NOXXON Pharma NV

Germany / Biotechnology
Paris
Bloomberg: ALNOX FP
ISIN: NL0012044762

Initiation of coverage

RATING	**BUY**
PRICE TARGET	**€40.00**
Return Potential	**86.1**%
Risk Rating	High

INNOVATIVE IMMUNOTHERAPY WITH HIGH POTENTIAL IN CANCER

Noxxon Pharma NV is a biotech company with a development stage immunotherapeutic product pipeline focusing on cancer. The company's drug candidates belong to a new class of drugs called Spiegelmers which are synthesized through the company's proprietary discovery platform. Noxxon currently has two innovative immuno-oncology (IO) drugs in phase I and phase II clinical trials that have potential to become the next pillar of cancer treatment. The lead drug candidate NOX-A12 significantly improves efficacy of most cancer treatments including the 'IO rising stars' checkpoint inhibitors and CAR-Ts. NOX-A12 has the ability to treat a broad range of cancers. We estimate sales potential for the product at €2.3bn. Phase II clinical trials in solid tumours are planned to start in Q4/16 or Q1/17. We expect positive news flow from NOX-A12 to add substantial value to Noxxon and have a positive impact on the share price. We initiate coverage of Noxxon with a Buy rating and a €40.00 price target.

NOX-A12 efficacy validated in phase II study for first indication The product has achieved very strong data in phase II trials for blood cancers, multiple myeloma (MM) and chronic lymphatic leukaemia (CLL), delivering objective response rates of 68% and 86% respectively. In our view, these results provide a sound basis for further development.

Attractive market potential and unmet medical need have prompted Noxxon to prioritise a phase II study of NOX-A12 on solid tumours This study will be in advanced pancreatic and colorectal cancer in combination with a checkpoint inhibitor. The pre-clinical data of NOX-A12 on solid tumours in combination with a checkpoint inhibitor are promising in our view.

Buy recommendation Our pipeline valuation model yields a price target of €40.00, which represents a return potential of 86.1% from the current level.

FINANCIAL HISTORY & PROJECTIONS

	2014	2015	2016E	2017E	2018E	2019E
Revenue (€m)	0.03	0.04	0.04	0.00	15.00	0.00
Y-o-y growth	n.a.	72.0%	-7.0%	-100.0%	n.a.	-100.0%
EBIT (€m)	-13.17	-14.83	-9.21	-4.98	8.97	-7.08
EBIT margin	n.a.	n.a.	n.a.	n.a.	59.8%	n.a.
Net income (€m)	-13.80	-16.10	-11.83	-4.98	8.98	-7.07
EPS (diluted) (€)	-47.22	-42.43	-5.90	-2.13	2.97	-2.34
DPS (€)	0.00	0.00	0.00	0.00	0.00	0.00
FCF (€m)	-13.05	-14.40	-10.61	-4.92	8.94	-7.11
Net gearing	n.a.	n.a.	n.a.	n.a.	-105.1%	-107.0%
Liquid assets (€m)	1.53	4.09	2.00	1.08	25.02	17.91

RISKS

Risks include, but are not limited to development, regulatory, competition and financing risks.

COMPANY PROFILE

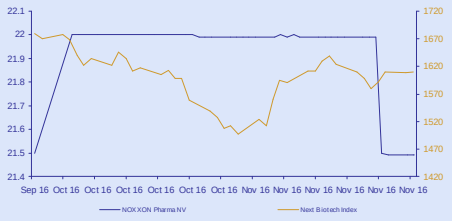
Noxxon Pharma NV is an immuno-therapeutic biotech company focused on the research and development of new drugs to treat cancer based on its proprietary Spiegelmer technology platform. The company is based in Berlin and currently has two drugs in phase I and phase II clinical trials to treat several types of cancer.

MARKET DATA

As of 29 Nov 2016	
Closing Price	€ 21.49
Shares outstanding	2.01m
Market Capitalisation	€ 43.11m
52-week Range	€ 21.49 / 22.00
Avg. Volume (12 Months)	53

Multiples	2015	2016E	2017E
P/E	n.a.	n.a.	n.a.
EV/Sales	1016.5	1092.8	n.a.
EV/EBIT	n.a.	n.a.	n.a.
Div. Yield	0.0%	0.0%	0.0%

STOCK OVERVIEW



COMPANY DATA

As of 30 Jun 2016	
Liquid Assets	€ 1.82m
Current Assets	€ 2.14m
Intangible Assets	€ 0.03m
Total Assets	€ 2.53m
Current Liabilities	€ 10.74m
Shareholders' Equity	€ -11.78m

SHAREHOLDERS

Kreos Capital IV Ltd.	17.8%
TVM Capital GmbH	16.0%
Sofinnova Capital V FCPR	15.8%
Other investors	36.7%
Freefloat	13.7%

Analyst: Christian Orquera, Tel. + 49 (0)30 80 93 96 93

CONTENTS **PAGE**

NOXXON Pharma NV – Executive Summary 1
Investment Case 3
SWOT Analysis 5
Valuation 7
Company Profile 9
Overview 9
The "Spiegelmer" Technology Platform Provides Competitive Advantage 10
Strategy: Developing Immunotherapeutics Against Cancer by Targeting the TME 11
Company History 12
Profile of the Lead Drug Candidate NOX-A12 13
Targeting the Chemokine CXCL12 13
Triple Mode of Action to Fight Cancer 14
Positioned as a Combination Therapy in Cancer Treatment 16
Early but Promising NOX-A12 Data in Advanced Solid Tumours 17
Pre-Clinical Data Proves Mechanism of Action 17
Planned Phase II Trial of NOX-A12 in Colorectal and Pancreatic Cancer 20
Robust Phase II Efficacy Data of NOX-A12 in MM 21
Clinical Development Status 21
Planned Future Clinical Studies of NOX-A12 in MM 22
Targeted Cancer Segments 22
High Unmet Medical Need in Advanced Solid Tumours 22
Pancreatic Cancer is a Fast-Moving-Killer with Few Treatment Options 23
Colorectal Cancer Among the Three Deadliest Cancers 24
MM not Curable, but Treatable 25
Financial History and Outlook 27
Financial History 27
Financial Outlook 28
Management 30
Management Board 30
Supervisory Board 30
Newsflow 32
Shareholders & Stock Information 32
Income Statement 33
Balance Sheet 34
Cash Flow Statement 35
Appendix 36
Positive Phase II Data of NOX-A12 in Chronic Lymphocytic Leukemia (CLL) 36
NOX-A12 in Glioblastoma, Orphan-Drug Indication with Encouraging Preclinical Data 36

INVESTMENT CASE

Proprietary technology platform generates a new highly efficient class of oligonucleotide aptamers called Spiegelmers In therapeutic use, Spiegelmers combine the benefits of the two largest drug classes, biological drugs and small chemical molecules, delivering high binding specificity and a favourable side-effect profile. Noxxon's Spiegelmers can address multiple types of disease-relevant targets including peptides and proteins and most importantly chemokines.

Noxxon's immuno-oncology (IO) pipeline promises an innovative approach in cancer treatment Noxxon has identified novel targets called "chemokines" which are located in the tumour microenvironment (TME) and play a relevant role in the immune system to fight against cancer. Chemokines serve as critical communication agents around the tumour which create a permissive microenvironment for tumour growth and metastasis. By blocking specific chemokines, Noxxon has developed novel therapeutics which make use of the immune system to fight cancer. IO drugs such as Noxxon's are poised to become the next pillar of cancer treatment.

NOX-A12 positioned as combination therapy within cancer treatment NOX-A12 offers a mode of action which is complementary to other cancer treatments including checkpoint inhibitors and CAR-T which are the current "rising stars" of immuno-oncology therapy. Academic studies have shown that tumours manage to keep the immune system's killer T-cells at a distance from the cancer cells. However, the destruction of cancer cells by killer T-cells requires that T-cells physically contact cancer cells and penetrate the tumour environment. This is facilitated by NOX-A12. Based on studies in both animals and patients, Noxxon has demonstrated that the combination therapy of NOX-A12 with other cancer drugs increases the efficacy of these treatments without additional significant side effects.

Due to triple mode of action, lead drug candidate NOX-A12 has the ability to treat broad range of cancers The Spiegelmer NOX-A12 targets CXCL12, a chemokine which regulates three key defence mechanisms of cancer cells. NOX-A12 can destroy the immune privilege of solid tumours, block recruitment of bone marrow-derived "repair" cells to solid tumours and mobilises blood cancer cells hiding in protective niches out of the bone marrow to be killed by the immune system. This drug candidate thus offers potential in three types of cancers - solid tumours, brain cancer and blood cancers.

NOX-A12 has delivered strong phase II data in two blood cancers - multiple myeloma (MM) and chronic lymphatic leukemia (CLL) The demonstrated objective response rates (ORR) of 68% in MM and 86% in CLL are encouraging. Comparable studies for standard of care treatments have shown ORR of 40%-51% in MM and 59% in CLL. These data provide a sound basis for further development of this drug.

Attractive prospects and unmet medical need, prompted switch in NOX-A12 development focus to advanced solid tumours Noxxon has identified advanced solid tumours which do not respond to checkpoint inhibitors, such as pancreatic and colorectal cancer, as a more attractive option for further development of NOX-A12. The fact that these solid tumours do not respond to checkpoint inhibitors - the "rising stars" of IO treatment - offers a unique therapeutic niche for NOX-A12. Furthermore, pre-clinical data has demonstrated that NOX-A12 acts synergistically with checkpoint inhibitors enabling T-cells to penetrate the tumour and kill cancer cells. Noxxon plans to start a phase II clinical trial in Q4/16 or Q1/17. This small clinical trial of 20 patients will provide valuable efficacy data after only 12-18 months, paving the way for a phase III registration study.

Noxxon shares appear significantly undervalued. We initiate coverage with a price target of €40.00 and a Buy recommendation Largely based on NOX-A12, our proprietary risk-adjusted sum-of-the-parts valuation model suggests a fair value for Noxxon of €119.8m or €40.00 per share. We believe our valuation is conservative, considering that the median value of licensing transactions in 2015 for IO drug candidates at a similar development stage was USD354m (€333m) - significantly more than our overall valuation of Noxxon. We believe investors do not yet appreciate the potential in the IO pipeline which Noxxon has developed since its shift in focus towards this area in 2013. During the next twelve months, we expect positive news flow from phase II clinical trials of NOX-A12 on solid tumours as well as on future cooperation agreements to trigger appreciation of Noxxon's share price.

SWOT ANALYSIS

STRENGTHS

- **Experienced management team** Mr. Aram Mangasarian, Ph.D. (CEO) and Dr. Matthias Baumann (CMO) are both highly qualified executives with over 40 years of combined experience in the pharmaceutical industry.
- **Successfully validated proprietary Spiegelmer platform** Spiegelmer technology enables the company to generate a new highly efficient class of molecules called aptamers. In therapeutic use, they combine the benefits of the two largest drug classes, biological drugs and small chemical molecules. The drug candidates generated through the platform have been tested by nearly 3,000 administrations to over 300 humans during the course of phase I and II clinical trials.
- **Unique immune-modulating lead drug candidate with triple mode of action** NOX-A12 has proved to be a highly specific and potent anti-cancer immunotherapeutic agent with a triple mechanism of action which enables use in a wide variety of cancers such as solid tumours (pancreatic cancer, colorectal cancer, lung cancer), glioblastoma (brain cancer) and blood cancers (multiple myeloma and chronic lymphatic leukaemia).
- **Robust phase II data in multiple myeloma (MM)** Noxxon's NOX-A12 phase II trial with 28 patients demonstrated a 68% objective response rate (ORR) for this type of cancer compared to 40%-51% for standard of care treatments.

WEAKNESSES

- **Early stage pipeline in phase I and phase II** Despite promising phase I/II efficacy data from NOX-A12 for MM, the company decided to switch focus to solid tumour indications which offer a higher unmet medical need. The new indication has strong pre-clinical efficacy data, however the response rate has still to be demonstrated on patients in a phase II clinical trial.
- **Limited financial latitude** The company secured €4.2m in a private placement before the listing and plans a further placement of some €3.0-4.0m before Q2/17. These funds will finance operations for 12-18 months including phase II trials of NOX-A12 in pancreatic and colorectal cancer. Potential trials for the drug in further indications such as multiple myeloma, CLL, brain cancer and lung cancer are "on hold" awaiting further financing.

OPPORTUNITIES

- **The progress of NOX-A12 in phase II clinical trials on solid tumours may create significant shareholder value** This small clinical trial with 20 patients will provide significant valuable efficacy data within only 12-18 months, paving the way for a phase III registration study.
- **Development deals with pharmaceutical companies** Noxxon aims to close a cooperative agreement during Q4/16 with a large pharmaceutical company which will provide an approved check point inhibitor for the phase II trials in combination with NOX-A12. A deal of this type will in our view validate the drug's potential and attract attention from the industry for further potential co-development deals.
- **Market potential expansion from further cancer indications and drug candidates** There is robust preclinical and clinical evidence of the high response rate produced by NOX-A12 in many solid tumours and blood cancers. The

successful phase II validation of the product in the first solid tumour types in combination with a checkpoint inhibitor could attract financing (e.g. investors or pharmaceutical companies seeking exposure to immuno-oncology) for development in further cancer types. Furthermore, preclinical data for the second drug candidate, NOX-E36, also suggests potential use in therapy of various solid tumours. These new indications and products hold out the prospect of significant additional market potential.

THREATS

- **Development and regulatory risks** Development of NOX-A12 may progress more slowly than expected. The product may fail to repeat the strong results shown during pre-clinical development (in laboratory and animal models) in the clinical trials on patients. Moreover, even if the drug achieves good results in clinical trials, there is still a risk that the regulatory agencies (FDA and EMEA) do not approve the drug or may request further trials.
- **Competitive risks** Noxxon's pipeline, particularly the lead drug candidate NOX-A12, may face competitive pressure. Several companies, including Bristol Myers, Merck & Co, Roche, Astra Zeneca, Novartis, are developing innovative immune therapies in solid tumours and blood cancers. Any unexpected breakthrough by one or more of these competitors could significantly hit Noxxon's potential revenues.
- **Financing risks** The company will need to raise funds to finance further development of its R&D portfolio. A difficult financing environment or negative results from clinical trials would be an impediment to raising more capital.

VALUATION

Biotechnology valuation is notoriously difficult since there is high risk in the development of the R&D pipeline, which leads to uncertainty in projecting cash flows. We have assessed Noxxon's fair value based on a sum-of-the-parts methodology. We believe this is the most appropriate valuation method for Noxxon because it reflects the implicit risk-adjusted value of every drug candidate in the R&D pipeline. Development risks, including clinical and regulatory risks, are taken into account as are market size and the expected timing of cash flows post-approval for each project.

We have used a risk-adjusted NPV model for each product line and key indication, namely NOX-A12 for the treatment of pancreatic cancer, colorectal cancer, multiple myeloma, glioblastoma (brain cancer) and lung cancer. We believe that NOX-12 has substantial value in further indications (e.g. CLL), and the second drug candidate NOX-E36 also has potential. However, these areas are currently not the main focus of the company and we consider them an upside to our valuation.

