factor for the onset of this autoimmune disease, we can only refer to the statistically determined prevalence when calculating the number of cases:

### GBC-forecast of DM-prevalence in Europe



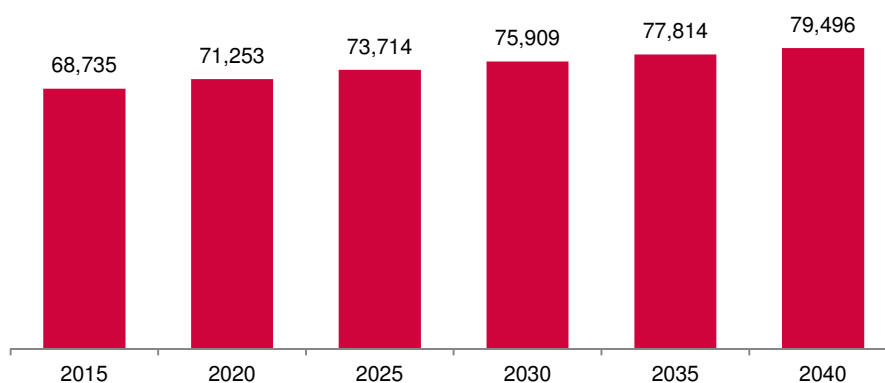
Source: European Medicines Agency; worldbank.org; GBC AG

### DM in the USA

The European data on DM have been confirmed in a long-term study conducted in the USA (1976-2007). A slightly higher DM prevalence of 21.4 per 100,000 inhabitants was identified in the state of Minnesota, which can be attributed to the ethnic composition of the population. The study also found that the black population was two times more likely to be diagnosed with the disease than those of Caucasian ethnicity.

Extrapolated to the total US population of approximately 321 million, this would mean that more than 68,000 people are diagnosed with DM. The conditions for orphan drug status would, therefore, be fulfilled. According to the Orphan Drug Designation programme (FDA), a disorder is rare if fewer than 200,000 people in the United States are affected. Once again, this is accompanied by an accelerated and less financially intensive approval process. We have calculated the following DM prevalence figures for the USA:

### GBC-forecast of DM-prevalence in the USA



Source: Incidence of Dermatomyositis and Clinically Amyopathic Dermatomyositis: A Population-Based Study in Olmsted County, Minnesota, Margo J. Reeder et al.; worldbank.org; GBC AG

## ANALYSIS OF THE COMPANY'S DEVELOPMENT

### Past development of the company

In €m	FY 2012	FY 2013	FY 2014	FY 2015
Total Sales*	0.12	0.04	0.16	1.18
EBIT	-8.24	-7.90	-9.65	-11.28
EAT	-7.15	-6.87	-7.51	-4.68

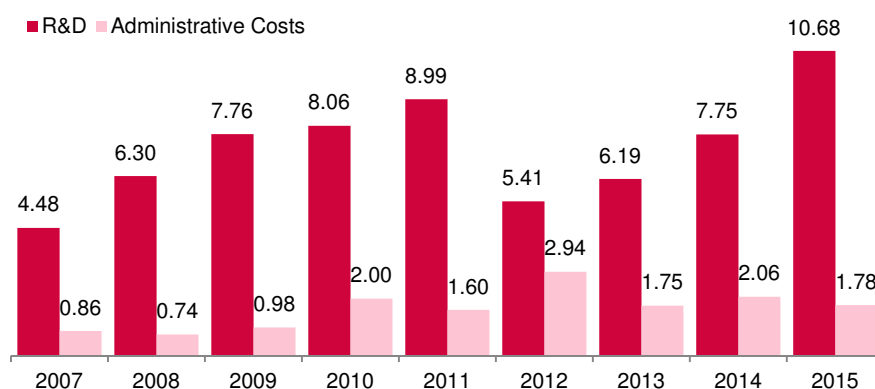
Source: Neovacs S.A.; GBC AG; \*incl. earning from research subsidies

As the IFN $\alpha$  kinoid developed by Neovacs is still in clinical development for all indications, the operative development of the company will be marked by a lack of marketing revenues, whereby expenses are associated with the research and clinical approval of the main product. This results in a typical situation for a research-based biotech company, which is primarily characterised by a negative result. During this phase, the focus is on financial resources as the basis for the financing of the further product development.

