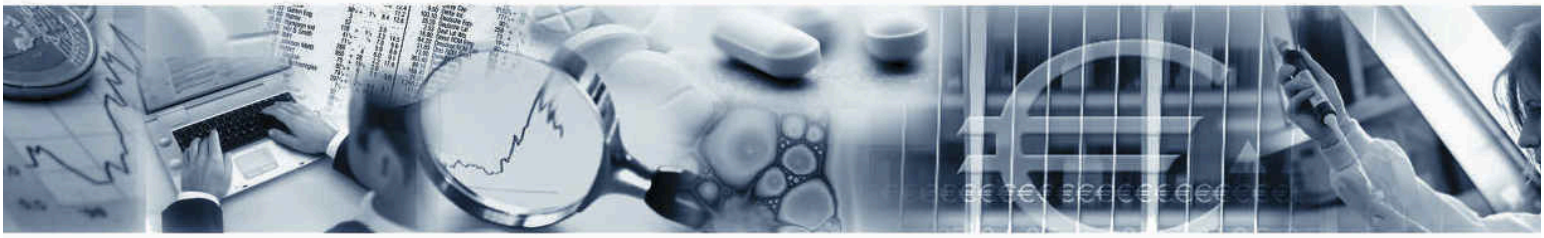


Research Note

Biofrontera AG

Full Speed Ahead with Ameluz

Biofrontera
Experts in dermatology

Chief Research Analyst

Marcel Wijma MSc

+1 (917) 460 6185 (US)

+31 (6) 8489 2954 (NL)

+61 (0) 426 4349 240 (AU)

m.wijma@leeuwenhoeck.com

http://www.leeuwenhoeck.com

Date: 30 September 2016

Name:	**Biofrontera AG**
Country:	**Germany**
Price:	**EUR 3.01**
ISIN Code:	**DE0006046113**
Reuters Code:	**B8F.DE**
Market Cap (EUR m):	**91.0**
EV (EUR m):	**80.8**
Cash & cash eq. (EUR m):	**10.2**
Shares outstanding (m):	**30.348**
Volume:	**23,736**
Free float:	**70%**
52-week Range:	**1.39-3.70**

EUR million (ending 30/6)	2014A	2015A	2016E
Total Income	3.096	4.138	5.500
Net (Loss)/Profit	(10.721)	(11.203)	(7.500)
Net loss per share (cents)	(0.49)	(0.48)	(0.25)
R&D costs	4.534	6.204	8.500
Cash increase/(decrease)	5.576	(4.550)	10.000
Cash and marketable sec.	8.509	3.959	10.173

Highlights

- Biofrontera AG (B8F.DE) is a biopharmaceutical company specializing in the development of dermatological drugs and medical cosmetics for the care and treatment of skin and inflammatory diseases. Biofrontera's lead product is Ameluz®, a prescription drug approved for use in Europe and the US for the treatment of mild to moderate actinic keratosis (AK) on the face and scalp in conjunction with photodynamic therapy (PDT). Biofrontera is the first small German pharmaceutical company to receive a centralized approval for a drug developed in-house. The Company intends to start sales of Ameluz in the US as of October 2016.

- Actinic keratosis is a superficial form of skin cancer, and there is a risk that it can spread to deeper layers of the skin and develop into a squamous cell carcinoma, which represents the second most dangerous form of skin cancer. The growth of actinic keratosis as a market has been steadily increasing in Europe, as patient awareness levels rise. In the US, the AK prevalence is estimated to be 6.5% of the population or 58 million people.