During the forecasting process, we adjusted our sales estimates and resulting cash flows for success probabilities to obtain risk-adjusted expected values. We base our probability coefficients on statistical sector studies, such as the Tufts CSDD, and on our own estimates. In this instance, we have derived a 32% probability of success for the drug candidates in phase I (solid tumours) and a 38% success probability for the drug candidates in phase II (multiple myeloma) clinical development. We consider NOX-A12 to be the most important value driver for the company.

Additionally, using the First Berlin methodology, which takes into account company-specific risk factors, we have derived a cost of equity (COE) of 21.1% for Noxxon. Based on a debt ratio of 0.0%, we arrive at a WACC of 21.1%, which we have used to discount projected cash flows. Including projected net cash of €23.1m and a present value of €9.0m for milestone payments, we value Noxxon at €119.8m, which implies a fair value of €40.00 per share on a fully diluted basis.

Using our ten-factor risk analysis, we have set a High risk rating for Noxxon. The main risk factors that we have identified are development, regulatory, competition and financing.

Figure 1: "Sum-of-the-parts" valuation model

Compound	Project[1]	Present Value	Patient Pop	Treatment Cost	Market Size	Market Share	Peak Sales	PACME Margin[2]	Discount Factor	Patent Life[3]	Time to Market
NOX-A12	Pancreatic cancer	€37.9M	94K	€65,913	€6,195.9M	6%	€714M	18%	21%	9	6 Years
NOX-A12	Colorectal cancer	€54.7M	360K	€65,913	€23,729M	3%	€958M	18%	21%	9	6 Years
NOX-A12	Multiple Myeloma	€11.2M	150K	€65,913	€9,887M	2%	€261M	18%	21%	7	7 Years
NOX-A12	Brain & lung cancer	€19.3M	431K	€65,913	€28,409M	1%	€450M	18%	21%	7	8 Years
PACME PV		€123.0M			€68,220M		€2,337M				
Costs PV[4]		€35.3M									
NPV		€87.8M									
Milestones PV		€9.0M									
Net cash (pro-forma)		€23.1M									
Fair Value		€119.8M									
Share Count (fully diluted)		2,996K									
Price Target		€40.00									

1) A project typically refers to a specific indication or, where necessary or relevant, a combination between indication and geographic market

2) PACME (Profit After Costs and Marketing Expenses) reflects the company's profit share on future revenues. This share may be derived in the form of royalties (outsourced marketing/manufacturing) or operating EBITDA margin (in-house model), or some mix of both (depending on the specific parameters of partnership agreements)

3) Remaining patent life after the point of approval

4) Includes company-level R&D, G&A, Financing Costs and CapEx; COGS and S&M are factored into the PACME margin for each project

Source: First Berlin Equity Research

Our sum-of-the-parts model shows that NOX-A12 in the indications colorectal and pancreatic cancer accounts for around 75% of the pipeline value. We estimate this drug is worth approximately €87.8m. We believe this value is quite conservative, since we have seen in- and out-licensing deals on drugs in preclinical through phase II trials within the immuno-oncology field worth much more than this figure. We calculate that the historical median value paid by pharmaceutical companies to license immuno-oncology drugs in late pre-clinical through phase II stage was USD354m (€333m). In table 1 we have summarised select immuno-oncology deals conducted in 2015 where financial information has been disclosed.

Table 1: Selected immuno-oncology deals in 2015

Licensee/licensor	Drug candidates/ targets	Description	Development stage	Total deal value USDm	Value per product USDm
Incyte/ Agenus	GITR, OX40, LAG-3, TIM-3	Checkpoint regulators	Pre-clinical	410	103
Johnson&Johnson/ Aduro	Undisclosed, currently two	LADD Immunotherapy	Late pre-clinical	817	408
Bristol Myers/ CytomiX	Four undisclosed programmes	IDO inhibitor	Pre-clinical	1.024	256
Genmab/ BioNTech	undisclosed programmes	Immunotherapeutics	Pre-clinical	undisclosed	300
Sanofi/ Regeneron	REGN2810	PD1 inhibitor	Phase I-II	1,800	1,800
Astra Zeneca/ Inovio Pharmac.	INO-3112	Cancer vaccine	Phase I-II	727	727
Johnson&Johnson/ Alligator Biosc.	ADC-1013	CD40 stimulant	Late pre-clinical	700	700
Sanofi/ BioNTech	mRNA programmes	mRNA immunotherapeutics	Pre-clinical	1,500	300

Source: First Berlin Equity Research, Companies

Estimation of price and sales potential

Pricing of comparable drugs such as checkpoint inhibitors (Yervoy USD85k p.a., Nivolumab USD130k p.a.) suggests that a sales price of USD70k (€65.9k) per patient per year should be achievable for NOX-A12. Our price estimate conservatively implies a discount to the peer drugs on the basis that NOX-A12 will be used in combination with a check point inhibitor. It may be challenging to achieve such a premium price for two drugs. In addition, we have assumed that due to the aggressiveness of the diseases, Noxxon will try to move rapidly from last-line to first- and second-line treatment.

We have assumed that Noxxon can achieve a market share in the range of 1-6% in the different indications. Based on statistical data on the incidence of the different cancer types (see table 4, page 22), we estimate sales potential of €2.3bn for NOX-A12. We believe our estimate is realistic, considering that 2020 consensus sales projections for peers' IO drugs such as Yervoy, Opdivo or MK-3475 amount to some USD3.4bn-3.6bn (€3.2bn-3.4bn) each, These drugs each target 2-3 cancer indications.

COMPANY PROFILE

OVERVIEW

Founded in 1997 and headquartered in Berlin, Noxxon Pharma NV is a clinical stage biotech company with a broad product pipeline focused on cancer diseases. The company's product candidates are synthesized through a proprietary discovery platform and belong to a new class of drugs called Spiegelmers.

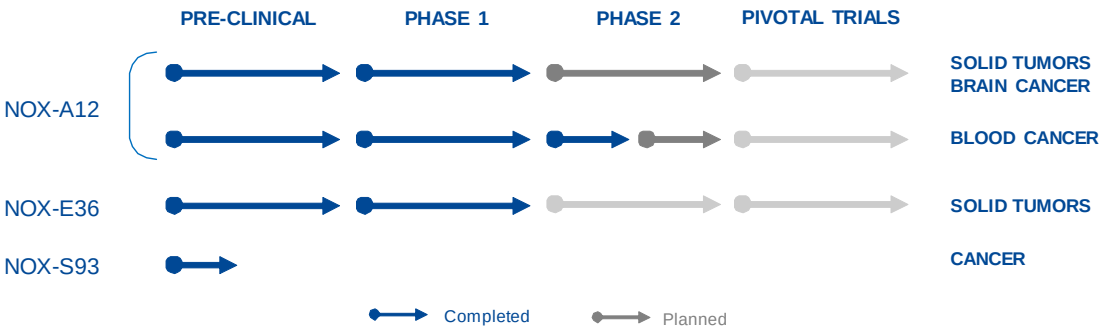
The company currently has two drugs in phase I and phase II clinical trials. The lead drug candidate, NOX-A12, is in phase II for blood cancers, multiple myeloma (MM) and chronic lymphatic leukaemia (CLL). NOX-A12 achieved strong data in phase II trials for MM and CLL, delivering objective response rates (ORR) of 68% and 86% respectively. In our view, these results provide a sound basis for further development.

Noxxon has decided to prioritise development efforts of NOX-A12 in two solid tumour cancers with high unmet medical need, pancreatic cancer and colorectal cancer. Glioblastoma/brain cancer may be added if additional funding of some €5-6m can be secured. Preclinical data for NOX-A12 in solid tumours looks promising. The company believes that the medical need in solid tumours is much higher than blood cancers. Furthermore, these tumours do not respond to checkpoint inhibitors, the "rising stars" of immuno-oncology therapy. The synergistic mode of action of the drugs creates an attractive market opportunity for combination therapy. We therefore share management's view that a focus on solid tumours will create greater shareholder value.

NOX-E36, the second drug candidate, is in phase I clinical development. The product's target, CCL2/MCP-1, is implicated in the spread of cancer and immune privilege of tumours. The company is conducting preclinical investigations to gain more data for future phase II trials.

In this report we focus on the lead drug candidate NOX-A12 and the three main indications, pancreatic, colorectal cancer and multiple myeloma, which are the main value drivers of the company.

Figure 2: Snapshot of the clinical stage R&D pipeline focusing on cancer



Source: First Berlin Equity Research, Noxxon Pharma NV

Euronext listing on 30 September 2016 opens doors for access to new funds In order to further finance pipeline development, the company decided to go public on the Alternext Paris Exchange. Noxxon placed 2.0m shares at €21.50, valuing the company at €43.0m. Noxxon shares were listed after €4.2m had been raised through a private placement mainly with its current shareholders. In the course of the listing, the sole debt holder Kreos agreed on the conversion of all of its €9.6m debt into equity, thereby becoming Noxxon's main shareholder (>21% after full conversion). However, €2.6m of this will only become effective if the company raises at least the same amount in equity before the end of March 2017. We

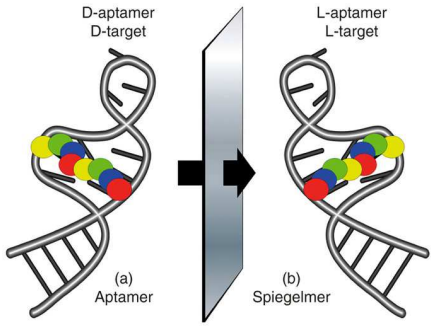
therefore anticipate that Noxxon will conduct a capital increase of some €3.0-4.0m within the next few months.

THE "SPIEGELMER" TECHNOLOGY PLATFORM PROVIDES COMPETITIVE ADVANTAGE

The proprietary platform enables the company to generate a new highly efficient class of molecules called Spiegelmers. Spiegelmers are oligonucleotide aptamers based on short segments of nucleic acids. In therapeutic use, they combine the benefits of the two largest drug classes, biological drugs and small chemical molecules. Their characteristics include the affinity and specificity of biologic drugs such as monoclonal antibodies. This translates into a favourable side-effect profile. Meanwhile, similarly to small molecules, they benefit from ease of manufacturing since they can be chemically synthesised thereby keeping production costs low (especially in comparison to highly complex, costly and difficult to scale biological drugs).

Furthermore, Spiegelmers are biologically stable and non-immunogenic. They are built on a backbone of mirror-image RNA or DNA (L-stereoisomers). By leveraging this "mirror-image chemistry", Spiegelmers solve two key problems that have limited the development of aptamers thus far. Firstly, aptamers quickly degrade in the body. Secondly, they have a high immunogenicity (recognized by the immune system triggering an immune reaction). Thanks to the mirror-image production technology of Spiegelmers, they are not recognized by enzymes called nucleases found throughout the body and are therefore not degraded in the blood. In a similar way, the immune system, which normally reacts to foreign RNA or DNA, does not recognize Spiegelmers making them immunologically passive. Spiegelmers are injectable compounds that can be administered intravenously or subcutaneously.

Figure 3: Spiegelmer's technology platform



Source: First Berlin Equity Research, Noxxon Pharma NV

Noxxon's Spiegelmer technology platform can address multiple types of target such as small molecules, peptides and proteins (e.g. chemokines). The platform has been fine-tuned to address chemokines and hormone peptides as binding targets. Through this technology platform the company has generated its first two drug candidates. The proprietary platform uses an in vitro screening process called SELEX (Systematic Evolution of Ligands by Exponential Enrichment).

Although aptamers were discovered more than 25 years ago, interest from the pharmaceutical community is only arising now. In our view, the main reason for this is the discovery of novel targets such as chemokines or peptide hormones. These targets act as key regulators in various areas, such as in the tumour microenvironment biology (TME), inflammation, tissue invasion and iron regulation, and therefore have high relevance for several diseases including cancer. Unfortunately, these novel targets can not be properly addressed by existing small molecules and monoclonal antibodies (Source: Haringman et al., 2006; Sandhu et al., 2013), producing an opportunity for molecules such as aptamers.

Noxxon's aptamers have shown encouraging results in accurately addressing such promising targets. This underscores the uniqueness of the technology platform.

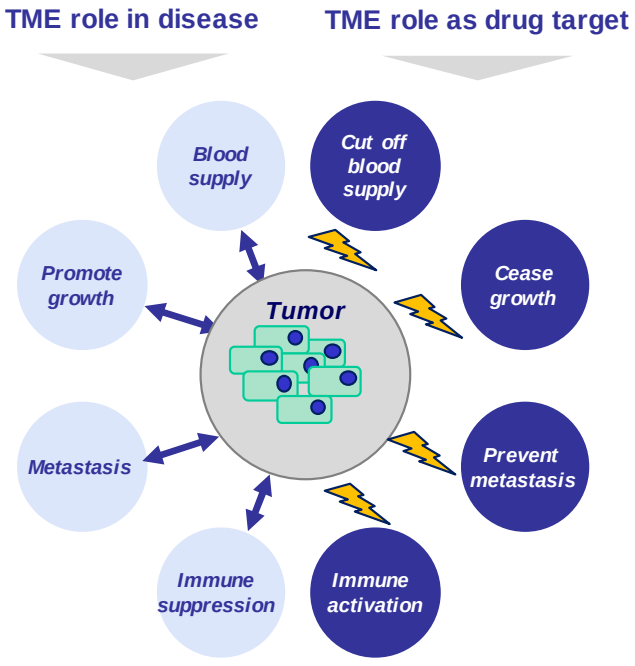
The Spiegelmer technology platform has been successfully validated. The drug candidates generated through the platform have been tested by nearly 3,000 administrations to over 300 humans in the course of phase I and II clinical trials. Spiegelmers have so far been shown to be biologically active and generally well-tolerated without relevant side effects.

STRATEGY: DEVELOPING IMMUNOTHERAPEUTICS AGAINST CANCER BY TARGETING THE TME

Noxxon has identified novel targets called chemokines which are located in the tumour microenvironment (TME) and play a relevant role in the immune system. Based on these findings, the company decided in 2013 to focus all its efforts on developing immunotherapeutic drug candidates against cancer. The basic concept of cancer immunotherapy or immuno-oncology (IO) is to utilize certain parts of the immune system to fight against the disease. This can be done by stimulating or supporting the immune system to attack cancer cells or by introducing immune system components into the body. Within the past few years research and development into cancer treatment has shown an increased focus on IO.

Evidence in IO indicates that the TME plays a critical role in all aspects of cancer biology, such as a cancer's growth, angiogenesis (blood vessel recruitment and growth utilised by the tumour to access blood supply), metastasis (spread of the tumour to other locations in the body) and progression. (Source: The importance of the tumour microenvironment in the therapeutic management of cancer, Pottier et.al, 2015). The TME is defined as the cellular environment in which cancer cells exist. This includes the surrounding blood vessels, immune cells, fibroblasts, signalling molecules, such as chemokines, and the extracellular matrix.

Figure 4: Role of the Tumour microenvironment (TME)



Source: First Berlin Equity Research, Noxxon NV

The TME can create a local immunosuppression which prevents tumours from being eliminated by the immune system. In addition, the TME can inhibit chemotherapy and immunotherapy-induced cell death. This is for example the case with so called “checkpoints” within the TME such as PD-1 and CTLA-1 which can downregulate immune response. In a similar way certain chemokines, such as Noxxon’s CXCL12, serve as a critical communication agent around the tumour to create a permissive microenvironment for tumour growth and metastasis.