The revenues are, for example, associated with research grants and income within the scope of IFN $\alpha$  kinoid licensing. Other operating income of €1.0 million relating to an exclusive licence agreement with South Korea concluded with Chong Kun Dang (CKD) Pharmaceutical Corp. was generated in the 2015 financial year. This is Neovacs' first licence agreement, and the yield level was consequently unusually high during the past financial year. In previous financial years, Neovacs received low-level research grants.

The essential expenses are associated with the development of the IFN $\alpha$  kinoids and are, therefore, attributable to the R&D area. As a rule, this expense item tends to increase as a result of clinical progress, as later study phases are usually accompanied by higher expenses. Upon entry into the phase IIa trial for the indication SLE and expansion to include the indication DM, the R&D expenses increased to €10.68 million during the 2015 financial year (previous year: €7.75 million) and were, therefore, above the level of the previous financial years:

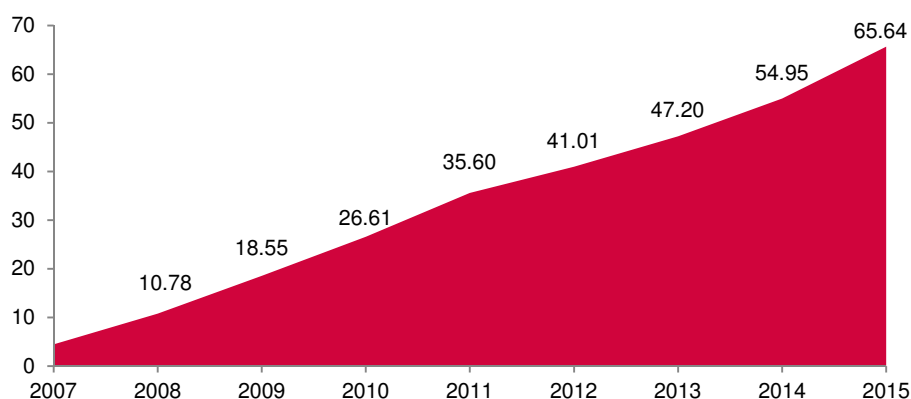
### Historical Development of R&D-expenses and administrative costs (in €m)



Source: Neovacs S.A.; GBC AG

Since 2007, the year of the oldest available Neovacs annual report, the research and development expenses have amounted to a total of €65.64 million. These almost exclusively relate to the development and clinical approval of IFN $\alpha$  kinoids and TNF kinoids.

### Cumulated R&D-expenses since 2007 (in €m)



Source: Neovacs S.A.; GBC AG

Administrative expenses, a second major cost item for Neovacs, have developed relatively constantly. Recently, the company has even been able to reduce these overhead costs to €1.78 million (previous year: €2.06 million), which demonstrates the generally lean cost structure of Neovacs.

As expected, Neovacs has, therefore, posted a negative result. Since the foundation of the company, the cumulative losses recognised in equity have amounted to €68.77 million as of 31.12.2015. During the 2015 financial year, Neovacs was even able to increase its after-tax profit to €-4.68 million (previous year: €-7.51 million). This is primarily due to an extraordinary result of €4.19 million, which is associated with investment grants from the "General Commission for Investment PIAVE" and "Bpifrance". Neovacs also received control and research refunds amounting to €2.57 million.

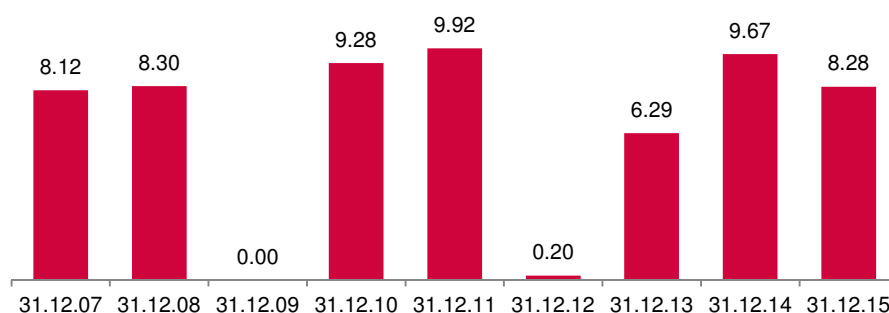
### Historical development of the balance figures

