Cyxone AB

Sweden / Biotechnology
Nasdaq First North
Bloomberg: CYXO SS
ISIN: SE0007815428

Initiation of coverage

RATING	**BUY**
PRICE TARGET	**SEK 13.50**
Return Potential	547.5%
Risk Rating	Speculative

INNOVATIVE DRUG CANDIDATES FOR AUTOIMMUNE DISEASES

Cyxone AB is a biotech company with a development stage product pipeline focusing on autoimmune diseases. The company's proprietary discovery technology is generating drug candidates which belong to a new class of drugs called Cyclotides. At present, Cyxone has two oral drugs, one in late preclinical and one in phase II clinical trials. Both have potential to significantly improve treatment of autoimmune diseases. T20K, the most advanced oral Cyclotide-based drug candidate for multiple sclerosis (MS), is set to start recruitment of patients for a phase I clinical trial before year-end. If successfully developed and approved, we see sales potential for the product in excess of SEK12.7bn (USD1.4bn). Rabeximod, the recently acquired lead drug candidate for rheumatoid arthritis (RA), has shown robust and statistically significant efficacy in a phase IIa trial. Preparations for a phase IIb trial are underway. We estimate sales potential for the product at SEK8.5bn (USD951m). In our view, positive results from the phase IIb trial should add substantial value to Cyxone and have a positive impact on the share price. We initiate coverage of Cyxone with a Buy rating and a SEK13.50 price target.

Rabeximod, Cyxone's most valuable asset, showed strong and statistically significant efficacy for RA in a phase IIa study, although the programme missed its primary endpoint Cyxone acquired the drug candidate from Oxypharma in 2017 for a bargain price of SEK10m (USD1.0m) plus royalties of 10% of profit. The product achieved sound ACR20 efficacy of 53.3% (vs. placebo 28.6%) in a phase II trial, but outside the stipulated schedule of 12 weeks. Rabeximod requires slightly longer than other drugs to unfold its full potential. Therefore, the phase IIb trial is planned to cover a period of 24 weeks. On 26 October the company raised SEK44.3m (USD5.0m) to finance the study.

Buy recommendation In our valuation, we focus on the most advanced products - Rabeximod and T20K. Our pipeline valuation model yields a price target of SEK13.50, which represents a return potential of 547.5% from the current level. (p.t.o.)

FINANCIAL HISTORY & PROJECTIONS

	2016	2017	2018E	2019E	2020E	2021E
Revenue (SEK m)	0.02	0.00	0.00	0.00	89.00	0.00
Y-o-y growth	n.a.	-100.0%	n.a.	n.a.	n.a.	-100.0%
EBIT (SEK m)	-4.16	-8.82	-13.92	-18.29	65.89	-29.27
EBIT margin	n.a.	n.a.	n.a.	n.a.	74.0%	n.a.
Net income (SEK m)	-4.16	-8.82	-13.91	-18.26	65.93	-29.24
EPS (diluted) (SEK)	-0.32	-0.50	-0.62	-0.43	1.37	-0.55
DPS (SEK)	0.00	0.00	0.00	0.00	0.00	0.00
FCF (SEK m)	-5.40	-11.37	-35.36	-43.87	38.11	-55.04
Net gearing	n.a.	n.a.	n.a.	-51.0%	-53.6%	-25.6%
Liquid assets (SEK m)	21.60	33.36	33.96	52.92	91.03	36.00

RISKS

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

COMPANY PROFILE

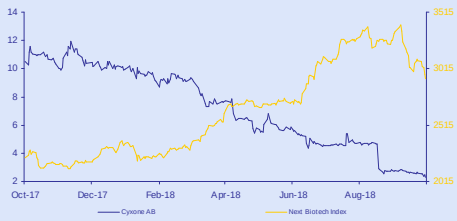
Cyxone AB is Swedish biotech company focused on the research and development of new drugs to treat autoimmune diseases. The company's proprietary discovery technology is generating drug candidates which belong to a new class of drugs called Cyclotides.Cyxone currently has two drugs in late preclinical and phase II clinical trials to treat multiple sclerosis and rheumatoid arthritis.