COMPANY HISTORY

Table 2: Key milestones in company’s history

Time	Corporate events
1997	Founded in Berlin, Germany as NOXXON Pharma AG.
1997-1999	€21m raised from venture capital funds. Optimization of the drug discovery process to identify Spiegelmers (mirror-image oligonucleotides).
2000	€21m venture capital financing round closed (Merlin Biosciences/DEWB Deutsche Effecten- und Wechsel-Beteiligungsgesellschaft AG).
2002	Operative and research focus on a smaller number of key projects.
2006	Research partnership with Pfizer Inc.
2007	€37m invested in the company by a syndicate of investors led by TVM Capital and Sofinnova Partners, enabling clinical development of the company’s pre-clinical assets.
2009	First successful administration of a Spiegelmer to a healthy volunteer, first-in-man studies for the lead drug candidates, NOX-A12 and NOX-E36
2010	€35m invested in Noxxon by new lead investor NGN Capital and syndicate members.
2011	Start of phase I clinical trials for the drug candidate NOX-H94.
2012	Product candidates NOX-A12 and NOX-E36 have shown been shown to be generally safe and well-tolerated after up to four weeks of treatment. Beginning of first NOX-A12 phase II studies in blood cancers.
2013 - 2015	€25m invested in the company by the current investors in order to finance further development of the lead drug candidates. Clinical proof-of-concept trials for NOX-A12 and NOX-E36. This data set provided a basis for future strategy including which products and indications to prioritize in later stage clinical development. The company refocused its business on cancer treatments.
2016	The company changed its structure and name to Noxxon Pharma NV, based in the Netherlands, which facilitated the listing on the Pan-European Stock Exchange, Euronext

Source: First Berlin Equity Research, Noxxon NV

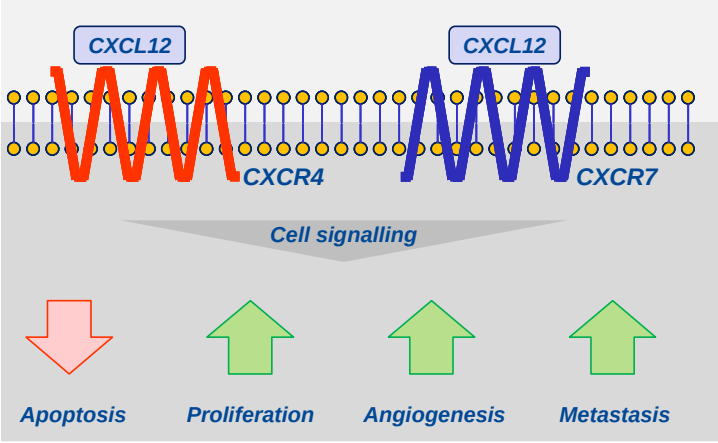
PROFILE OF THE LEAD DRUG CANDIDATE NOX-A12

TARGETING THE CHEMOKINE CXCL12

Noxxon's lead product candidate NOX-A12, also known as olaptesed pegol, is a Spiegelmer that targets CXCL12, a key chemokine in the tumour microenvironment (TME) that is normally involved in cell migration (Source: Guo et al., 2015). CXCL12, also known as stromal cell-derived factor-1 (SDF-1), is secreted by supporting cells in the bone marrow and lymph nodes which maintain blood-forming stem cells and white blood cells in these tissues. CXCL12 has two distinct receptors, CXCR4 and CXCR7. Recent scientific findings show that CXCL12, which binds to both its specific receptors, plays an important role in the TME (Source: Liu et al., 2014, Azab et al., 2014). As can be seen in figure 5, CXCL12, through its receptors CXCR4 and CXCR7, affects tumour progression by four mechanisms:

- Reducing tumour cell death (apoptosis)
- Promoting tumour proliferation
- Promoting new blood vessel formation
- Promoting metastasis

Figure 5: Chemokine CXCL12 cell signalling in cancer



Source: First Berlin Equity Research, Noxxon NV

These findings validate Noxxon's therapeutic approach in addressing the full CXCL12 axis and not only one of the receptors. We note that leading pharmaceutical players such as Bristol Myers, Sanofi and Eli Lilly all target only the receptor CXCR4. We therefore believe Noxxon's drug candidate is superior to its peers. For example, pre-clinical data shows that NOX-A12 is 1,000 times more potent than Sanofi's drug Mozobil/plerixaflor which is a drug that has been approved and marketed for mobilising stem cells into the blood stream for collection and transplantation in patients with NHL and multiple myeloma.

Table 3: Immuno-oncology therapies in development targeting CXCR4

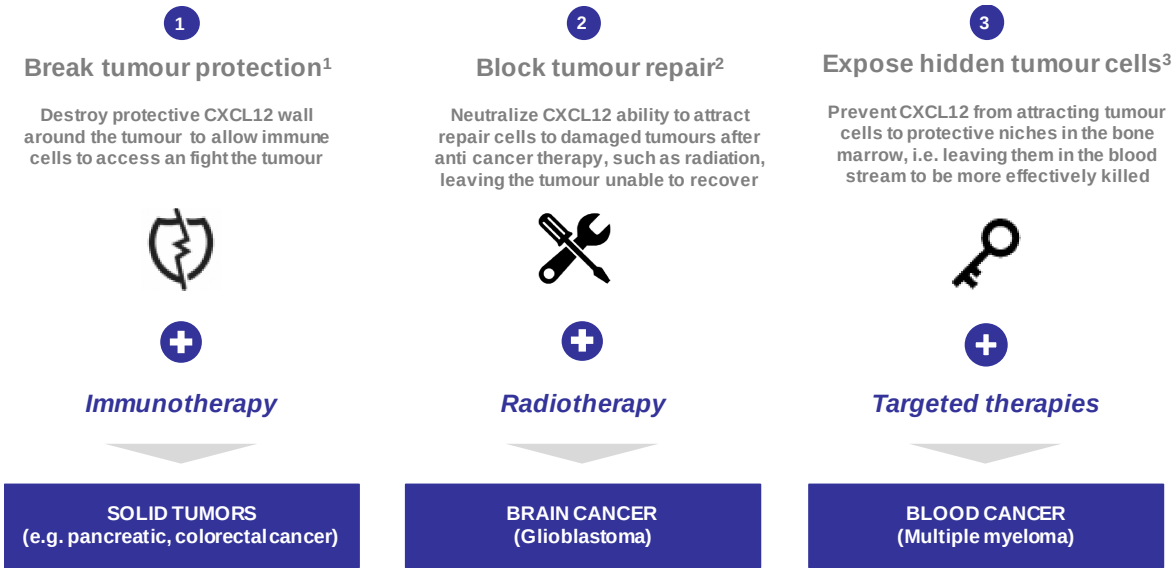
Company	Drug candidate	Description	Development stage	Selected indication
Bristol Myers	ulocluplumab	monoclonal antibody	Phase I-II	AML, solid tumours
Sanofi	Mozobil/plerixaflor	small molecule	Phase I-II	Multiple Myeloma
Elly Lilly	LY-2510924	Peptide	Phase II	Metastatic RCC, lung cancer
X4 Pharmaceuticals	X4P-001	small molecule	Phase I-II	RCC
BiolineRX	BL-8040	peptide	Phase II	AML, pancreatic
TaiGen	burixafor	small molecule	Phase II	Stem cell mobilisation
Polyphor	Pol-6326	peptide	Phase I	Metastatic breast cancer

Source: First Berlin Equity Research, Noxxon NV, ClinicalTrials.gov

TRIPLE MODE OF ACTION TO FIGHT CANCER

Preclinical data and results from two phase II trials provide firm evidence of the ability of NOX-A12 to effectively target the CXCL12 chemokine within the TME and hence destroy the immune privilege of solid tumours, block recruitment of bone marrow-derived "repair" cells to solid tumours and mobilise cancer cells from protective niches in blood cancers. We give an overview of NOX-A12 mode of action below:

Figure 6: NOX-12 triple mode of action



1. Feig, C. et al. PNAS (2013); Fearon, D. Cancer Immunol. Research (2014; Poznansky, M., Nature America (2000)
2. Liu, S. et al. Neuro-Oncology (2013); Castro, B. & Aghi, M. Neuro-Oncology (2014)
3. Rocarro et al. Cell reports (2014); Marasca, R. & Maffei, R., Blood (2014)

Source: First Berlin Equity Research, Noxxon NV

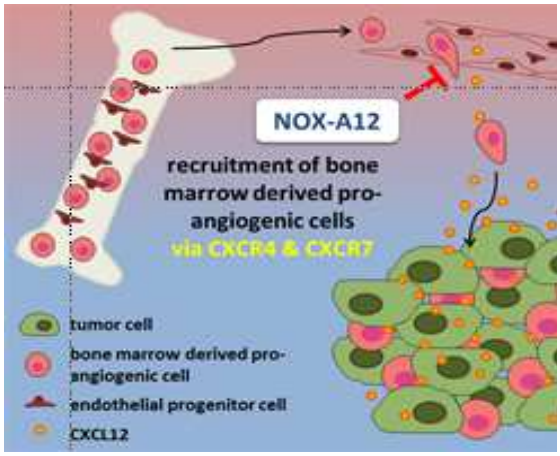
Based on the properties of the drug's target CXCL12, Noxxon has identified three major areas in which NOX-A12 can modulate the TME with an anti-CXCL12 approach. The drug candidate will create significant medical benefit to patients with: solid tumours, brain cancer and blood cancer.

I) Breaking the "protecting wall" in solid tumours CXCL12 mediates an immune suppressive effect in solid tumours. The chemokine binds to cancer cells and excludes the immune system's killing T-cells through a mechanism that depends on signalling by the CXCL12 receptor, CXCR4. Hence it forms a biochemical wall around the tumour, preventing killer T-cells from entering the inner tumour region. Two preclinical studies conducted in mice models, Feig 2013 and Fearon 2014, showed that blocking CXCR4 signalling can permit killer T-cells to penetrate the tumour. We analyse the results of these studies in detail in the chapter "pre-clinical data on solid tumours", on page 18.

II) Blocking tumour repair in brain cancer (glioblastoma) CXCL12 is believed to help the repair of tumour cells damaged by radiation or chemotherapy by attracting pro-angiogenic cells from the bone marrow. In studies conducted by the company's collaborators at Stanford University using animal models of glioblastoma, irradiation was shown to induce the recruitment of bone marrow-derived cells to form blood vessels and generally support tumour growth. NOX-A12 blocks recruitment of bone marrow-derived

"repair" cells to solid tumours damaged by initial therapy thereby preventing the resumption of their growth. This mechanism is particularly relevant in brain cancer.

Figure 7: NOX-A12 blocks tumour repair cells[1]

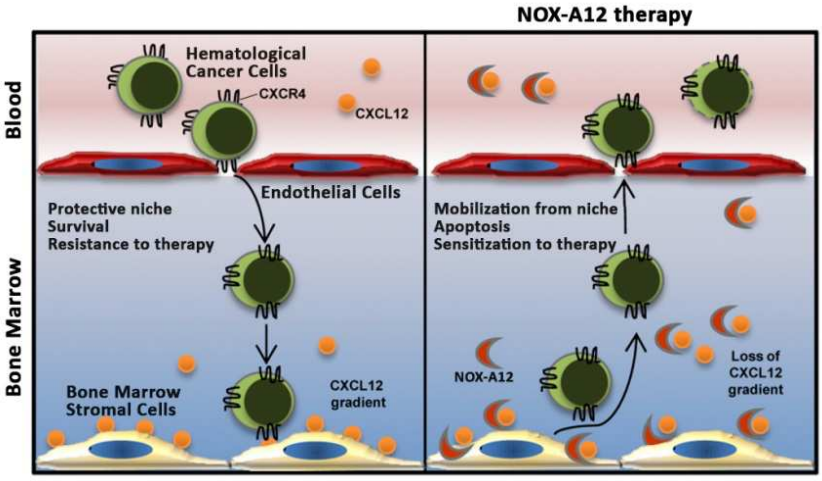


Source: First Berlin Equity Research, Noxxon NV

A preclinical study showed that treatment with NOX-A12 in combination with radiation leads to tumour shrinkage to undetectable levels. Other treatments (e.g. clinically used combination of temozolomide and radiation) were able to stabilize the growth of these tumours but did not result in significant size reduction. After treatment was stopped, only 2 out of 6 rats treated with NOX-A12 and radiation had tumour recurrence.

III) Exposing hidden tumour cells in multiple myeloma (MM) The chemokine CXCL12 enables blood cancer cells to migrate to the bone marrow. In bone marrow, blood cancer cells are more difficult to target and kill through existing treatments (Source: Guo et al., 2015; Roccaro et al., 2014). By blocking CXCL12 and eliminating the gradient, NOX-A12 triggers these blood cancer cells to migrate out of the bone marrow into the blood stream, where they can subsequently be more easily targeted by other treatment, as illustrated on the right-hand side of figure 8. Noxxon believes that inhibiting CXCL12 in blood cancer, such as MM, can provide significant benefit in combination with other therapies.

Figure 8: Role of CXCL12 in haematological cancers and the effect of NOX-A12



Source: First Berlin Equity Research, Noxxon

In addition to the role of the chemokine CXCL12, in certain leukaemic cells CXCL12 is itself a survival factor for tumour cells, which suggests that inhibition of CXCL12 may also have a

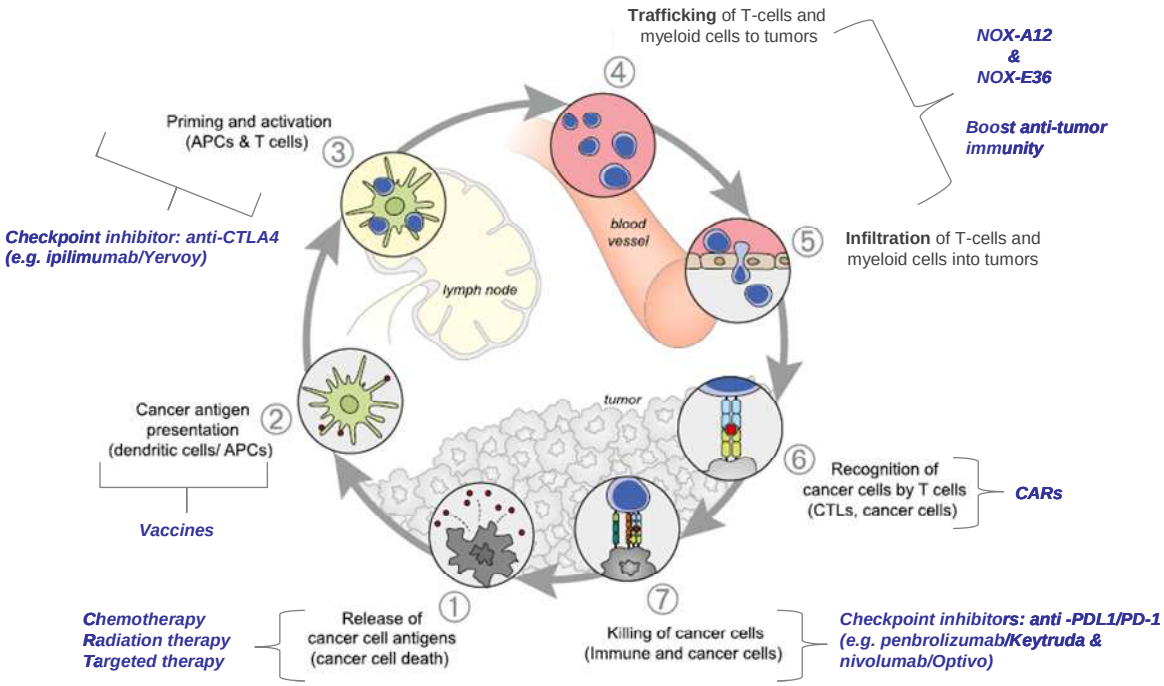
direct anti-tumour effect in some leukaemias. It has also been shown that CXCL12 can recruit regulatory T-cells to the bone-marrow, a key component of the microenvironment for haematological cancers, and these regulatory T-cells may form an immunosuppressive niche (Source: Dürr et al., 2010). A recent study reported that CXCL12 secreted by bone marrow stroma cells can attract CXCR4-expressing MM cells to the bone marrow niches and protect them from chemotherapy- and immunotherapy- induced cell death (Source: Roccaro et al., 2014).