in €m	31/12/2012	31/12/2013	31/12/2014	31/12/2015
Shareholder's Capital	3.88	3.72	5.87	6.37
Losses carried forward	-49.70	-56.57	-64.08	-68.77
Equity ratio	60.0%	47.0%	62.7%	55.1%
Liquid Assets	0.16	0.22	1.98	0.88
Financial Assets	4.34	4.01	5.62	6.09
Capital increase	0.20	6.29	9.67	8.28
Operating Cashflow	-6.33	-7.00	-8.05	-7.69
Investment Cashflow	-0.03	-0.04	0.00	-0.12
Financing Cashflow	0.18	6.71	9.67	8.28

Source: Neovacs S.A.; GBC AG

In order to cover the financial requirements for the clinical development of the IFN $\alpha$  kinoids and TNF kinoids while also facing a lack of operative liquidity inflows, Neovacs S.A. has performed a series of capital increases and has received several government investment grants over the past few financial years. On the basis of the financing cash flow, a total of €60.06 million has been received since the 2007 financial year, which is roughly at the same level as the R&D expenses incurred over the same period.

### Capital increases 2007 - 2015 (in €m)

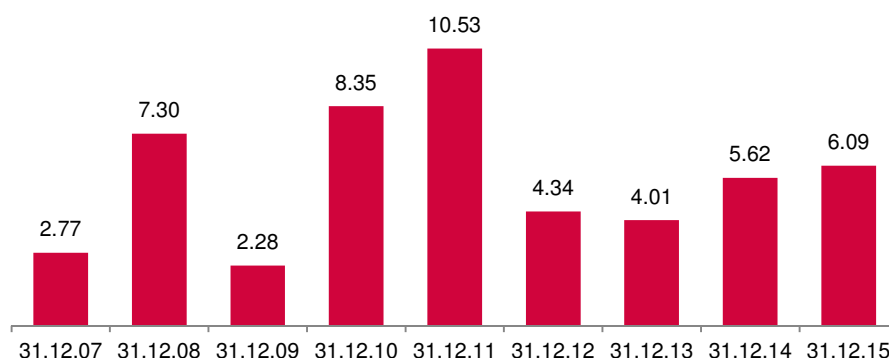


Source: Neovacs S.A.; GBC AG

During the 2015 financial year, for example, a capital increase of €7.5 million (issuance of 7.5 million shares) was executed, which was fully subscribed by US institutional investors. A further 1.55 million shares were also issued within a standby equity agreement with Kepler Cheuvreux, thereby generating €8.28 million net.

As a result of these corporate actions, Neovacs was able to cover its operative liquidity outflows and was even in a position to increase its short-term liquid funds. As a result of the issue proceeds exceeding the liquidity consumption over the past financial years, the short-term liquid assets (including short-term securities) increased to €6.09 million (31.12.14: €5.62 million):

### Short term liquidity (in €m)



Source: Neovacs S.A.; GBC AG

The liquidity of the company is, therefore, currently considered to be sufficient. Including the grants from the "Investments for the future" programme (€5.0 million), up-front fees from the CKD partnership (€1.0 million) and the equity agreement with Kepler Cheuvreux (up to €13.0 million), we have calculated a cash reach of 2.5 years on the basis of the current cash burn.

The losses carried forward, which have developed consistently as a result of the capital measures, are an important asset in the company's equity. As a result, future tax expenses will continue to be low, even if operating profits are generated in the future. As at 31.12.2015, the accumulated losses amounted to €68.77 million (31.12.14: €64.08 million).