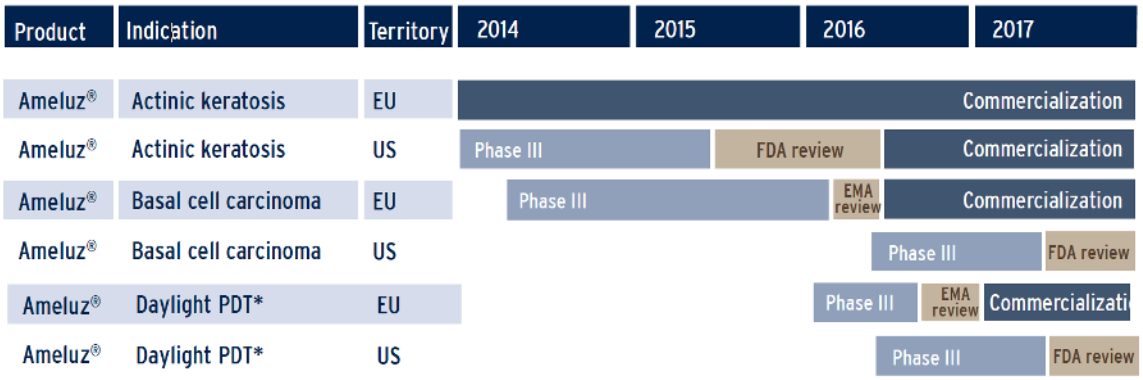
- In December 2011, Ameluz® was approved in Europe for the treatment of AK. This approval has aided the Company's transition from being fully research-oriented towards becoming an integrated pharmaceutical company specializing in dermatology products. Currently, Biofrontera sells Ameluz® via its own sales team to dermatologists in Germany, Spain and the UK. Ameluz is distributed in other EU member states, as well as in Israel and Switzerland, by licensing partners.

- In the past 12 months, the company achieved major milestones with the approval for Ameluz® by the FDA in the US and the announcement of the positive Phase III results of Ameluz in BCC. There are a number of key milestones to focus on in the next 1-6 months, which include: launch of Ameluz® in the US, approval Ameluz for BCC in Europe and the results of a Phase III study with Ameluz and daylight PDT. We also expect that the company will make an IPO on the NASDAQ in 2017H1.

- **Based on our NPV valuation, we believe that Biofrontera is still substantially undervalued at the current share price of EUR 3.00. Using our risk adjusted NPV model, we have increased our valuation of the Company's total value from EUR 120-165 million to EUR 250-300 million, or EUR 8-10 per share with the expectation that the sales of Ameluz will increase rapidly in the US for AK as well as revenues from newly approved indication in BCC and daylight PDT. This represents a substantial upside from the current share price.**

Pipeline: Focus on Ameluz®

After the approval of Ameluz for AK in the US, Biofrontera is focused on the commercial launch of Ameluz in the US in October 2016 and also aims at the approval of Ameluz® in other geographic regions and for other skin diseases. The company already filed Ameluz for BCC in Europe and will conclude a Phase III study of Ameluz in combination with daylight PDT before the end of the year.Each of these developments offer important growth drivers for an accerlation of Ameluz revenues.



Ameluz® approved in the FDA for AK following superior Phase III results

In May 2016, the US FDA granted approval for Ameluz® in combination with the BF-RhodoLED® lamp in the USA. The company had submitted the approval application to the FDA in early July 2015. Ameluz® and BF-RhodoLED® have to be approved as a combination of a drug and a medi-cal device in the USA, making the approval application unusually complex. The FDA performed extensive review and inspections in the months following the application. Unconditional approval was subsequently granted for the lesion-directed and field-directed treatment of mild to moderate actinic keratoses on the face and scalp. This means that Biofrontera has access to the largest healthcare market in the world, and preparations for the planned market launch in October 2016 are well underway. Biofrontera managed to hire the top

sales persons with excellent customer networks from its competitor DUSA as well oher dermatology companies

In the phase III approval trials, Ameluz® showed excellent healing rates and demonstrated significant superiority compared to the approved comparator product, which was tested in parallel. In the first phase III trial in which the drug was combined with an LED lamp, all keratoses were completely removed in 87% of patients treated with Ame-luz®, and in terms of the number of individual keratosis lesions, as many as 96% were completely eradicated (all values stated are ITT (intent to treat) values). In the second phase III approval trial, the effectiveness of Ameluz® was tested in comparison with the approved standard medication. The results of the trial provided evidence that Ameluz® was clearly superior to the competitor product already available in Europe at the time. Based on the average for all lamps used in the treatment, Ameluz® resulted in the complete healing of actinic keratoses in 78% of patients, whereas the competitor product already approved at the time achieved a healing rate of only 64%. With LED lamps, the healing rates increased to 85% for Ameluz® and 68% for the competitor product. The side-effect profile was comparable for both products.