By blocking CXCL12, NOX-A12 offers a novel and complementary approach aimed at the signalling of a key chemokine, which is thought to play an important role in tumour cell growth, survival, migration, drug resistance, as well as in bone destruction.

POSITIONED AS A COMBINATION THERAPY IN CANCER TREATMENT

The development of immunotherapy has achieved a relevant inflection point in the race to find a cure for cancer. For the first time, durable responses in a subset of cancer patients have been reported for a broad range of drug candidates such as checkpoint inhibitors (e.g. Hamid et al, 2013). Leading cancer experts recognize the large potential of checkpoint inhibitors (blocking the target that the tumour is using to turn off the immune system) for long-term elimination of cancer cells (Source: Lee et.al 2015, Guo et al., 2015). However, many patients still do not respond, leading researchers to explore new mechanisms of boosting the immune system, or slowing down the cancer's ability to evade it. According to leading scientists Chen and Mellman, in order that an anti-cancer immune therapy can lead to effective and durable killing of cancer cells, several events within the cancer immunity cycle (see figure 9 below) have to take place.

Figure 9: NOXXON drugs address key steps (4 & 5) in the cancer-immunity cycle that synergize with other drugs such as checkpoint inhibitors (7)



Source: First Berlin Equity Research, Noxxon, Chen & Mellman 2013 Immunity

Most drugs target only one of these events, which is why combination therapy using drugs with different pathways and acting synergistically can produce superior results. In view of these synergies, cancer experts in the scientific community and the pharmaceutical industry

see the future of cancer therapy in immuno-oncology combinations. The leading pharmaceutical companies such as Bristol Myers, Roche, Merck, Pfizer, Astra Zeneca, are aggressively combining immunotherapeutic drugs from their own pipelines while also partnering with competitors' products to expand their immune-oncology combination pipelines (Source: Immuno-oncology combinations, Reuters Cortellis competitive Intelligence).

NOX-A12 offers a complementary mode of action to other cancer treatments including the current standards of care (such as chemotherapy and radiotherapy) and the latest "rising stars" of immuno-oncology therapeutics such as checkpoint inhibitors and CAR-T approaches. The destruction of cancer cells by killer T-cells, requires not only that cancer-specific T-cells are activated and recognize cancer cells (e.g. with help from checkpoint inhibitors), but also that these T-cells physically contact cancer cells and penetrate the tumour environment (e.g. as NOX-A12 does). Many academic studies have demonstrated that exclusion of killer T-cells from the vicinity of cancer cells correlates with a poor long-term clinical outcome.

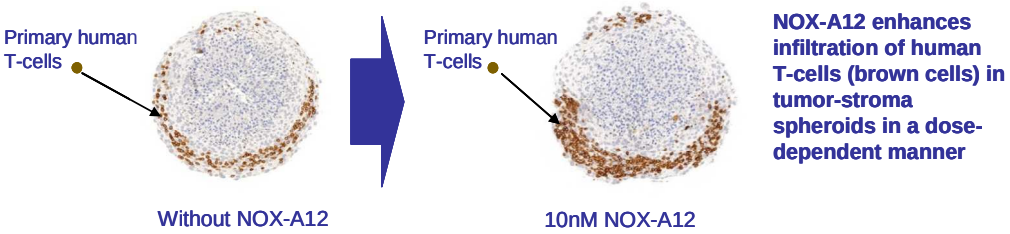
As a result, NOX-A12 is positioned to become a "must-have" combination partner for a wide range of cancer treatments. Based on work in animal models and patients, Noxxon has demonstrated that a combination therapy of cancer compounds with NOX-A12 increases the efficacy of these treatments without adding significant side effects (Source: Guo et al., 2015; Lazennec & Richmond, 2010; Würth et al., 2014; Bouyssou et al., 2015).

EARLY BUT PROMISING NOX-A12 DATA IN ADVANCED SOLID TUMOURS

PRE-CLINICAL DATA PROVES MECHANISM OF ACTION

In-vitro: NOX-A12 increases access of T-cells to the tumour by up to 3 times Noxxon has investigated the influence of NOX-A12 T-cell infiltration into tumour tissue by using a three-dimensional cell culture (tumour-stroma spheroid model) that mimics the complexity of the TME. In the study, a tumour cell line (colorectal or pancreatic cancer) together with CXCL12 were allowed to form in a cell culture over two days. These cell cultures were then incubated with different concentrations of NOX-A12 and then human T-cells isolated from the blood were added. In the next step cell cultures were harvested and T-cell infiltration was assessed (see figure 10).

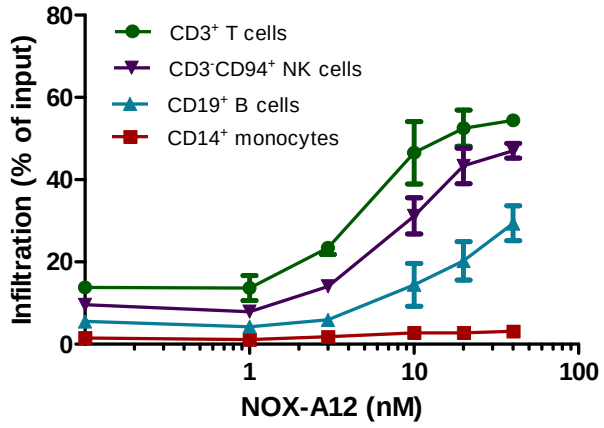
Figure 10: NOX-A12 increase T-cell access to the tumour



Source: First Berlin Equity Research, Noxxon (Zboralski, D., 2016).

NOX-A12 increased the number of T-cells in the tumours depending on the dose. At the optimal concentration of 10 nanomolar of NOX-A12, analyses revealed a two- to three-fold increase in T-cell infiltration of the tumour. As shown in the figure below, enhanced T-cell infiltration in the presence of NOX-A12 was corroborated by immuno-histochemistry.

Figure 11: NOX-A12 promotes T-cell and NK cell infiltration in a solid tumour model

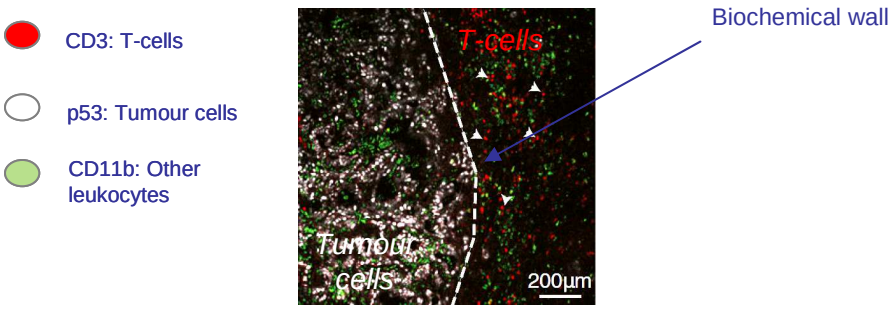


Source: First Berlin Equity Research, Noxxon NV

In this model system, NOX-A12 increased T-cell migration into the tumour. In addition, NOX-A12 alone increased T-cell infiltration and activation. In our view, this data confirms the underlying hypothesis that the inhibition of CXCL12 by NOX-A12 will be able to increase the efficacy of anti-cancer therapies, such as checkpoint inhibitors and CAR-T approaches, by enabling the direct contact of T-cells with solid tumours.

CXCL12 regulates a"biochemical wall" that protects tumour cells from attack by T cells CXCL12 mediates an immune suppressive effect in cancer cells. Hence it forms a biochemical wall around the tumour, excluding killer T-cells to enter the inner tumour region as seen in the figure below. Two preclinical studies in mice models, Feig in 2013 and Fearon, in 2014, suggest that the mechanism of immune suppression may effect a more fundamental step involving the interaction of killer T-cells with the tumour than the currently highly successful PD-1/PD-L1 immune checkpoint drugs do.

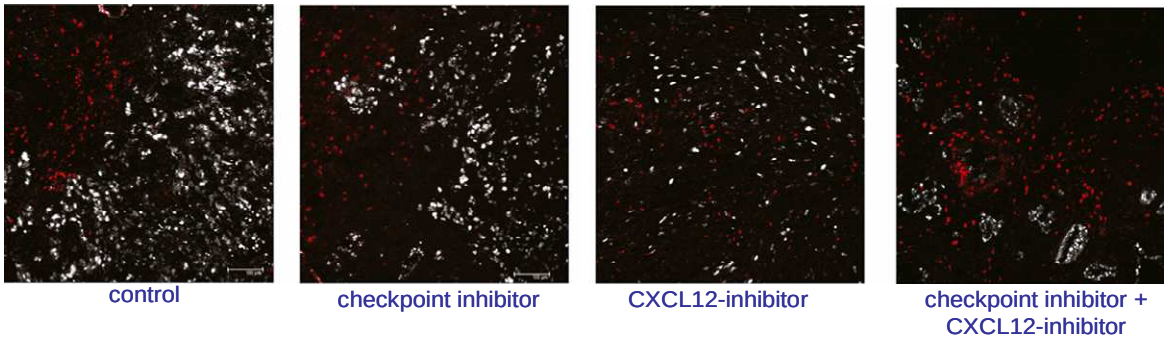
Figure 12: Tumour protection via CXCL12 "biochemical wall"



Source: First Berlin Equity Research, Noxxon NV, Publications Feig at al 2013 and Fearon at al 2014

The above-mentioned studies also show that NOX-A12 (CXCL-12 inhibitor) was capable of destroying tumour immune privilege by breaking down the biochemical wall to unleash the full potential of tumour immunotherapy. This mechanism is relevant in advanced solid tumours that are being addressed by immunotherapy.

Figure 13: Therapeutic comparison in a murine pancreatic cancer model



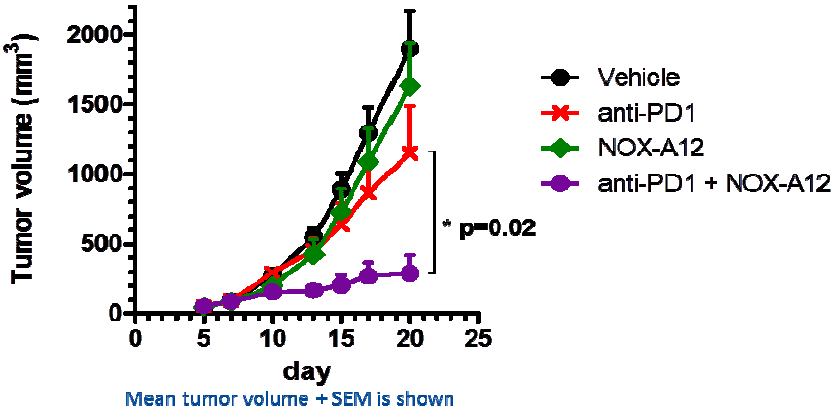
Source: First Berlin Equity Research, Noxxon NV, Publications Feig at al 2013 and Fearon at al 2014

The Fearon study compared the effects of the PD-L1 checkpoint-inhibitor alone, a CXCL12-inhibitor alone, and the PD-L1 checkpoint-inhibitor in combination with the CXCL12-inhibitor in a murine pancreatic cancer model (see figure 13). The study showed that the anti PD-L1 alone had no effect, whereas the CXCL-12 inhibitor increased the accumulation of T cells in the tumour area slowing tumour growth. Moreover, the combination therapy of anti-PD-L1 and CXCL12-inhibitor acted synergistically inducing rapid T-cell accumulation among cancer cells and greatly diminishing cancer cells and the tumour volume.

A further in-vitro study demonstrates synergies between NOX-A12 and checkpoint inhibitor Both NOX-A12 and a PD-1 inhibitor were added to a tumour model at different doses. The highest doses almost doubled T-cell activation. A detailed quantitative analysis revealed that NOX-A12 and the PD-1 inhibitor act synergistically (Source: Noxxon, Zboralski, 2016).

In-vivo study establishes rationale of the combination NOX-A12+checkpoint inhibitor Noxxon recently generated recently new data studying the combination NOX-A12 with checkpoint inhibitors in an animal model. The company used a colon cancer model which is only poorly responsive to checkpoint inhibition and analysed various therapies in a tumour growth study. As illustrated in the figure below, the combination of NOX-A12 plus the checkpoint inhibitor anti-PD-1 was the only therapy that showed a statistically significant reduction in tumour growth compared to the other groups tested. The combination therapy allowed stable or reduced tumour size in the majority of animals.

Figure 14: Combination therapy NOX-A12 + checkpoint inhibitor significantly reduces tumour growth in animal model of colon cancer

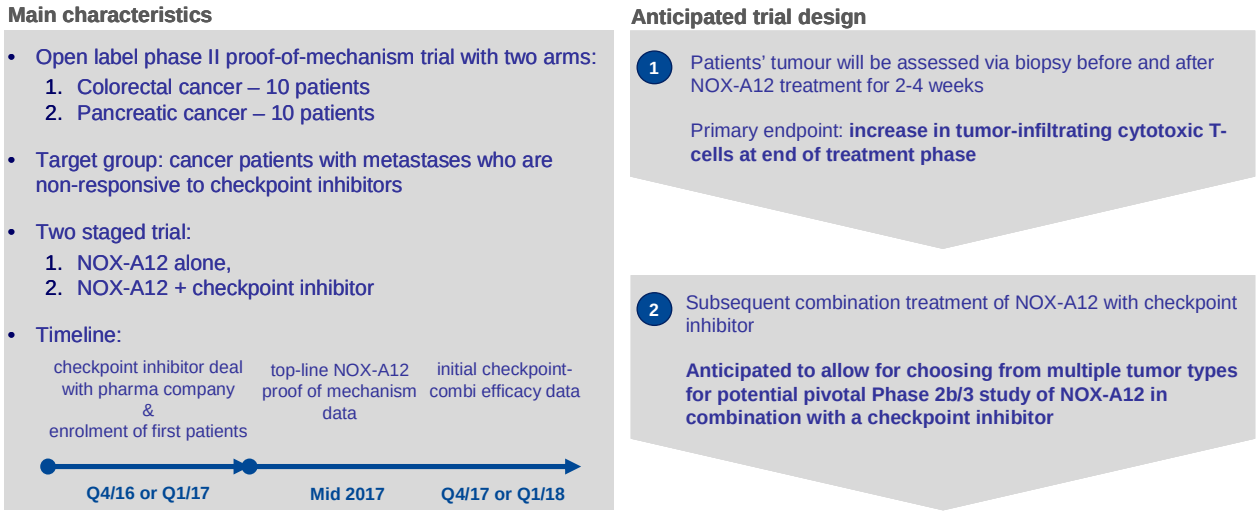


Source: First Berlin Equity Research, Noxxon NV

PLANNED PHASE II TRIAL OF NOX-A12 IN COLORECTAL AND PANCREATIC CANCER

A nonstandard phase II trial Noxxon intends to conduct a "proof-of-mechanism" study of NOX-A12 in two types of advanced solid tumours: colorectal and pancreatic cancer. This open label phase II trial will include approximately 10 patients for each indication, 20 patients in total.