## FORECAST AND MODEL ASSUMPTIONS

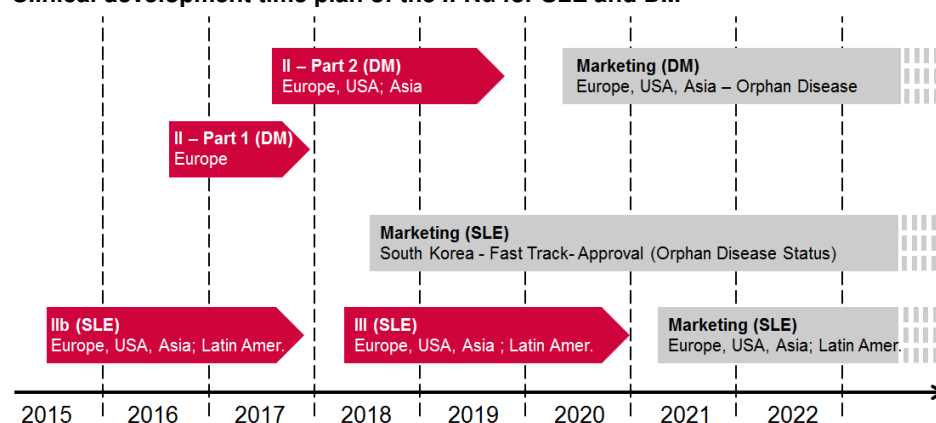
in €m	FY 2016e	FY 2017e	FY 2018e	FY 2019e	FY 2020e	FY 2021e	FY 2022e	FY 2023e
Sales	0.00	0.00	5.11	2.66	18.08	128.30	190.54	253.24
EBIT	-7.26	-8.57	-11.77	-19.09	-5.48	81.25	124.09	167.06
Net Income	-7.36	-8.67	-11.87	-19.19	-5.58	81.15	123.99	116.84
EPS	-0.21	-0.21	-0.26	-0.36	-0.10	1.41	2.15	2.02

Source: GBC AG

### Commercial strategy and authorisation schedule

We have prepared an approval schedule for the two indications SLE and DM to be used as a basis for our sales and earnings forecasts. While the current project pipeline of Neovacs S.A. also includes further indications and other kinoids based on different cytokines, this is seen as evidence of Neovacs technology's development potential. As the development of the IFN $\alpha$  kinoid for the indications SLE and DM is currently at the most advanced stage, we base the following forecasts solely on these two areas.

#### Clinical development time plan of the IFN $\alpha$ for SLE and DM



Source: GBC AG

The ongoing phase IIb study for the SLE indication (IFN-K-002) involves a total of 178 patients in 19 countries in Europe, Asia, Latin America and, since April 2016, the USA. The aim of this study is to demonstrate the biological and clinical efficacy of IFN-K. We expect the first results to be available in the middle of the 2017 financial year. Subsequently, Neovacs should promptly begin the final phase III trials to enable the marketing of IFN-K in the abovementioned countries from mid-2021.

However, Neovacs will not begin to earn marketing revenues until the 2018 financial year. This is based on our assumption that SLE could be classified as an orphan disease (rare disease) in South Korea, which would avoid the costly and time-intensive final phase III trials. To be classified as a rare disease in South Korea, prevalence must be below 20,000. According to our findings, there are approximately 16,000 diagnosed patients in South Korea, so classification as an orphan disease is likely. Neovacs intends to promptly request classification of SLE as an orphan disease in South Korea. Neovacs concluded an exclusive licensing agreement with Seoul-based Chong Kun Dang (CKD) Pharmaceutical Corp. at the end of 2015 for distribution in the South Korean market.

Orphan disease status is likely to be achieved worldwide for the indication DM (dermatomyositis) due to its significantly lower prevalence, which would lead to faster and less costly clinical approval overall. We initially expect approval to be granted in Europe, the USA and Asia, whereby we have conservatively included only Europe and the USA as