122 Patients, Placebo-controlled, double-blind, multicenter study (DE)

Treatment group (ITT)	Ameluz®		Placebo
	LED narrow band lamp	Broad spectrum lamp	
Patient complete response*	**87% (27/31)**	**53% (26/49)**	**13% (5/40)**
Lesion complete response	**96%**	**70%**	**22%**
Severe erythema**	9.3%	0%	0%
Moderate edema **	32.0%	0%	0%
Moderate induration**	22.2%	0%	0%
Severe pain during illumination***	32.9%	7.1%	1.5%

* Primary endpoint: all of the 4-8 lesions per patient had to be totally cleared
** Application side effects are transient and disappear within one week
*** Results of integrated analysis

- **570 patient, Three-arm study with Ameluz®, Metvix®, Placebo, 3:3:1**
- **Multinational (CH, AT, DE), placebo controlled, observer-blinded study**
- **Ameluz® was significantly superior ($p<0.05$) to Metvix® on the primary endpoint**
- **54% of the Ameluz®* patients required only one PDT with LED lamps**

Clinical end point (ITT)	Ameluz®	Metvix®	Placebo
Complete patient clearance** (all lamps)	78%	64%	17%
Complete lesion clearance (all lamps)	90%	83%	37%
Complete patient clearance with narrow/broad spectrum lamps	narrow 85% broad 71%	narrow 68% broad 61%	narrow 13% broad 22%
Complete patient clearance after 1st PDT (all lamps)	48%	37%	4%

* Development name: BF-200 ALA
** Clinical endpoint: average of all lamps

Clinical end point (ITT)	Ameluz®	Placebo
Complete patient clearance	91% (50/55)	22% (7/32)
Complete lesion clearance	94%	33%
Complete patient clearance after 1st PDT	62%	9%
Complete lesion clearance after 1st PDT	84%	22%

The overall advantages of Ameluz® in terms of effectiveness, handling, user friendliness and cosmetic results, as well as the clear superiority of PDT in the treatment of actinic keratoses, will encourage dermatologists to focus on this treatment option in the future. This will be helped by the expansion of the range of indications to include basal cell carcinoma, which the company is currently striving to achieve, as the vast majority of PDT treatments are for this indication, particularly in Great Britain and Spain.

Ameluz® in development for other indications (BCC and daylight PDT)

Biofrontera has conducted a phase III trial for the extension of the European approval to include the indication basal cell carcinoma (BCC). BCCs are the most common invasive tumors affecting humans, accounting for approximately 80% of all invasive white skin cancers. Around

30% of all Caucasians develop at least one BCC in their life-time, and cases are increasing rapidly worldwide due to increased exposure to UV light. Surgical removal is the most frequent treatment currently used in Germany but this can lead to clearly visible scarring, whereas treatment with photodynamic therapy (PDT), which is an alternative particularly in the treatment of thin BCCs, gives rise to excellent cosmetic results. In the pivotal phase III trial, a total of 278 patients were treated. The trial was conduct-ed under the clinical supervision of Prof. Colin Morton (UK) and Prof. Markus Szeimies (Germany) and was carried out at 27 clinical trial centers in the UK and Germany. Patient recruitment for the trial, which was conducted in direct comparison with the competitor product Metvix®, was completed in May 2015 and the last patient completed the trial in November 2015. The results of the trial have been available since January 2016. The results confirm the company's positive expectations. In the clinical trial, the effectiveness and safety of Ameluz® were compared with that of Metvix®, a drug already approved in the EU for the treatment of BCC. Non-aggressive (superficial and nodu-lar) BCCs with a thickness of up to 2 mm were included in the trial. Ameluz® achieved the complete elimination of all BCCs from the patient in 93.4% of cases compared to 91.8% with Metvix®. There were greater differences in the case of thicker BCCs. With Ameluz®, 89.3% of the nodular carcinomas were completely removed, compared to only 78.6% with Metvix®.

Based on the results of this phase III trial, Biofrontera applied to the European Medicines Agency for approval for the treatment of BCC with Ameluz® in July 2016. The inspection of the application by the agency is expected to take around six months. In June 2016, the first patient was treated in a phase III clinical trial to evaluate the safety and efficacy of Ameluz® in combination with daylight photodynamic therapy (PDT) in comparison with Metvix® for the treatment of mild to moderate actinic keratosis. The head-to-head, randomized, observer-blinded, multi-center trial encompassing around 50 patients is being carried out at eight trial centers in Spain and Germany. All of the participants have between three and nine mild to moderate actinic keratoses (Olsen grade 1 and 2) in each of two comparable treat-ment areas on