Figure 15: Overview of the planned phase II trial



Source: First Berlin Equity Research, Noxxon NV

Noxxon expects to enrol the first patient in this phase II trial in Q4/16 or Q1/17. First top-line data evaluating NOX-A12 alone and initial data for the combination with a checkpoint inhibitor will likely be published in mid-2017 and Q4/17 respectively. A key enrolment criterion for the trial will be accessibility to the tumour, since a main goal during the first stage will be to evaluate the effect of NOX-A12 on the number of tumour-infiltrating killer T-cells. In order to be able to measure the number of infiltrating T-cells, the company will conduct a biopsy to collect cancer tissue specimens before and after the application of NOX-A12.

Secondly, the company plans to continue NOX-A12/checkpoint inhibitor combination treatment. This second part of the study has the potential to provide additional information on the safety and efficacy of NOX-A12/checkpoint inhibitor combination in a small number of cancer patients. Since participating patients will have tumours at an advanced stage, which are metastised and non-responsive to checkpoint monotherapy, even a small proportion of responders would be of high relevance. In addition, in these populations, the anticipated low number of responders required to gain regulatory approval can translate into short development timelines. Hence, the company believes a positive outcome of this proof-of-mechanism trial would be sufficient to support the conduct of a registration pivotal double-blind, randomized trial of NOX-A12 in combination with a checkpoint inhibitor against placebo.

Noxxon is negotiating a potential collaboration agreement The company is currently aiming to collaborate with a pharmaceutical company which owns a marketed checkpoint inhibitor. The pharmaceutical company would provide Noxxon with the checkpoint inhibitor for the company's clinical trials free of charge. The deal is expected to be closed during Q4/16. In our view this milestone is very important for Noxxon, since a deal with a leading pharmaceutical company in the cancer field will validate the potential of NOX-A12.

ROBUST PHASE II EFFICACY DATA OF NOX-A12 IN MM

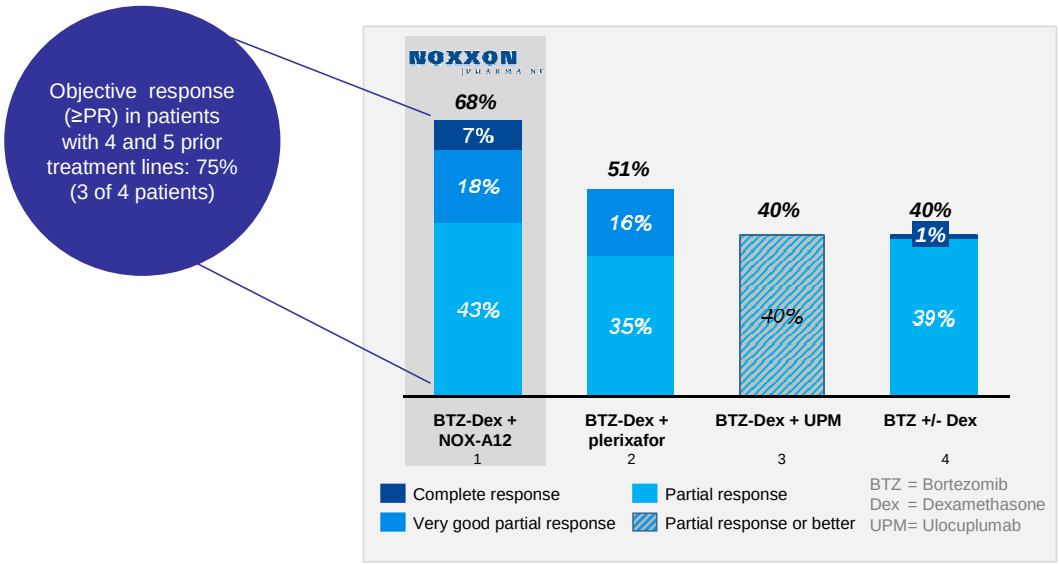
CLINICAL DEVELOPMENT STATUS

Phase I clinical trials in healthy volunteers A first-in-human phase I clinical trial (open and uncontrolled) to determine safety and tolerability was conducted in 48 healthy subjects. The purpose was to examine their response to single ascending doses of NOX-A12 ranging from 0.05 to 10.8 mg/kg. All administered doses were well tolerated, without producing significant side effects. In line with CXCL12 inhibition, NOX-A12 induced a dose-dependent mobilisation of white blood cells and hematopoietic stem cells into the peripheral blood.

Phase II clinical trial showed superior efficacy for the combination NOX-A12/Velcade Noxxon completed a multi-center, open-label, single-arm phase II clinical trial evaluating the safety and preliminary efficacy of a combination of NOX-A12 with Velcade (bortezomib) and dexamethasone, known as VD, in 28 previously treated patients with MM. VD is a standard of care regimen for MM patients in this particular stage of the disease.

Although patients in the phase II trial had advanced and refractory disease, these patients achieved an objective response rate of 68%. Two patients (7%) obtained a complete response, five patients (18%) obtained a very good partial response and an additional twelve obtained a partial response (43%), as shown in the figure below.

Figure 16: Response rates in a phase II clinical trial of NOX-A12 in MM compared to relevant comparator trials



Source: First Berlin Equity Research, Noxxon NV

Interestingly, NOX-A12 showed an overall response rate of 75% (3 of 4) in late-stage patients who had already received 4 or 5 prior lines of treatment. Generally, such patients have lower overall rates of response.

Noxxon conducted a comparison of the results with results of established treatments in comparable open-label clinical trials. A study using the combination Velcade (BTZ/bortezomib) +CXCR4 antagonist Mozobil (plerixafor) showed an overall response rate

of 51%. A second study using Velcade with or without dexamethasone, resulted in an overall response rate of 40%. A third relevant study using the combination Velcade+CXCR4 antagonist UPM/Ulocuplumab showed an overall response rate of 40%. None of the trials showed complete responses.

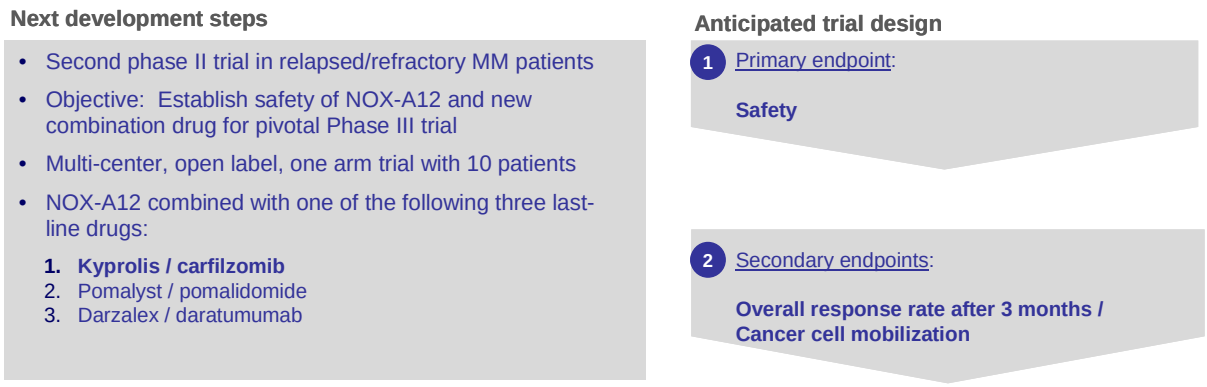
The overall safety profile of NOX-A12 was also positive, since the product did not generate additional adverse events and there were no treatment related changes in liver enzymes.

PLANNED FUTURE CLINICAL STUDIES OF NOX-A12 IN MM

Based on the promising top-line results of the phase II clinical trial in MM and on the input that the company has received from the regulatory agencies in the United States, Germany and Sweden, Noxxon has designed a clinical development plan to reach market approval.

First, Noxxon plans to complete a second single-armed, open-label, phase II trial with escalating doses of NOX-A12 on top of one of three potential combination compounds, Kyprolis, Pomalyst or Darzalex. The trial will include 10 relapsed and refractory MM patients. The company believes positive data from this trial would be sufficient to progress NOX-A12 into the pivotal phase III trial.

Figure 17: Overview of the planned second phase II trial



Source: First Berlin Equity Research, Noxxon NV

Assuming a positive outcome in this trial, the company will then likely conduct a single pivotal double-blind, placebo-controlled phase III trial with the selected combination partner drug both in Europe and the United States. Based on preliminary discussions with European and U.S. regulators the company believes that a potentially pivotal trial would include approximately 400 patients, half of whom will be treated with NOX-A12 or placebo on top of the chosen combination drug partner. The primary endpoint would be progression-free survival.

TARGETED CANCER SEGMENTS

HIGH UNMET MEDICAL NEED IN ADVANCED SOLID TUMOURS

Cancer is a leading cause of death and generates among the highest costs to healthcare systems around the globe. Due to low specificity, traditional chemotherapy usually applied to treat cancer also kills healthy cells, is poorly tolerated and has therapeutic and safety limitations. Tumour resistance is a further obstacle to effective treatment. Current research is therefore focusing on treatment approaches that limit damage to healthy cells and more specifically target cancerous cells such as growth factor inhibitors, anti-angiogenesis factors and immune therapy.

However, the unmet medical need in certain solid tumours remains very high. When the cancer is not detected before it spreads outside of the location in which it arises, this greatly increases the risk for patients that treatment will not be successful. The five-year survival statistics for solid cancers highlight a clear need for better treatments for these patient groups.

Table 4: Overview survival rates for solid tumours

Cancer type	Five year survival rate	Median duration of survival	Est. new cases in US & EU-5
Pancreatic cancer	1-3% (patients stage IV*)	6-12 months	94k
Colorectal cancer	11% (patients stage IV*)	6-24 months	360k
Brain cancer (glioblastoma)	<10%	15 months	25k
Lung cancer	1-2% (patients stage IV*)	8 months	409k

**Stage IV cancer is defined when metastasis have spread to other parts of the body.*

Source: First Berlin Equity Research, Noxxon, U.S. National Cancer Institute's SEER database, American Cancer society, Roche,

Noxxon has identified advanced solid tumours that do not respond to checkpoint inhibitors, such as pancreatic cancer and some 85% of colorectal cancers, without defective mismatch repair (Source: Brahmer et al., 2012, Sunshine & Taube 2015, and Kerr & Midgley 2010), as a highly attractive option for further development of NOX-A12 based on the very high unmet medical need.

PANCREATIC CANCER IS A FAST-MOVING-KILLER WITH FEW TREATMENT OPTIONS

Little progress achieved in the treatment of pancreatic cancer so far Pancreatic cancer is one of the few cancers for which survival has not improved substantially over nearly 40 years. This cancer is expected to be the second deadliest malignancy in the USA by 2020 (Garrid-Laguna et al, 2015). It is an aggressive and deadly disease with few symptoms until the cancer is advanced. The vast majority of pancreatic cancer cases are diagnosed in late stage; more than half of patients are diagnosed once the disease has metastasised. As a result, this type of cancer is one of the most difficult to treat and this is reflected in the low survival rate (see table 4). Only about 25% of patients survive more than one year after diagnosis. The average life expectancy after diagnosis with metastatic disease is just three to six months.

Surgical resection is the only potentially curative treatment for this disease. Unfortunately, because of the late presentation, only 15-20% of patients are candidates for pancreatectomy. Furthermore, prognosis is poor, even after a complete resection. The disease recurs in approximately 80% of these patients, all of whom will die within five years of recurrence. In the case of non-surgical candidates, chemotherapy, possibly with radiation or targeted therapy, is considered first-line therapy. However, the outcome is very poor. Enrolling in clinical trials is a good alternative for these set of patients.

Competitive environment in pancreatic cancer The focus of our analysis of competitor's development programmes is on immunotherapies. We believe this category of products has good prospects of producing a substantial improvement in survival rates in pancreatic cancer and becoming the backbone of treatment (similar to what checkpoint inhibitors have achieved in skin and lung cancer). Our overview on table 5 shows that Bristol Myers and Astra Zeneca have a leading role in immuno-oncology in this cancer setting, with two drug candidates in phase III and phase II/ phase II-III respectively. We note that the majority of

products are checkpoint inhibitors, which act synergistically with NOX-A12. We therefore believe that NOX-A12 can further improve the results achieved by these products.

Table 5: Immuno-oncology therapies in development for pancreatic cancer

Company	Drug candidate	Description	Development stage
Bristol Myers	Opdivo/nivolumab + Yervoy/ Ipilimumab	PD1 inhibitor + CTLA-4 inhibitor	Phase III
Bristol Myers	Yervoy	CTLA-4 inhibitor	Phase III
Astra Zeneca	durvalumab	PD-L1 inhibitor	Phase II-III
Astra Zeneca	tremelimumab	CTLA-4 inhibitor	Phase II
Merck & Co	Keytruda/pembrolizumab	PD1 inhibitor	Phase II
Aduro Biotech	CRS-207 Gvax	Vaccine + vaccine	Phase II
BiolineRX	BL-8040	CXCR4 inhibitor	Phase II
NewLink Genetics	indoximod	IDO inhibitor	Phase I/II
Daichi Sankyo	PLX 7486	CSF1R inhibitor	Phase I
Astra Zeneca	Pexidartinib	CSF1R inhibitor	Phase I

Source: First Berlin Equity Research, ClinicalTrials.gov, Aids Insight

COLORECTAL CANCER AMONG THE THREE DEADLIEST CANCERS

Incidence and mortality of CRC Colorectal cancer (CRC) is the third most common cancer worldwide, with an estimated incidence of more than 1.4m new cases per year. An estimated 694,000 deaths from CRC occur worldwide every year, accounting for 8.5% of all cancer deaths and making it the fourth most common cause of death from cancer (Source: Ferlay et all, GLOBOCAN -Cancer Incidence and Mortality Worldwide). Diet plays a major role in the aetiology of the disease as under 10% of cases can be linked to genetic predisposition. Surgery is the mainstay of curative therapy but about 50% will relapse due to the presence of micro-metastases. Without any treatment the median survival after detection of metastases is less than 12 months.