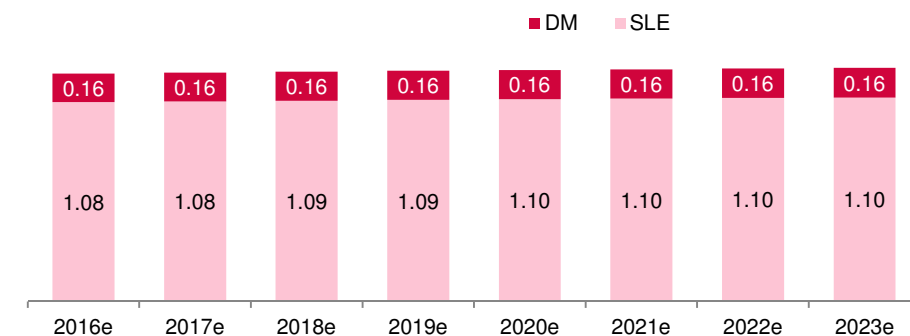
approval regions in our forecasts. In accordance with our expectations, the market launch should take place in 2020.

Neovacs may, in principle, pursue out-licensing of the projects, in a similar way as for the South Korean market. A regional or global out-licensing would result in revenue from upfront and milestone payments, and the financing expenses for clinical product development would thus be considerably lower. In the marketing phase, Neovacs would collect revenue-based royalties. As a result of continued lacking concretisation, however, we have not yet taken this fundamental strategy into account. We will not take this into account in our sales and earnings forecasts, and, consequently, in our valuation model, until a licence agreement is concluded in the same way as for the South Korean market.

### Sales forecasts 2016-2023

Our sales forecasts are initially based on the number of all patients diagnosed with SLE and DM in the regions addressed by Neovacs (Europe, US, Asia). Based on the calculated prevalence and incidence figures (see Market and market environment section) and taking the population figures into account, we have assumed the following indication-based (SLE: Europe, Asia, USA; DM: Europe; USA) population:

#### Basis of our Sales-Forecast: Prevalence of SLE und DM (in Million Cases)



Source: GBC AG

However, as not all SLE and DM patients can be treated with IFN $\alpha$  kinoid (no IFN $\alpha$  signature) and as some of the diagnostic preparation is still incomplete, we have made a 30% deduction from the population determined on the basis of the market statistics.

We expect average costs of approximately €20,000 for treatment with the Neovacs product (the price may vary between regions). On the basis of current findings, a follow-up dose is also likely to be required after five years, which will subsequently have a positive impact on sales figures. Our price assumption is a verifiable and even conservative assumption, particularly when compared with the only product currently approved specifically for the treatment of SLE, Belimumab (tradename Benlysta<sup>®</sup>). According to the National Institute of Health (NIH), annual treatment with Benlysta<sup>®</sup> costs approximately USD 35,000. It should be noted that Benlysta<sup>®</sup> is used for the treatment of symptoms and is, therefore, accompanied by corresponding costs as the disease worsens. Due to the verified long-lasting effect of IFN $\alpha$ -K (in patients of a phase I/IIa trial, anti-IFN $\alpha$  antibodies were still detected four years later), a single treatment cycle with the Neovacs product is to be expected. This is an important argument, particularly in light of the legal compensation options.

### SLE in Europe, USA and Asia

In Mio. €	FY 2016e	FY 2017e	FY 2018e	FY 2019e	FY 2020e	FY 2021e	FY 2022e	FY 2023e
Patient population	1,062,694	1,067,017	1,071,140	1,075,043	1,078,711	1,082,139	1,085,311	1,088,219
Reduction 30%	743,886	746,912	749,798	752,530	755,097	757,498	759,718	761,753
Market share	-	-	-	-	-	0.5%	0.8%	1.0%
Treated patients	-	-	-	-	-	3,787	5,698	7,618
Price/treatment cycle	-	-	-	-	-	25,000	25,000	25,000
<b>Sales Neovacs</b>	-	-	-	-	-	<b>94.69</b>	<b>142.45</b>	<b>190.44</b>