the face and/or scalp. The drug for each treatment site will be selected at random. The last patient is expected to conclude treatment by the end of 2016. Daylight PDT offers a convenient and painless alternative to PDT with a specialized lamp. The topical medication is activated by exposure to natural or artificial daylight. Among the many benefits, this saves physician office visit time for the patient. A label extension to include daylight PDT would allow Biofrontera to compete directly with patient-administered topical drugs as well as cryotherapy. We are excited to begin this clinical trial to determine additional methods of effectively treating patients with superficial skin cancer. The primary endpoint of the trial is the total clearance rate for all lesions at each treatment site twelve weeks after treatment. The secondary clinical endpoint includes evaluating the safety of the drug and supplementary efficacy parameters. The trial is being co-led by Dr. Susana Puig, Research Director at the Biomedical Research Institute August Pi I Sunyer and a professor at the University of Barcelona, as the coordinating investigator in Spain and Prof. Thomas Dirschka, founder of the private dermatology practice Centro Derm, as the coordinating investigator in Germany.

Biofrontera Group anticipates that Ameluz® in combination with BF-RhodoLED® will compete in the United States with currently marketed Levulan® Kerastick in combination with the lamp BLU-U®, manufactured and distributed in the United States by Dusa Pharmaceuticals, Inc, a Sun Pharma (India) company. In Europe Ameluz® is sold independently from a light source. Its major competitor is Metvix®, a drug owned and distributed by Galderma. Comparisons with both Metvix® and also Levulan show that Ameluz® has superior efficacy (see also below).

	Ameluz®*	Levulan®**
Efficacy (3 months after last of 1 or 2 PDTs)	~ 90%	~ 65%
Efficacy scalp	~ 82%	~ 50%
P_{12m}*CR	~ 60%	~ 31%
Lamp	red light	blue light
Application	gel ***	liquid
Incubation time	3 hr	14-18 hr
Illumination time	10 mins	16 mins
Skin rejuvenation	Described in label	Not covered by label
Treatment area	field	lesion
Est. revenue in USA (2016)		USD 160 MM****

* all Ameluz® data are with LED lamps only
** all Levulan® data are with BLU-U only
*** enhanced penetration and easier application
**** forecast based on Dusa Pharmaceuticals financial reports

PDT: Fast growing skin cancer treatment

The treatment of actinic keratosis with Ameluz® is based on photodynamic therapy (PDT). In a PDT, the respective lesion is treated by applying a drug topically to the relevant parts of the skin, which then delivers the active substance (ALA = aminolevulinic acid) into the cells, where it is metabolized into a molecule ring that can absorb energy from light at certain wavelengths. By shining light onto the skin the reaction is triggered and will selectively kill tumorous cells. The international treatment directives list PDT as gold standard for the removal of actinic keratosis, particularly for patients with large areas of keratoses. Biofrontera Group offers a drug with such an active substance, Ameluz®, as well as an optimal light source called BF-RhodoLED®.

Source: Biofrontera

BF-RhodoLED® is a lamp designed for photodynamic therapy (PDT). It uses LEDs emitting red light at a wavelength of approx. 635 nm. Light at this wavelength, which is ideally suited for PDT illumination with drugs containing ALA or methyl ALA, is red but is still below the warming infrared range. The BF-RhodoLED® lamp combines a controlled and consistent emission of light at the required wavelength with simplicity, user-friendliness and energy efficiency. The light energy and fan power settings can be adjusted during a PDT treatment session in order to reduce any discomfort caused by the treatment. No other lamp on the market offers comparable power and flexibility. BF-RhodoLED® has been CE-certified since November 2012 and is distributed throughout the EU. For the purpose of sales operations in the USA, the final assembly of the PDT lamp has been transferred to Biofrontera's facilities and performed by the company itself since July 2016, meaning that Biofrontera is the responsible manufacturer from the FDA's perspective.

The availability of topical PDT therapies for the treatment of AK and BCC has now become well established with the availability of DUSA's (now SUN Pharma's) Levulan® (only in the US) and Galderma's Metvix® (only in Europe). Levulan® is FDA approved for the treatment of minimally to moderately thick AK of the face or scalp.

Acceleration in Revenues for Ameluz imminent

With its central European approval, Ameluz® can be sold and distributed in all EU countries as well as in Norway, Iceland, and Liechtenstein. To date, the company has commenced sales in Germany, the UK, Spain, Austria, the Netherlands, Luxembourg, Belgium, Denmark, Sweden, Nor-way, Switzerland, and Slovenia. The drug is available in these countries at a pharmacy retail price of between just under EUR 200 and approx. EUR 270 per 2g tube.