Treatment of CRC Standard therapeutic first-line treatment for colorectal cancer is currently chemotherapy with either Irinotecan + 5-FU + Leucovorin (known as FOLFIRI regimen and mainly used in the US), or Oxaliplatin + 5-FU + Leucovorin (known as FOLFOX regimen and mainly used in Europe). The third chemotherapeutic alternative is Oxaliplatin + capecitabine (known as XELOX or CAPOX). In most cases it is recommended that the VEGF-blocker bevacizumab (Avastin), which inhibits tumour vascularisation and growth, is administered together with chemotherapy. If the cancer returns, second-line treatment entails administration of another of the three chemotherapeutic regimens, in combination with a VEGF-blocker such as bevacizumab (Avastin), aflibercept (Zaltrap), and ramucirumab (Cyramza). Further first-line treatment options are EGFR-blockers such as cetuximab (Erbitux) and panitumumab (Vectibix) in combination with chemotherapy in a subset of patients with RAS wild-type mutation. In patients without the mutation, the EGFR-blockers are prescribed as a second or third line therapy. Additional second or third line treatment options are targeted therapeutic drugs such as ziv-aflibercept (Zaltrap) or regorafenib (Stlvarga) (Source: Uptodate.com, cancer.net, Merck, Roche).

Potential of immuno-oncology in CRC and competitive environment About 85% are known not to have increased mutational load due to DNA mismatch-repair deficiencies. Leading scientists believe that these tumours are likely to be susceptible to immunotherapeutic targeting, because such tumours stimulate the immune system. Results of a trial using the checkpoint inhibitor Keytruda published last year in The New England Journal of Medicine, reinforce this hypothesis (Dung T.Le et al, 2015). We therefore see high potential for immuno-oncology in this disease.

For reference, we have identified potentially competing immuno-oncology drug candidates in development for metastatic colorectal cancer. These drug candidates target 2nd and 3rd line therapy with relapse patients. The majority of the drug candidates are checkpoint inhibitors. Roche, Bristol Myers and Merck & Co have the lead in this area.

Table 6: Immuno-oncology therapies in development for CRC

Company	Drug candidate	Description	Development stage
Roche	Tecentriq /atezolizumab	PD-L1 inhibitor	Phase III
Bristol Myers	Yervoy/ipilimumab	CTLA-4 inhibitor	Phase III
Merck & Co	Keytruda/pembrolizumab	Anti-PD1	Phase III
Astra Zeneca	durvalumab	PD-L1 inhibitor	Phase II
Bristol Myers	Opdivo/nivolumab	PD1 inhibitor	Phase I-II
Aduro Biotech	CRS-207 Gvax	Vaccine + vaccine	Phase II
Astra Zeneca	pexidartinib	CSF1R inhibitor	Phase I
Roche	emactuzumab	CSF1R inhibitor	Phase I
Astra Zeneca	tremelimumab	CTLA-4 inhibitor	Phase I

Source: First Berlin Equity Research, ClinicalTrials.gov, Aids Insight

MM NOT CURABLE, BUT TREATABLE

MM is the second most common blood cancer This disease is characterised by the overproduction and accumulation of monoclonal plasma cells, a type of white blood cell normally responsible for producing antibodies in the bone marrow. The median age for an MM patient at diagnosis is about 69 years and as the average age of the population increases, the incidence of this disease is expected to increase. The majority of patients with MM relapses and eventually becomes drug-resistant, or refractory, to treatments.

Dynamic development in the therapeutic treatment of MM Improvements in treatment have improved the five-year survival rate for MM patients from 30% to over 45% during the past 20 years (Source: SEER Cancer Statistics Review, 2015). However, the five-year survival rate is still the lowest of the blood cancer diseases. New treatments include autologous stem cell transplantation, proteasome inhibitors, such as bortezomib (Velcade) and immunomodulatory drugs or drug candidates, such as lenalidomide (Revlimid), which are currently the backbone of MM treatment.

The development pipeline in the industry is crowded A wide variety of new drugs or drug candidates are already approved or are being evaluated in relapsed or refractory patients. For advanced MM patients, chemotherapy is the most widely used frontline option plus bone marrow transplant if the patients are eligible. For relapsed patients, Amgen's new proteasome inhibitor carfilzomib (Kyprolis) in combination with Revlimid and dexamethasone has demonstrated superior efficacy to drugs approved so far. The product increased progression-free survival (PFS) by 50% to 18.7 months against Valcade and may well become the new standard of care. Additionally, in 2015 we see four new drugs of high relevance which received approval in the US or Europe for patients who have received at least one to three prior therapies:

- the CS1 antibody elotuzumab (Empliciti) in combination with Revlimid and dexamethasone which has shown data comparable to Kyprolis with better dosing (once vs. twice a week)
- the proteasome inhibitor ixazomib (Ninlaro) in combination with Revlimid and dexamethasone which extended PFS by 40% to 20.6 months

- the antibody daratumumab (Darzalex) for patients who have received at least three prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent, reduced risk of disease progression by 65% compared to Revlimid.
- the immunomodulatory drug pomalidomide (Pomalyst/Imnovid) in combination with dexamethasone, for patients who have received at least two prior treatment regimens, including both Revlimid and Velcade. The drug increased PFS by 100% to 3.6 months.

Competitive environment in MM There are currently many clinical trials underway testing the safety and efficacy of new therapies for MM. We give an overview of the development programmes testing cell- or antibody-based immuno-oncology therapies in table 7.

Table 7: Immuno-oncology therapies in development for MM

Company	Drug candidate	Description	Development stage
Bristol Myers	Opdivo/nivolumab	PD1 inhibitor	Phase III
Merck & Co	Keytruda/pembrolizumab	PD1 inhibitor	Phase III
Novartis	CTL019	CAR-T	Phase II
Celyad	CAR-NKG2D	CAR-NK	Phase I-II
Astra Zeneca	Durvalumab	PD-L1 inhibitor	Phase I-II
Medivation	Pidilizumab+Revlimid	PD1 inhibitor + VEGF inhibitor	Phase I-II
Roche	Tecentriq /atezolizumab	PD-L1 inhibitor	Phase I
Bluebird Bio	BB2121	CAR-T	Phase I

Source: First Berlin Equity Research, ClinicalTrials.gov, Aids Insight

MM seems less attractive for Noxxon compared to solid tumours Despite significant efforts and the advent of new treatment options, MM remains a difficult-to-treat disease characterized by repeated treatment cycles, high cost and unmet medical need. However, Noxxon believes that this need is lower than the need in those advanced solid tumours which do not respond to checkpoint inhibitors, such as colorectal and pancreatic cancers. Moreover, Noxxon will still need to conduct a second phase II clinical trial in MM before NOX-A12 is phase III-ready. Noxxon believes that the next big value-adding step in NOX-A12 clinical development in MM will be completion of the pivotal phase III study itself. However, in advanced solid tumours, significant value can be created rapidly with the small proof-of-concept phase II study.

FINANCIAL HISTORY AND OUTLOOK

FINANCIAL HISTORY

Income Statement H1/16

Noxxon's financial statement is typical of an early stage R&D biotech company. The company has generated small-scale revenues from the sale of oligonucleotides to its scientific collaborators. The collaborators use these chemical compounds for research purposes. The revenues are not part of the strategic focus of the company and we expect them to be discontinued in the future. Revenues increased to €32k in H1/16 (up from €23k in H1/15) due to higher demand for oligonucleotides.

In July 2015 the company implemented a restructuring process to focus on the lead drug candidate NOX-A12. These strategic measures lead to downsizing of the total headcount from approx. 50 in 2015 to 26 full time employees by 31 July 2016. As a result, general and administrative expenses declined significantly to €2.4m in H1/16 (H1/15: €3.4m). General and administrative expenses also benefited from lower legal and consulting expenses of €1.5m (H1/15: €2.0m) for preparation of the capital increase and stock exchange listing. Research and development expenses declined by 18.7% to €3.2m (H1/15: €3.9m) mainly due to effects of the restructuring process. EBIT came in at €-5.4m (H1/15: €-7.3m). The net financial result increased to €-2.6m (H1/15:€-0.6m) and reflects growth in debt financing. Noxxon reported a net loss of €8.0m, (H1/15: €7.9m) corresponding to €-16.02 per share (H1/15:€-23.32).

Table 8: Income Statement H1/16 and H1/15 (selected items)

All figures in EUR '000	H1/16	H1/15	*Delta*
Revenue	**32**	**23**	***39%***
General and administrative	2,395	3,439	*-30%*
Research and development	3,197	3,933	*-19%*
EBIT	**-5,357**	**-7,342**	***-27%***
Net income / loss	-8,010	-7,932	*1%*
EPS (€)	-16.02	-23.32	*-31%*

Source: Noxxon NV

Balance Sheet H1/16

At the end of H1/16, Noxxon's equity position decreased to €-11.8m from €-7.0m at the end of FY/15. The company's cash position decreased to €1.8m (FY/15: €4.1m). Short and long term financial liabilities with Kreos Kapital increased to €11.1m in H1/16 (FY/15: €8.9m). As is typical of a biotech company, Noxxon is highly dependent on raising new funds to finance operations and further pipeline development. In H1/16 Noxxon raised €3.3m from existing investors. In addition, prior to the listing on 30 September 2016, the company raised a further €4.2m from existing investors and converted €7.0m out of Kreos' €9.6m debt outstanding. The remaining debt of €2.6m with Kreos can be converted if Noxxon manages to raise at least the same amount through a capital increase.

Table 9: Balance Sheet H1/16 and FY/15 (selected items)

All figures in EUR '000	H1/16	FY/15	*Delta*
Liquid funds	1,815	4,093	*-56%*
Net debt	9,266	4,787	*94%*
Total Assets	2,532	6,041	*-58%*
Equity	-11,784	-7,032	*68%*
Equity ratio	*-465%*	*-116%*	-

Source: Noxxon NV

Cash Flows H1/16

In H1/16, cash flow from operating activities came in at €-5.2m (H1/15: €-7.0m) and cash flow from financing activities amounted to €2.9m (H1/15: €7.4m) with the decrease being due to lower financing activity through debt and equity. Thus net cash flow came in at €-2.3m (H1/15: €0.4m).

Table 10: Cash flow statement H1/16 and H1/15 (selected items)

All figures in EUR '000	H1/16	H1/15	*Delta*
Operating cash flow	-5,211	-6,957	*-25%*
Cash flow from investing	0	-7	*n.a.*
Cash flow from financing	2,933	7,388	*-60%*
Net cash flow	-2,278	424	*-637%*

Source: Noxxon NV

FINANCIAL OUTLOOK

We have modelled non-core revenues of €40k in 2016, but have assumed that the company discontinues selling nucleotides from 2017 on due to the focus of resources on the core business. With regard to upfront and milestone payments, it is difficult to predict the conditions under which Noxxon will be able to negotiate. These will depend on the quality of the phase II trials data and on management's preference for upfront payments or royalties. We have assumed the company will finance further pipeline development until a sustainable breakeven is achieved in 2023 through a combination of raising funds from investors and upfront payments from licensing to pharmaceutical partners. We also assume that the phase II trial will deliver positive data. We project that the out-licensing of NOX-A12 will lead to upfront payments in 2018 of €15m for EU phase III development and distribution rights in the pancreatic/colorectal indication. We expect that Noxxon will still complete phase II trials of NOX-A12 in further indications, in order to maximise royalty conditions. The pharmaceutical partner will be responsible for the expensive phase III trials.

Our 2016 projections were the baseline for our projections going forward. Considering the company's successful restructuring and downsizing measures over the period 2015-2016, we project OPEX to decline from €14.9m in 2015 to €9.2m in 2016 and €5.0 in 2017. The company's plan foresees that the headcount will fall from 26 full-time employees in 2016 to 10-12 as of Q1/17. We expect that the new structure will remain stable over the next few years. We have projected that OPEX will slightly increase to €7.5m in 2020 due to higher research and development expenses. Our OPEX curve assumes that the company will spend €26.8m in research and development in the period 2016-2020. In our view this budget is sufficient to complete phase II clinical trials for NOX-A12 in all five relevant cancer indications (pancreatic, colorectal, MM, lung and glioblastoma).

Table 11: Revenue, EBIT, net income forecasts

All figures in EUR '000	2014	2015	2016E	2017E	2018E	2019E	2020E
Revenue	25	43	40	0	0	0	0
Upfront & milestone payments	0	0	0	0	15,000	0	0
OPEX	13,191	14,873	9,247	4,980	6,030	7,083	7,538
EBIT	-13,166	-14,830	-9,207	-4,980	8,970	-7,083	-7,538
Net income / loss	-13,798	-16,102	-11,834	-4,984	8,975	-7,072	-7,531

Source: First Berlin Equity Research

Our financial forecast assumes that Noxxon will be able to successfully convert financial debt of €2.6m with Kreos Capital by carrying out a capital increase of €4.0m during Q1/17. As a result, we forecast no financial debt on Noxxon's balance sheet by 2017 year end and going forward. Based on current low interest rates, we project a net financial result close to zero in the forecasting period.

Going forward, we model revenue and net earnings until 2028. We have taken typical industry development timeframes into consideration. We expect the company to generate first revenues and achieve break-even in 2023 due to the marketing of NOX-A12 in its first two indications, pancreatic and colorectal cancer. We estimate Noxxon will need cash in the range of €38m to fund operations (mainly research and development projects) over the next 6 years until revenues begin in 2023. We projected that the company will raise capital of €15.0m in 2018 and €8.0m in 2022, which combined with the above-mentioned upfront payment covers the company's funding requirement until 2023.

MANAGEMENT

MANAGEMENT BOARD

Aram Mangasarian, Ph.D., is the CEO of Noxxon. He joined the company in May 2010 as Chief Business Officer. Mr. Mangasarian brings over fifteen years of experience in biotechnology and pharmaceutical business development to Noxxon. Prior to joining Noxxon, Mr. Mangasarian served as Vice-President of Business Development for Novexel from October 2005 to March 2010. In this position he closed the licensing agreement for North American rights to the NXL104 beta-lactamase inhibitor, now known as avibactam, with Forest Laboratories in January 2008. Aram Mangasarian, Ph.D. was a member of the team that negotiated the acquisition of Novexel by AstraZeneca in March 2010. From May 2000 to October 2005, Mr. Mangasarian served in a variety of roles at ExonHit Therapeutics (now Diaxonhit), eventually heading the business development function as Vice-President. He concluded a number of important agreements for ExonHit, in particular the strategic alliance with Allergan.

Matthias Baumann joined Noxxon in February 2011 as Chief Medical Officer. From 2002 to 2010 he served as Chief Scientific Officer and Managing Director of the German-based company FOCUS Clinical Drug Development GmbH, a contract research organization (CRO) specialized in early clinical studies and exploratory development. In this role he was responsible for the design and execution of progressing drug candidates from the preclinical stage to clinical proof of concept. Before joining FOCUS, Dr. Baumann was with the Swiss pharmaceutical and diagnostics company, Hoffmann-La Roche Ltd., from 1998 to 2002. As Medical Officer he conducted clinical studies for the qualification of biomarkers and diagnostics in various therapeutic areas, including cardiovascular, metabolism and oncology. Dr. Baumann started his career in the pharmaceutical industry in 1990 at Boehringer Mannheim GmbH, where he held the positions of Program Manager and Clinical R&D Department Head.