MARKET DATA

	As of 10/29/2018
Closing Price	SEK 2.09
Shares outstanding	37.46m
Market Capitalisation	SEK 78.10m
52-week Range	SEK 2.09 / 11.97
Avg. Volume (12 Months)	86,223

Multiples	2017	2018E	2019E
P/E	n.a.	n.a.	n.a.
EV/Sales	n.a.	n.a.	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 2018
Liquid Assets	SEK 17.82m
Current Assets	SEK 18.09m
Intangible Assets	SEK 14.90m
Total Assets	SEK 32.99m
Current Liabilities	SEK 2.36m
Shareholders' Equity	SEK 30.63m

SHAREHOLDERS

Accequa AB	30.2%
OxyPharma AB	9.7%
Avanza Pension	3.5%
Nordnet Pensionsförsäkring	3.2%
Others	53.4%

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INVESTMENT CASE

Cyxone's proprietary technology enables generation of a new highly efficient class of circular peptides called Cyclotides Cyclotides are a new class of drugs synthesized through the company's proprietary discovery technology. This patent-protected technology has the potential to generate new engineered Cyclotides, so called mutant Cyclotides, with improved pharmacological properties compared to the original proteins found in plants. Pre-clinical studies showed that Cyclotides can successfully address multiple types of autoimmune disease such as multiple sclerosis (MS) and rheumatoid arthritis (RA). Additionally, Cyclotides have demonstrated stability suited for oral administration and a favourable side-effect profile in therapeutic use, which make them an ideal compound for drug development.

T20K is set to start phase I studies during Q4/18 T20K is the first oral drug candidate against multiple sclerosis (MS) engineered with Cyxone's Cyclotide technology. The drug is in late pre-clinical development for MS. Enrolment of patients for a phase I clinical trial is due to start before the end of the year. Preclinical data for T20K in MS look promising. The product has shown clear immune suppression activity without the typical undesired side effects. If successfully developed and approved, we conservatively see peak sales for T20K of SEK12.7bn (USD1.4bn)

Market for MS drugs expanding at a CAGR of 6.3% to 2025 The global MS drugs market was valued at USD16.1bn in 2016, and is expected to reach USD27.3bn by 2025, expanding at a CAGR of 6.3% during this period. Moreover, the market for oral medications is expected to grow even more strongly (Source: Credence Research, 2017). The increasing base of patients suffering from MS as well as rising demand for novel more potent drugs are main growth drivers. Competitors' oral drugs, such as Tecfidera and the recently launched Ocrevus, are projected to achieve peak sales in excess of USD4bn (Source: Pharma intelligence, 2018).

The lead drug candidate Rabeximod against rheumatoid arthritis (RA) has delivered strong data in a first phase IIa study In order to expand the development pipeline, in 2017 the company acquired the drug candidate Rabeximod against RA. In 2009 the originator OxyPharma conducted a phase IIa study with Rabeximod including 224 patients. The product demonstrated statistically significant ($p<0.0198$) efficacy measured in accordance with ACR20 criteria. 53.3% of patients benefited from the treatment during the follow-up period at week 16, against 28.6% efficacy with placebo. Unfortunately, the trial design stipulated review of the data at week 12, which is why the programme missed its primary endpoint despite showing significant efficacy during the follow-up period. Lack of financing led the originator to put the programme on hold.

Phase IIb study in moderate to severe RA is planned and preparations for the trial are underway – the recent capital increase amounting to SEK44.3m secured sufficient funding Cyxone intends to conduct a phase IIb study of Rabeximod in approx. 200-250 RA patients. Because the phase IIa study failed due to its short duration, the company has designed the trial to last 24 weeks (6 months). First top-line data will likely be published in H2/20. This clinical trial will provide valuable efficacy data paving the way for a potential licensing deal with a pharmaceutical partner to conduct the phase III registration study and market the drug. We estimate sales potential for the product at SEK8.5bn (USD951m).

Market opportunity for RA medications looks attractive based on unmet medical need The global RA drugs market was valued at USD20.3bn in 2016 and is expected to reach USD30.4bn by 2025, expanding at a CAGR of 4.6% in the period (Source: Grand View Research, 2018). The RA market is likely to see strong growth in coming years as new

products such as JAK and IL-6 inhibitors and also new biosimilar options reach the market. However RA is a complex disease to treat, and at least one third of patients remain or become unresponsive to treatment (Hyrich et al., 2007). Available oral drugs have significant safety shortcomings. Therefore, oral drugs with a superior efficacy and safety profile will see strong demand. At present, market expectations of oral drugs are high. For example, Evaluate Pharma's projections foresee blockbuster sales potential for competitors' JAK-inhibitors (oral) such as Abbvie's Updactinib (USD2.6bn by 2024) and Gilead's Filgotinib (USD 1.4bn by 2024).