### SLE in South Korea

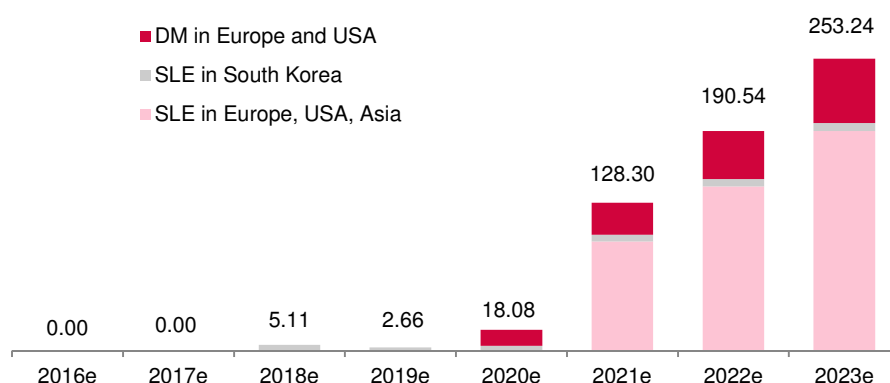
In Mio. €	FY 2016e	FY 2017e	FY 2018e	FY 2019e	FY 2020e	FY 2021e	FY 2022e	FY 2023e
Patient population	16,267	16,327	16,385	16,439	16,490	16,540	16,586	16,631
Reduction 30%	11,387	11,429	11,469	11,507	11,543	11,578	11,610	11,642
Market share	-	-	2.3%	5.6%	8.7%	11.7%	12.6%	9.6%
Treated patients	-	-	260	640	1,000	1,360	1,460	1,600
Price/treatment cycle	-	-	15,000	15,000	15,000	15,000	15,000	15,000
Revenue licence partner	-	-	3.90	9.60	15.00	20.40	21.90	24.00
Licence fee	-	-	10%	10%	10%	10%	10%	10%
Revenue Neovacs*	-	-	1.11	2.66	4.25	5.84	6.29	6.88
Milestone + up-front	-	-	4,00	-	-	-	-	-
<b>Sales Neovacs</b>	-	-	<b>5.11</b>	<b>2.66</b>	<b>4.25</b>	<b>5.84</b>	<b>6.29</b>	<b>6.88</b>

\*Licence fee + production revenues

### DM in Europe and USA

In Mio. €	FY 2016e	FY 2017e	FY 2018e	FY 2019e	FY 2020e	FY 2021e	FY 2022e	FY 2023e
Patient population	155,770	156,361	156,949	157,532	158,106	158,675	159,232	159,774
Reduction 30%	109,039	109,453	109,864	110,272	110,675	111,072	111,462	111,842
Market share	-	-	-	-	0.5%	1.0%	1.5%	2.0%
Treated patients	-	-	-	-	553	1,111	1,672	2,237
Price/treatment cycle	-	-	-	-	25,000	25,000	25,000	25,000
<b>Sales Neovacs</b>	-	-	-	-	<b>13.83</b>	<b>27.77</b>	<b>41.80</b>	<b>55.92</b>

### Sales forecasts 2016-2023 (in €m)



Source: GBC AG

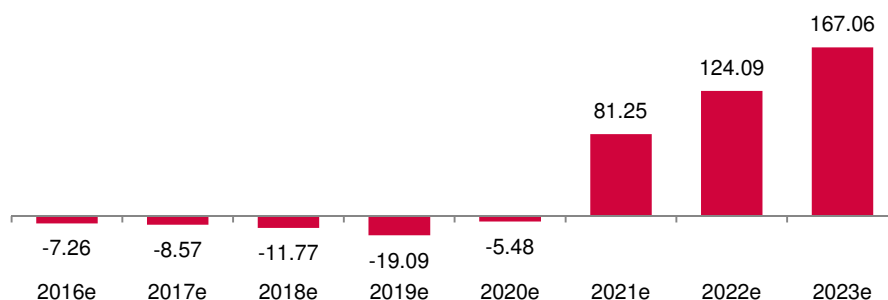


## Earnings forecast 2016 – 2023

Until the marketing phase, the cost situation of Neovacs will be mainly impacted by expenses associated with clinical product development. For both indications, we anticipate clinical registration costs of €50 million, the same amount we have allocated to the upcoming financial years according to our projected study progress. The company earnings will correspondingly be in the negative range, as expected.