SUPERVISORY BOARD

Dr. Birner, Mr. Köhler, Dr. Litzka and Dr. PetitBon are representatives of TVM Capital GmbH, DEWB AG, Edmond de Rothschild Investment Partners SCA and Kreos Capital, respectively, who are among the principal shareholders of the company.

Dr. Hubert Birner is Chairman of Noxxon's Supervisory Board. Since 2000 he has worked as the investment manager for the venture capital firm, TVM Capital, and is currently Managing Partner at TVM Capital's Munich and Montreal offices. He is responsible for numerous active investments in Europe as well as the United States. He currently serves as Chairman/Member of the Board of several biotech companies such as Argos Therapeutics Inc., leonnanodrugs GmbH, Spepharm Holdings BV, Proteon Therapeutics Inc. For many years, he was the Chairman/Vice Chairman of Direvo Biotech AG and Jerini AG, which were acquired in 2008 by Bayer HealthCare AG and Shire Ltd., respectively. Before joining TVM Capital, he was Head of Business Development Europe and Director of Marketing for Germany at Zeneca. Dr. Birner joined Zeneca from McKinsey. He was also Assistant Professor of Biochemistry at the Ludwig-Maximilians-University in Munich. He holds an MBA from Harvard Business School and a doctoral degree in biochemistry from Ludwig-Maximilians-University Munich, where he graduated summa cum laude.

Bertram Köhler joined DEWB Deutsche Effecten- und Wechsel-Beteiligungsgesellschaft AG in August 2000 and has served as member of the Board of Directors of DEWB Deutsche Effecten- und Wechsel-Beteiligungsgesellschaft AG since June 2005. Since 2012, Mr. Köhler has served as Chief Executive Officer of DEWB Deutsche Effecten- und Wechsel-Beteiligungsgesellschaft AG. Prior to his activity at DEWB Deutsche Effecten- und Wechsel-

Beteiligungsgesellschaft AG, Mr. Köhler was a risk management consultant at Commerzbank AG, where he led projects in the area of company reorganisations, mergers and acquisitions and turnaround-situations. Currently, he also serves on the Board of Directors of Nanotron Technologies Ltd., LemnaTec GmbH, DirectPhotonics Industries GmbH. He holds a university diploma in economics as “Diplom-Kaufmann”.

Dr. Olivier Litzka has been a Partner with Paris-based Edmond de Rothschild Investment Partners (EdRIP) since 2006. He invests primarily in European and secondarily in American biotechnology and medical technology companies. In addition to being a member of the Supervisory Board of Noxxon Pharma AG, he currently serves on the board of Allecra Therapeutics GmbH, Probiodrug AG, SuperSonic Imagine and JenaValve Technology GmbH, and served on the board of Novexel, Sapiens and Endosense up until their respective acquisitions. Before joining EdRIP, Olivier Litzka spent six years with 3i’s life science venture capital practice, based first in Munich and then in Paris. In this position, he served on the boards of several portfolio companies and made a range of international investments. Before joining 3i in 2000, he worked as a strategy consultant with Mercer Management Consulting for several years, both in Munich and Paris. Dr. Litzka holds a Ph.D. in molecular microbiology from the University of Munich.

Dr. Maurizio PetitBon is general partner and co-founder of Kreos Capital where he focuses on healthcare investments. Prior to co-founding Kreos, Dr. PetitBon was Managing Partner of PMA Europe, London, a consulting partnership focused on assisting private equity firms and corporate clients in evaluating investment opportunities in technology companies. Prior to that, he was principal consultant at SRI International, in Menlo Park, California and London where he advised a number of U.S., European and Japanese technology companies on business development and M&A strategies. He also held a number of managerial positions at Emerson Electric, Digital Equipment and Xerox. Dr. PetitBon holds a doctoral degree in mechanical engineering from the University of Rome and a Master of Business Administration from INSEAD in Fontainebleau, France.

Dr. J. Donald deBethizy served as President and Chief Executive Officer of Santaris Pharma A/S, in Denmark and the U.S., until September 2014, when the company was sold to Roche. He served as Executive Chairman of Contera Pharma ApS until it was sold to Bukwang Pharma in November 2014. Dr. deBethizy was co-founder and Chief Executive Officer of Targacept, Inc., U.S., a public biotechnology company listed on NASDAQ. He completed a postdoctoral fellowship at the Chemical Industry Institute of Toxicology at Research Triangle Park, NC, and is a Diplomate of the American Board of Toxicology. Dr. deBethizy has held adjunct appointments at Duke University, at Wake Forest University School of Medicine and Wake Forest University Babcock School of Management. He also currently serves on the Board of Directors of Newron Pharmaceuticals SpA, arGEN-X N.V., Rigontec GmbH, and Serendex Pharmaceuticals A/S.

Dr. Walter Wenninger has over 30 years of experience in research and development, financial, business, and operating management in the pharmaceutical industry. He joined Bayer Pharma in 1968, where he held executive management positions in Germany, the United States and Europe within the life science business of Bayer AG. From 1994 to 2000, Dr. Wenninger served as a member of the Management board of Bayer AG. Following his retirement from Bayer, Dr. Wenninger has been involved in the strategic positioning and development of several companies and organisations. He currently serves on the advisory group for the board of Novo A/S, Denmark. He has been a member of the executive committee of the German Cardiac Research Foundation, the executive committee of the Robert-Koch-Foundation, and until recently was a long time member of the Board of Trustees of the German Cancer Research Center. Dr. Wenninger graduated from the Ludwig-Maximilians-University Munich in veterinary medicine with a Ph.D. and with a degree in economics as “Diplom-Kaufmann”.

NEWSFLOW

In our view, Noxxon's stock price will be driven by news about its pipeline. We expect the company to make a number of announcements during the coming 12-18 months which will act as catalysts for the stock. These include:

- Deal for delivery agreement of checkpoint inhibitor drug material for phase II studies of NOX-A12 with a pharmaceutical company in Q4/16.
- Enrolment of first patients for phase II studies of NOX-A12 in combination with a checkpoint inhibitor in pancreatic and colorectal cancer in Q4/16 or Q1/17.
- Publication of interim top-line proof of mechanism data for phase II studies of NOX-A12 in pancreatic and colorectal cancer, around mid 2017.
- Publication of final proof of mechanism data for NOX-A12, as well as initial efficacy data for NOX-A12 from phase II studies in combination with a checkpoint inhibitor in pancreatic and colorectal cancer in Q4/17 or Q1/18.
- Publication of final efficacy data from NOX-A12 phase II studies in combination with a checkpoint inhibitor in pancreatic and colorectal cancer, around mid 2018.

SHAREHOLDERS & STOCK INFORMATION

Stock Information	
ISIN	NL0012044762
WKN	A2ASSB
Bloomberg ticker	ALNOX FP
No. of issued shares	2,006,097
Country	France
Sector	Healthcare
Subsector	Biotechnology

Source: Paris stock exchange, First Berlin Equity Research

Shareholder Structure	
Kreos Capital IV Ltd.	17.8%
TVM Capital GmbH	16.0%
Sofinnova Capital V FCPR	15.8%
DEWB AG	12.3%
Edmond de Rothschild Investment	10.5%
NGN BioMed Opportunity LP	10.0%
Seventure Partners	3.9%
Others	13.7%

Source: NOXXON Pharma NV

INCOME STATEMENT

All figures in EUR '000	2014	2015	2016E	2017E	2018E	2019E	2020E
Revenue	**25**	**43**	**40**	**0**	**0**	**0**	**0**
Upfront & milestone payments	**0**	**0**	**0**	**0**	**15,000**	**0**	**0**
Total revenue	**25**	**43**	**40**	**0**	**15,000**	**0**	**0**
General and administrative	3,107	7,319	3,832	1,000	1,050	1,103	1,158
Research and development	10,154	7,587	5,435	4,000	5,000	6,000	6,400
Other operating income (expense)	70	33	20	20	20	20	20
Operating income (EBIT)	**-13,166**	**-14,830**	**-9,207**	**-4,980**	**8,970**	**-7,083**	**-7,538**
Net financial result	-629	-1,294	-2,627	-4	5	11	7
Pre-tax income (EBT)	**-13,795**	**-16,124**	**-11,834**	**-4,984**	**8,975**	**-7,072**	**-7,531**
Income taxes	-3	22	0	0	0	0	0
Net income / loss	**-13,798**	**-16,102**	**-11,834**	**-4,984**	**8,975**	**-7,072**	**-7,531**
Diluted EPS	**-47.22**	**-42.43**	**-5.90**	**-2.13**	**2.97**	**-2.34**	**-2.49**
EBITDA	**-12,887**	**-14,612**	**-9,057**	**-4,880**	**9,020**	**-7,003**	**-7,438**
Ratios							
EBIT-Margin on total revenue	n.a.	n.a.	n.a.	n.a.	59.8%	n.a.	n.a.
EBITDA margin on total revenue	n.a.	n.a.	n.a.	n.a.	60.1%	n.a.	n.a.
Net Margin on total revenue	n.a.	n.a.	n.a.	n.a.	59.8%	n.a.	n.a.
Expenses as % of Revenues							
General and administrative	n.a.	n.a.	n.a.	n.a.	7.0%	n.a.	n.a.
Research and development	n.a.	n.a.	n.a.	n.a.	33.3%	n.a.	n.a.
Y-Y Growth							
Total revenue	n.a.	72.0%	-7.0%	-100.0%	n.a.	-100.0%	n.a.
Operating income	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Net income/ loss	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

BALANCE SHEET

All figures in EUR '000	2014	2015	2016E	2017E	2018E	2019E	2020E
Assets							
Current Assets, Total	**2,067**	**5,364**	**2,778**	**1,874**	**25,849**	**18,777**	**11,246**
Cash and Cash Equivalents	1,527	4,093	2,000	1,079	25,022	17,912	10,347
Receivables	0	3	8	5	5	10	10
Inventories	38	13	10	0	0	0	0
Other Current Assets	502	1,096	601	631	663	696	730
Financial Assets	0	159	159	159	159	159	159
Non-Current Assets, Total	**1,023**	**677**	**547**	**467**	**467**	**467**	**467**
Property, Plant & Equipment	772	603	493	425	425	425	425
Goodwill & Other Intangibles	251	74	55	43	43	43	43
Total Assets	**3,090**	**6,041**	**3,325**	**2,341**	**26,316**	**19,244**	**11,713**
Shareholders' Equity & Debt							
Current Liabilities, Total	**5,177**	**6,783**	**5,103**	**2,503**	**2,503**	**2,503**	**2,503**
Short-Term Debt	2,167	2,591	2,600	0	0	0	0
Accounts Payable	2,485	3,174	1,600	1,600	1,600	1,600	1,600
Other current liabilities	525	1,018	903	903	903	903	903
Longterm Liabilities, Total	**4,156**	**6,290**	**1**	**1**	**1**	**1**	**1**
Long Term Debt	4,152	6,289	0	0	0	0	0
Other Liabilities	4	1	1	1	1	1	1
Shareholders Equity	**-6,243**	**-7,032**	**-1,779**	**-163**	**23,812**	**16,740**	**9,209**
Total Consolidated Equity and Debt	**3,090**	**6,041**	**3,325**	**2,341**	**26,316**	**19,244**	**11,713**
Ratios							
Current ratio (x)	0.40	0.79	0.54	0.75	10.33	7.50	4.49
Quick ratio (x)	0.39	0.79	0.54	0.75	10.33	7.50	4.49
Net gearing	n.a.	n.a.	n.a.	n.a.	-105.1%	-107.0%	-112.4%
Book value per share (€)	n.a.	n.a.	n.a.	n.a.	7.88	5.54	3.05
Net debt	4,792	4,787	600	-1,079	-25,022	-17,912	-10,347
Equity ratio	-202.0%	-116.4%	-53.5%	-7.0%	90.5%	87.0%	78.6%

CASH FLOW STATEMENT

All figures in EUR '000	2014	2015	2016E	2017E	2018E	2019E	2020E
Net income	**-13,798**	**-16,102**	**-11,834**	**-4,984**	**8,975**	**-7,072**	**-7,531**
Depreciation and amortization	279	218	150	100	50	80	100
Interest, net	629	1,294	2,627	4	-5	-11	-7
Tax provision	3	-22	0	0	0	0	0
Changes in Working Capital	569	857	-1,196	-17	-32	-38	-35
Other Adjustments	-141	273	0	0	0	0	0
Cash interest net	-546	-915	-335	-4	5	11	7
Operating cash flow	**-13,005**	**-14,397**	**-10,588**	**-4,901**	**8,994**	**-7,030**	**-7,465**
CapEx	-42	-8	-20	-20	-50	-80	-100
Investments in Intangibles	-5	0	0	0	0	0	0
Free cash flow	**-13,052**	**-14,405**	**-10,608**	**-4,921**	**8,944**	**-7,110**	**-7,565**
Debt Financing, net	6,429	1,942	720	0	0	0	0
Equity Financing, net	0	9,328	7,795	4,000	15,000	0	0
Other financing activities	3,039	5,701	0	0	0	0	0
Cash flow from financing	**9,468**	**16,971**	**8,515**	**4,000**	**15,000**	**0**	**0**
Net cash flows	**-3,584**	**2,566**	**-2,093**	**-921**	**23,944**	**-7,110**	**-7,565**
Cash, start of the year	5,111	1,527	4,093	2,000	1,079	25,022	17,912
Cash, end of the year	**1,527**	**4,093**	**2,000**	**1,079**	**25,022**	**17,912**	**10,347**
EBITDA/share	**-44.13**	**-38.55**	**-4.51**	**-2.09**	**2.99**	**-2.32**	**-2.46**
Y-Y Growth							
Operating Cashflow	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Free cashflow	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
EBITDA/share	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

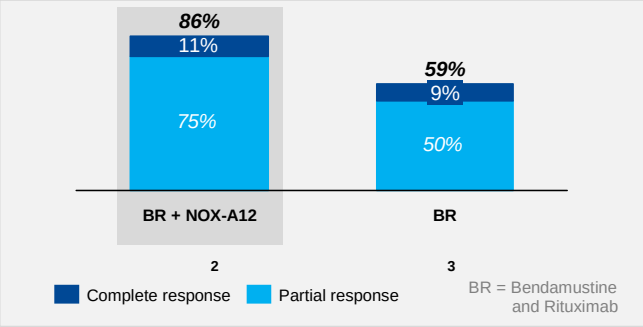
APPENDIX

POSITIVE PHASE II DATA OF NOX-A12 IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

Noxxon conducted an open-label, uncontrolled, single arm phase II clinical trial, in 28 previously treated patients with a second blood cancer - CLL. This study evaluated the safety and efficacy of NOX-A12 in combination with bendamustine and rituximab. The top-line results confirmed that NOX-A12 was safe and generally well tolerated. The treatment phase has been completed and patient follow-up will continue through 2017.

Patients in this trial reached an overall response rate of 86%, with three patients (11%) obtaining a complete response and an additional 21 a partial response (75%) as shown in the figure below. Of the remaining patients with chronic lymphocytic leukaemia, 11%, or three patients, were classified as having progressive disease and 4%, or one patient, was classified as not evaluable. Historical results from a peer's comparable open-label clinical trial using only bendamustine and rituximab showed an overall response rate of 59%.