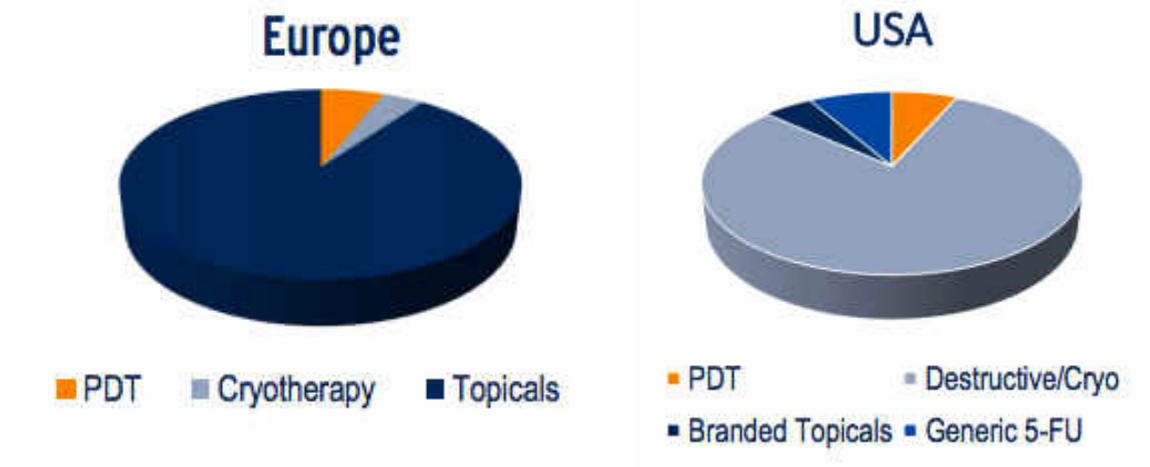
Ameluz® is marketed in Germany and, since March 2015, also in Spain by Biofrontera's own field sales force, and in other European countries using marketing partners. In the UK and Denmark, Biofrontera also started with its own sales operation, and the contract with a local marketing company was terminated in mid-2015.

Distribution to public pharmacies generally takes place via pharmaceutical wholesalers, whereas hospital pharmacies are supplied directly. In addition to regular visits by the field sales force to dermatologists, Biofrontera has presented Ameluz® at the major dermatological conferences both in Germany and in other European countries since it was introduced onto the market. The response from dermatologists has been extraordinarily positive. The market share of Ameluz® in the segment of PDT drugs dispensed by German public pharmacies is consistently over 70%. In spite of this, Ameluz® still only has a small share of the overall market for preparations used to treat actin-ic keratosis, because only approximately 5% of patients are treated with proprietary medicinal products for photodynamic therapy (PDT). Although PDT achieves by far the highest healing rates, the complexity of the treatment and the time required by medical practices to administer it have so far prevented significant market penetration in the statutory health insurance sector. In this sector in Germany, doctors do not usually receive any compensation from statutory health insurance for performing PDT.

The treatment of actinic keratosis using daylight therapy will play an increasingly important role in Europe in the future. The competitor drug Metvix® has already obtained approval and has recently begun to be specifically marketed for daylight application under the brand name Luxerm®. As this removes the need for additional PDT treatment at the physician's office and the drug can be administered by the patient, daylight PDT can be expected to be prescribed far more frequently in the future as an alternative to purely topical creams. Biofrontera is currently conducting a phase III clinical trial of daylight PDT and also expects to obtain approval in 2017H1.

Approval for basal cell carcinoma (BCC) is a prerequisite for the widespread use of Ameluz® in hospitals, as basal cell carcinoma is mainly treated there, whereas this is only very rarely the case for actinic keratosis. This indication plays an essential role for the breakthrough of Ameluz®, particularly elsewhere in Europe, where dermatologists are predominantly based in hospitals. BCCs are the most common invasive tumors that affect humans and account for 50-80% of all invasive white skin cancers. Around 30% of all Caucasians develop at least one BCC in their life-time, and this is a rapidly growing trend around the world due to increased exposure to UV light. BCCs are normally removed surgically, often resulting in substantial scarring. Treatment with photodynamic therapy (PDT) is a highly effective alternative which also leads to excellent cosmetic results. According to a market study published in 2014 by Technavio, the international market for actinic keratosis medications is expected to grow by approx. 8% annually, from approx. USD 546 million to USD 942 million in 2020. During the same period, however, the market for basal cell carcinoma medications is expected to grow at a phenomenal rate, from approx. USD 236 million today to nearly USD 5 billion, because the availability of new drugs (Ameluz® is mentioned in this context) will mean that fewer and fewer patients undergo operations.