As soon as marketing has begun, Neovacs S.A. will also cover the production of IFN $\alpha$ -K. In this regard, a joint venture agreement has been concluded with the US company Stellar Biotechnologies, Inc. (70% Neovacs / 30% Stellar). Stellar is the global leading manufacturer of keyhole limpet hemocyanin (KLH), the carrier protein for IFN $\alpha$ -K. The production of IFN $\alpha$ -K is to be covered by this joint venture. As a result, the company will be able to generate additional production revenue, even in the event of out-licensing (see CKD licence agreement). We anticipate a gross profit of 70.0% which, in the case of marketing, suggests a generally high profit margin as it is typical for biotech companies:

### EBIT-forecast 2016 – 2023 (in €m)



Source: GBC AG

## Key evaluation parameters

As the clinical development of IFN $\alpha$ -K is currently in a phase II study, the marketing probability is still subject to great uncertainty. Joseph A. DiMasi, Director of the Tufts Center for the Study of Drug Development, has identified statistics for the probability of occurrence depending on the clinical trial phases in a meta-analysis of clinical studies (published in the Journal of Health Economics). The probability of a drug in phase II trials being approved for market is 22.8%. If the drug is in phase III trials, the marketing probability increases significantly to 58.5%.

To determine the fair enterprise value, we have assumed a probability of 22.8% in the DCF model according to the latest approval progress. The risk will then be reduced upon entry into the third trial phase.

We have also taken the current capital increase into account in our valuation model by issuing 9.46 million shares (gross issue proceeds: €8.05 million). The successful completion of this capital measure appears likely within the context of a pre-agreed subscription rate of 50.9%. Upon completion of this capital increase, the number of shares in Neovacs will increase to 41.52 million.

## Valuation

### *Model assumptions*

We rated Neovacs S.A. using a two-stage DCF model. Starting with the specific consolidated estimates for the years 2016-2023 in the first phase, a residual value is determined in the second phase by means of a perpetual annuity. As the final value, we assume a growth rate of 3.0 % and we have set 60.0 % as the target EBITDA margin.

### *Determining the capital costs*

The weighted average cost of capital (WACC) of Neovacs S.A. is calculated from the equity cost and the cost of debt. The market premium, the company-specific beta, as well as the risk-free interest rate have to be determined in order to determine the equity cost.

The risk-free interest rate is derived from the current structured interest rate curves for risk-free bonds in accordance with the recommendations from the "Fachausschuss für Unternehmensbewertung und Betriebswirtschaft" (FAUB, Special Committee for Business Valuation and Business Management) of the "Institut der Wirtschaftsprüfer in Deutschland e.V." (Institute of Public Auditors in Germany). This is based on the zero bond interest rate calculated using the Svensson Method published by the German Bundesbank. In order to compensate for short-term market fluctuations, the average returns for the previous three months are used and the result is rounded up to the nearest 0.25 basis points. **The value currently used for the risk-free interest rate is 1.00 %.**

We set the historical market premium of 5.50 % as a reasonable expectation of the market premium. This is supported by historical analyses of equity market returns. The market premium reflects in a percentage the improved return expected from equity markets relative to low-risk government bonds.

According to GBC estimates, a beta of 2.04 is currently determined.

Using the premises provided, the equity cost is calculated at 12.20 % (beta multiplied by risk premium plus risk-free interest rate). As we assume a sustainable weighting of the equity cost of 100 %, the result is a weighted average cost of capital (WACC) of 12.20 %.

### *Evaluation results*

The discounting of future cash flows is based on the entity approach. In our calculation, the result for the corresponding weighted average cost of capital (WACC) is 12.20%. The resulting fair value per share at the end of the 2016 financial year corresponds to the stock price target of €2.90. In the DCF model, we assumed a marketing probability of 22.8% on the basis of current phase II trials (source: Journal of Health Economics; The price of innovation: new estimates of drug development costs), which accordingly reduces the fair value of the company. In the event of the successful continuation of the clinical approval process, the probability of occurrence and, therefore, the fair value of the company will increase.