Figure 18: Response rate of NOX-A12 in CLL phase II study compared to BR alone



Source: Noxxon NV

CLL is a competitive market; new combination therapies have delivered response rates in the 68%-83% range Based on Noxxon's pre-clinical and clinical experience with the monoclonal antibody, rituximab, the company believes that NOX-A12 may also be an ideal combination drug for many cancer-targeting monoclonal antibody cancer therapies. Despite positive clinical trial results in CLL, Noxxon prefers to focus the further development of NOX-A12 on MM. CLL is a highly crowded market and medical need is comparatively low. Recently, CLL combination therapies such as BR + Ibrutinib (Chanan-Khan et al., 2016) and BR + Idelalisib (Barrientos et al., ASCO 2016) delivered objective response rates of 83% and 68% respectively in Phase III studies.

NOX-A12 IN GLIOBLASTOMA, ORPHAN-DRUG INDICATION WITH ENCOURAGING PRECLINICAL DATA

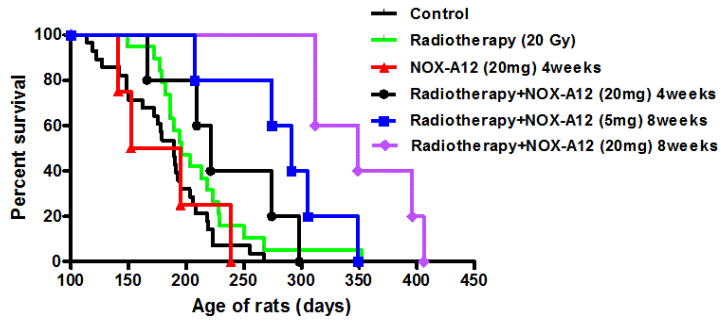
Glioblastoma is a particularly aggressive type of brain cancer in which tumour cells invade surrounding tissue, rendering surgical treatment and chemotherapy less effective. The median survival time for patients with glioblastoma is approximately one year from initial diagnosis (Source: Chauffer et al., 2014). Current therapies for glioblastoma primarily consist of surgery, radiation and temozolomide/Temodar (a DNA-alkylating agent), which are able to temporarily control tumour growth in only approximately 20% of patients.

In-vivo pre-clinical research

A pre-clinical study using a rat model of carcinogen-induced glioblastoma showed that NOX-A12 used in combination with radiation therapy led to an increase in survival time. The

strongest effects on survival took place at the highest dose and the longest duration of therapy. Based on the results, the researchers believe the main driver of efficacy may be the duration of therapy.

Figure 19: NOX-A12 used in combination with irradiation significantly prolongs survival in a rat glioblastoma model

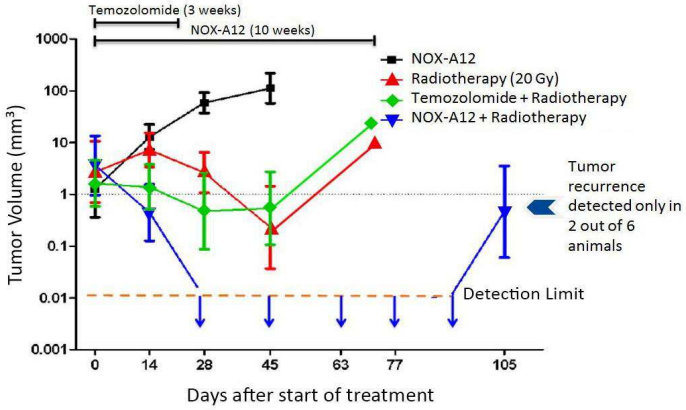


Source: Noxxon NV, Liu et al., 2014.

Similar to the results in the MM pre-clinical studies, NOX-A12 alone showed no positive effects. The reason is that NOX-A12 does not directly attack the tumour, but rather blocks the recruitment of “repair” cells.

Researchers from Stanford University conducted a further pre-clinical study. In this study, NOX-A12 in combination with radiation therapy lead to tumour shrinkage to volume levels undetectable by magnetic resonance imaging (MRI) in 100% of the animals tested. Moreover, NOX-A12 responses were durable in two thirds of animals after cessation of treatment. The other treatments, temozolomide and radiation, were able to stabilise the growth of these tumours but they did not result in significant reduction in their size.

Figure 20: NOX-A12 used in combination with irradiation produces tumour shrinkage in a rat model of glioblastoma



Source: Noxxon NV, Liu et al., 2014

For the phase II trials, Noxxon plans to target inoperable glioblastoma patients who are resistant to Temodar/temozolomide. The company believes that even small improvements in efficacy would be readily apparent after a short treatment period. Glioblastoma is an orphan drug indication in the US and Europe. As a result, the trial size and duration required to gain regulatory approval is expected to be limited. Noxxon plans a phase II study in 18 patients to evaluate safety, tolerability and the rate of progression-free survival after six months. Noxxon believes that NOX-A12 will work synergistically with standard therapies such as irradiation, chemotherapy and anti-angiogenesis drugs such as bevacizumab (Avastin from Genentech/Roche).

FIRST BERLIN RECOMMENDATION & PRICE TARGET HISTORY

Report No.:	Date of publication	Previous day closing price	Recommendation	Price target
Initial Report	Today	€21.49	Buy	€40.00

Authored by: Christian Orquera, Analyst

Company responsible for preparation:

First Berlin Equity Research GmbH
Mohrenstraße 34
10117 Berlin

Tel. + 49 (0)30 80 93 96 93 Fax +49 (0)30 - 80 93 96 87

info@firstberlin.com
www.firstberlin.com

Person responsible for forwarding or distributing this financial analysis: Martin Bailey

Copyright© 2016 First Berlin Equity Research GmbH No part of this financial analysis may be copied, photocopied, duplicated or distributed in any form or media whatsoever without prior written permission from First Berlin Equity Research GmbH. First Berlin Equity Research GmbH shall be identified as the source in the case of quotations. Further information is available on request.

INFORMATION PURSUANT TO SECTION 34b OF THE GERMAN SECURITIES TRADING ACT [WPHG] AND THE GERMAN ORDINANCE ON THE ANALYSIS OF FINANCIAL INSTRUMENTS [FINANV]

First Berlin Equity Research GmbH (hereinafter referred to as: "First Berlin") prepares financial analyses while taking the relevant regulatory provisions, in particular the German Securities Trading Act [WpHG] and the German Ordinance on the Analysis of Financial Instruments [FinAnV], into consideration. In the following First Berlin provides investors with information about the statutory provisions that are to be observed in the preparation of financial analyses.

CONFLICTS OF INTEREST

In accordance with Section 34b Paragraph 1 p. 2 No. 2 of the German Securities Trading Act [WpHG] financial analyses may only be passed on or publicly distributed if circumstances or relations which may cause conflicts of interest among the authors, the legal entities responsible for such preparation or companies associated with them are disclosed along with the financial analysis.

First Berlin offers a range of services that go beyond the preparation of financial analyses. Although First Berlin strives to avoid conflicts of interest wherever possible, First Berlin may maintain the following relations with the analysed company, which in particular may constitute a potential conflict of interest (further information and data may be provided on request):

- The author, First Berlin, or a company associated with First Berlin holds an interest of more than five percent in the share capital of the analysed company;
- The author, First Berlin, or a company associated with First Berlin provided investment banking or consulting services for the analysed company within the past twelve months for which remuneration was or was to be paid;
- The author, First Berlin, or a company associated with First Berlin reached an agreement with the analysed company for preparation of a financial analysis for which remuneration is owed;
- The author, First Berlin, or a company associated with First Berlin has other significant financial interests in the analysed company;

In order to avoid and, if necessary, manage possible conflicts of interest both the author of the financial analysis and First Berlin shall be obliged to neither hold nor in any way trade the securities of the company analyzed. The remuneration of the author of the financial analysis stands in no direct or indirect connection with the recommendations or opinions represented in the financial analysis. Furthermore, the remuneration of the author of the financial analysis is neither coupled directly to financial transactions nor to stock exchange trading volume or asset management fees.

If despite these measures one or more of the aforementioned conflicts of interest cannot be avoided on the part of the author or First Berlin, then reference shall be made to such conflict of interest.

PRICE TARGET DATES

Unless otherwise indicated, current prices refer to the closing prices of the previous trading day.

AGREEMENT WITH THE ANALYSED COMPANY AND MAINTENANCE OF OBJECTIVITY

The present financial analysis is based on the author's own knowledge and research. The author prepared this study without any direct or indirect influence exerted on the part of the analysed company. Parts of the financial analysis were possibly provided to the analysed company prior to publication in order to avoid inaccuracies in the representation of facts. However, no substantial changes were made at the request of the analysed company following any such provision.

ASSET VALUATION SYSTEM

First Berlin's system for asset valuation is divided into an asset recommendation and a risk assessment.

ASSET RECOMMENDATION

The recommendations determined in accordance with the share price trend anticipated by First Berlin in the respectively indicated investment period are as follows:

STRONG BUY: An expected favourable price trend of more than 50% combined with sizeable confidence in the quality and forecast security of management.

BUY: An expected favourable price trend of more than 25% percent.

ADD: An expected favourable price trend of between 0% and 25%.

REDUCE: An expected negative price trend of between 0% and -15%.

SELL: An expected negative price trend of more than -15%.

RISK ASSESSMENT

The First Berlin categories for risk assessment are low, average, high and speculative. They are determined by ten factors: Corporate governance, quality of earnings, management strength, balance sheet and financial risk, competitive position, standard of financial disclosure, regulatory and political uncertainty, strength of brandname, market capitalisation and free float. These risk factors are incorporated into the First Berlin valuation models and are thus included in the target prices. First Berlin customers may request the models.

INVESTMENT HORIZON

Unless otherwise stated in the financial analysis, the ratings refer to an investment period of twelve months.

UPDATES

At the time of publication of this financial analysis it is not certain whether, when and on what occasion an update will be provided. In general First Berlin strives to review the financial analysis for its topicality and, if required, to update it in a very timely manner in connection with the reporting obligations of the analysed company or on the occasion of ad hoc notifications.

SUBJECT TO CHANGE

The opinions contained in the financial analysis reflect the assessment of the author on the day of publication of the financial analysis. The author of the financial analysis reserves the right to change such opinion without prior notification.

Legally required information regarding

- **key sources of information in the preparation of this research report**
- **valuation methods and principles**
- **sensitivity of valuation parameters**

can be accessed through the following internet link: http://firstberlin.com/disclaimer-english-link/

SUPERVISORY AUTHORITY: Bundesanstalt für Finanzdienstleistungsaufsicht (German Federal Financial Supervisory Authority) [BaFin], Graurheindorferstraße 108, 53117 Bonn and Lurgiallee 12, 60439 Frankfurt

EXCLUSION OF LIABILITY (DISCLAIMER)

RELIABILITY OF INFORMATION AND SOURCES OF INFORMATION

The information contained in this study is based on sources considered by the author to be reliable. Comprehensive verification of the accuracy and completeness of information and the reliability of sources of information has neither been carried out by the author nor by First Berlin. As a result no warranty of any kind whatsoever shall be assumed for the accuracy and completeness of information and the reliability of sources of information, and neither the author nor First Berlin, nor the person responsible for passing on or distributing the financial analysis shall be liable for any direct or indirect damage incurred through reliance on the accuracy and completeness of information and the reliability of sources of information.

RELIABILITY OF ESTIMATES AND FORECASTS

The author of the financial analysis made estimates and forecasts to the best of the author's knowledge. These estimates and forecasts reflect the author's personal opinion and judgement. The premises for estimates and forecasts as well as the author's perspective on such premises are subject to constant change. Expectations with regard to the future performance of a financial instrument are the result of a measurement at a single point in time and may change at any time. The result of a financial analysis always describes only one possible future development – the one that is most probable from the perspective of the author – of a number of possible future developments.

Any and all market values or target prices indicated for the company analysed in this financial analysis may not be achieved due to various risk factors, including but not limited to market volatility, sector volatility, the actions of the analysed company, economic climate, failure to achieve earnings and/or sales forecasts, unavailability of complete and precise information and/or a subsequently occurring event which affects the underlying assumptions of the author and/or other sources on which the author relies in this document. Past performance is not an indicator of future results; past values cannot be carried over into the future.

Consequently, no warranty of any kind whatsoever shall be assumed for the accuracy of estimates and forecasts, and neither the author nor First Berlin, nor the person responsible for passing on or distributing the financial analysis shall be liable for any direct or indirect damage incurred through reliance on the correctness of estimates and forecasts.

INFORMATION PURPOSES, NO RECOMMENDATION, SOLICITATION, NO OFFER FOR THE PURCHASE OF SECURITIES

The present financial analysis serves information purposes. It is intended to support institutional investors in making their own investment decisions; however in no way provide the investor with investment advice. Neither the author, nor First Berlin, nor the person responsible for passing on or distributing the financial analysis shall be considered to be acting as an investment advisor or portfolio manager vis-à-vis an investor. Each investor must form his own independent opinion with regard to the suitability of an investment in view of his own investment objectives, experience, tax situation, financial position and other circumstances.

The financial analysis does not represent a recommendation or solicitation and is not an offer for the purchase of the security specified in this financial analysis. Consequently, neither the author nor First Berlin, nor the person responsible for passing on or distributing the financial analysis shall as a result be liable for losses incurred through direct or indirect employment or use of any kind whatsoever of information or statements arising out of this financial analysis.

A decision concerning an investment in securities should take place on the basis of independent investment analyses and procedures as well as other studies including, but not limited to, information memoranda, sales or issuing prospectuses and not on the basis of this document.

NO ESTABLISHMENT OF CONTRACTUAL OBLIGATIONS

By taking note of this financial analysis the recipient neither becomes a customer of First Berlin, nor does First Berlin incur any contractual, quasi-contractual or pre-contractual obligations and/or responsibilities toward the recipient. In particular no information contract shall be established between First Berlin and the recipient of this information.

NO OBLIGATION TO UPDATE

First Berlin, the author and/or the person responsible for passing on or distributing the financial analysis shall not be obliged to update the financial analysis. Investors must keep themselves informed about the current course of business and any changes in the current course of business of the analysed company.

DUPLICATION

Dispatch or duplication of this document is not permitted without the prior written consent of First Berlin.

SEVERABILITY

Should any provision of this disclaimer prove to be illegal, invalid or unenforceable under the respectively applicable law, then such provision shall be treated as if it were not an integral component of this disclaimer; in no way shall it affect the legality, validity or enforceability of the remaining provisions.

APPLICABLE LAW, PLACE OF JURISDICTION

The preparation of this financial analysis shall be subject to the law obtaining in the Federal Republic of Germany. The place of jurisdiction for any disputes shall be Berlin (Germany).

NOTICE OF DISCLAIMER

By taking note of this financial analysis the recipient confirms the binding nature of the above explanations.

By using this document or relying on it in any manner whatsoever the recipient accepts the above restrictions as binding for the recipient.

QUALIFIED INSTITUTIONAL INVESTORS

First Berlin financial analyses are intended exclusively for qualified institutional investors.

This report is not intended for distribution in the USA, Canada and/or the United Kingdom (Great Britain).