AK Market in Europe and US



In Switzerland, both the approval and the reimbursement approval were issued in December 2015. Market launch took place at the beginning of 2016. In Israel, approval for Ameluz® was granted by the Israeli health agency in April 2016 and marketing is expected to start in the next few months.

The contracts with the respective sales partners have been concluded in such a way that Biofrontera has received no down-payment, or only a modest down-payment, and the regional partners purchase Ameluz® from Biofrontera at a price that is linked to their own sales price. Biofrontera's share of the sales price varies considerably depending on the market conditions in each country, ranging from 35% to 60% of net revenue.

Biofrontera has already started preparations for its sales operation in the USA. With the help of a consulting firm specializing in market access and a team of medical advisors, Biofrontera started to analyze the actinic keratosis drug market and the reimbursement mechanisms in the US

healthcare system last year. Biofrontera was also able to draw on the experience of DUSA Pharmaceuticals Inc. with a competitor product already sold and distributed in the USA, Levulan Kerastick®. Sales in the USA will be handled via a wholly-owned subsidiary, Biofrontera Inc., which was established for this purpose back in March 2015. Key posts in the USA have already been filled with highly qualified and experienced local employees, with further appointments to follow in the near future. After approval was granted by the FDA on May 10, 2016, the plan is to launch Ameluz® on the US market in October 2016. As the drug and lamp are approved as a combined product in the USA, the speed of market penetration in the USA will depend in particular on how quickly the BF-RhodoLED® PDT lamp is positioned on the market.

Indication and relevant drug market	Product market potential	Ameluz® market potential
NMSC indications		
AK conventional PDT in Europe	> 15 MM	> 10 MM
AK conventional PDT in USA	> 250 MM	> 150 MM
AK daylight PDT (competing with all topical drugs in Europe)	> 100 MM	> 70 MM
AK daylight PDT (competing with all topical drugs in USA)	> 500 MM	> 200 MM
BCC in Europe	> 200 MM	> 100 MM
BCC in USA	> 700 MM	> 300 MM
Other indications		
cervical cancer (phase III)	> 1 Bn	> 300 MM
warts	> 300 MM	> 50 MM

Milestones: Ticking all the boxes

In the past 12 months, Biofrontera managed to achieve important mile stones with the approval of Ameluz in the US and the positive Phase III with Ameluz in BCC in Europe. For the coming months, there are a number of key milestones to focus on. Each of these milestones can potentially trigger the share price of Biofrontera further.

2015/2016:

- July 2015: NDA submission Ameluz® for AK in the USA ☑
- September 2015: Acceptance to file Ameluz® ☑
- October 2015: 74 day letter from FDA ☑
- 10 May 2016: Final review and approval of Ameluz® in the US ☑
- 2015Q4: Approval of Ameluz® in Israel and Switzerland ☑
- 2015Q4: BCC phase III study results ☑
- **October 2016: Commercial launch Ameluz® for AK in the US**
- 2016Q4: Results Phase III study daylight PDT with Ameluz
- 2017Q1 Approval for BCC in Europe
- 2017Q2: Approval for daylight PDT in Europe
- 2017H1: Scheduled IPO on NASDAQ

Analyst: Marcel Wijma MSc

Marcel Wijma, Chief Research Officer and managing partner, has a longstanding history in financial biotech research. After selling Van Leeuwenhoeck Research (VLR) to SNS Securities in 2006, he established an award winning analyst team in biotech/life sciences at SNS Securities. In 2009, Marcel was awarded by Financial Times/Starmine as being one of the Top-3 biotech analysts in Europe. Later that year, Marcel purchased VLR from SNS Securities after which the company was reconstituted. At VLR, he leads the professional VLR research organisation, which is augmented by selected external financial researchers with a specialisation in Life Sciences. Mr. Wijma has a Masters degree in Financial Economics from Erasmus University in Rotterdam.

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