## DCF-Modell

### Neovacs S.A. - Discounted Cashflow (DCF) model scenario

Value driver of the DCF - model after the estimate phase:

#### final - phase

Eternal growth rate	3,0%
Eternal EBITA - margin	60,0%
Effective tax rate in final phase	35,0%

#### two phases DCF - model:

phase in €m	estimate								final value
	FY 16e	FY 17e	FY 18e	FY 19e	FY 20e	FY 21e	FY 22e	FY 23e	
Revenue	0,00	0,00	5,11	2,66	18,08	128,30	190,54	253,24	
Revenue change	-	-	-	-47,9%	579,9%	609,4%	48,5%	32,9%	3,0%
Revenue to fixed assets	-7,21	-8,51	-11,70	-19,09	-5,48	81,25	124,09	167,06	
EBITDA	n.def.	n.def.	neg.	neg.	neg.	63,3%	65,1%	66,0%	
EBITDA-Margin	-7,26	-8,57	-11,77	-19,09	-5,48	81,25	124,09	167,06	
EBITA	n.def.	n.def.	neg.	neg.	neg.	63,3%	65,1%	66,0%	60,0%
EBITA-Margin	0,00	0,00	0,00	0,00	0,00	0,00	0,00	-50,12	
Taxes on EBITA	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%	0,0%	30,0%	35,0%
Taxes to EBITA	-7,26	-8,57	-11,77	-19,09	-5,48	81,25	124,09	116,95	
EBI (NOPLAT)	neg.	neg.	neg.	neg.	neg.	1032,2%	194,6%	104,0%	69,6%
Return on capital									
	0,90	0,70	1,00	1,01	6,87	48,75	72,40	96,23	
Working Capital (WC)	n.def.	n.def.	19,6%	38,0%	38,0%	38,0%	38,0%	38,0%	
WC to revenue	-0,12	0,20	-0,30	-0,01	-5,86	-41,88	-23,65	-23,83	
Investment in WC	0,10	0,15	0,20	0,50	1,00	15,00	40,00	50,00	
Operating fixed assets (OAV)	-0,05	-0,06	-0,07	-0,01	-0,03	-0,06	-0,90	-2,40	
Depreciation on OAV	50,0%	40,0%	35,0%	6,0%	6,0%	6,0%	6,0%	6,0%	
Depreciation to OAV	-0,09	-0,11	-0,12	-0,31	-0,53	-14,06	-25,90	-12,40	
Investment in OAV	1,00	0,85	1,20	1,51	7,87	63,75	112,40	146,23	
Capital employed	-7,21	-8,51	-11,70	-19,09	-5,48	81,25	124,09	167,06	
EBITDA	0,00	0,00	0,00	0,00	0,00	0,00	0,00	-50,12	
Taxes on EBITA	-0,21	0,09	-0,42	-0,32	-6,39	-55,94	-49,55	-36,23	
Total investment	-0,09	-0,11	-0,12	-0,31	-0,53	-14,06	-25,90	-12,40	
Investment in OAV	-0,12	0,20	-0,30	-0,01	-5,86	-41,88	-23,65	-23,83	
Investment in WC	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	
Investment in Goodwill	-7,42	-8,42	-12,12	-19,41	-11,87	25,31	74,53	80,72	1058,45
Free cashflows									

Value operating business (due date)	522,25	594,36
Net present value explicit free Cash-flows	49,30	63,73
Net present value of terminal value	472,95	530,63
Net debt	-5,54	-5,44
Value of equity	527,79	599,80
Probability of marketing	22,8%	22,8%
Value of share capital	120,34	136,75
Outstanding shares in m	41,52	44,84
Fair value per share in €	2,90	3,05

#### Cost of capital:

Risk free rate	1,0%
Market risk premium	5,5%
Beta	2,04
Cost of equity	12,2%
Target weight	100,0%
Cost of debt	4,5%
Target weight	0,0%
Taxshield	28,7%

WACC	12,2%
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Return on capital	WACC				
	10,2%	11,2%	12,2%	13,2%	14,2%
50%	2,93	2,47	2,12	1,84	1,62
60%	3,50	2,94	2,51	2,17	1,90
70%	4,07	3,40	2,90	2,50	2,19
80%	4,63	3,87	3,29	2,83	2,47
90%	5,20	4,34	3,68	3,16	2,75

## ANNEX

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