Cyxone shares are significantly undervalued in our view. We initiate coverage with a price target of SEK13.50 and a Buy recommendation Our proprietary risk-adjusted sum-of-the-parts valuation model suggests fair value for Cyxone of SEK709.2m (USD79.7m) or SEK13.50 (USD1.52) per share. We believe our valuation is conservative, given that the median value of licensing transactions in the last decade for RA and MS drug candidates at a similar development stage was USD450m (SEK4.0bn) per drug - significantly more than our overall valuation of Cyxone. At current levels, we see the Cyxone stock as significantly undervalued. During the next 12-24 months, we expect positive news flow from phase II clinical trials of Rabeximod in RA and of T20K in MS to trigger appreciation of Cyxone's share price.

SWOT ANALYSIS

STRENGTHS

- **Experienced management team** Mr. Kjell Stenberg, Ph.D., (CEO) and Mr. Ola Skanung (CFO) are both highly qualified executives with over 60 years of combined experience in the pharmaceutical, biotech and other high tech industries.

- **Innovative-patent protected Cyclotide technology** The technology enables the company to generate a new highly efficient class of circular peptide-molecules called Cyclotides. Importantly, in therapeutic use, Cyclotides are chemically very stable making them suitable for oral administration (e.g. first oral drug candidate T20K against MS) and show a favourable safety profile.

- **Lead drug candidate Rabeximod already demonstrated statistically significant efficacy in first phase II study in RA** Unfortunately, the drug seems to achieve its full efficacy a bit more slowly than previously believed. The phase II trial including 224 patients delivered a strong and statistically significant therapeutic effect in week 16 (during the follow up period), 4 weeks later than stipulated in the trial. As a result, the required phase IIb trial which will have a longer duration, involves lower risk in our view.

WEAKNESSES

- **Early stage pipeline with only two programmes, one in pre-clinical and one in phase II** While the lead programme Rabeximod has already demonstrated safety and first efficacy in a still small number of patients, the second drug candidate T20K has only been studied in animal models. Despite its strong pre-clinical efficacy data, the safety and response rate has yet to be demonstrated in humans.

- **Limited financial latitude** The company secured SEK25.0m in a placement during the listing and received a further SEK23.1m through warrant conversions in FY/17. These funds will finance operations for 12-18 months including the phase I trial of T20K in MS. The planned phase IIb trial for lead drug candidate Rabeximod in RA will be financed with the recently raised gross proceeds of SEK44.3m.

OPPORTUNITIES

- **The progress of Rabeximod in phase IIb clinical trials may create significant shareholder value** This clinical trial with approx. 200-250 patients will provide significant valuable efficacy data within only 18-24 months, paving the way for a phase III registration study and a potential development partnership with a big pharmaceutical company.

- **Development deals with pharmaceutical companies can lead to significant up front and milestone payments** Upon completion of key development milestones with the drug candidates Rabeximod (after phase IIb) and T20K (either after phase I other phase II), Cyxone aims to close a licensing agreement with pharmaceutical companies. In our view, deals of this type will validate the drugs' potential and provide additional funds through potential upfront and milestone payments.

- **Market potential expansion from further inflammation and autoimmune indications and drug candidates** There is robust preclinical evidence of the potential efficacy of Rabeximod and T20K in several autoimmune diseases. Rabeximod has been studied in RA and MS. Besides MS, T20K shows promise in Irritable Bowel Syndrome (IBS). Furthermore, Cyclotides have shown the potential to treat or prevent a wide range of autoimmune disorders, hypersensitivity disorders, and lymphocyte-mediated inflammation. These new indications and products hold out the prospect of significant additional market potential.

THREATS

- **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.

- **Development and regulatory risks** Development of the lead drug candidate Rabeximod 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) and particularly in the phase IIa clinical trial on patients. Moreover, even if the drug achieves good results in clinical trials, there is still a risk that the regulatory agencies (FDA and EMA) will not approve the drug or may request further trials.

- **Competitive risks** Cyxone's pipeline, particularly the RA lead drug candidate Rabeximod, may face competitive pressure. Several leading pharmaceutical and biotech companies, including AbbVie, Eli Lilly, Gilead/Galapagos and Astellas Pharma, are developing innovative oral drugs for RA. Any unexpected breakthrough by one or more of these competitors could significantly hit Cyxone's potential revenues. The same applies for the second drug candidate T20K.

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 Cyxone's fair value based on a sum-of-the-parts methodology. We believe this is the most appropriate valuation method for Cyxone 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 the lead drug candidate Rabeximod for the treatment of rheumatoid arthritis and T20K for the treatment of multiple sclerosis. We believe that Rabeximod has value in further indications (e.g. multiple sclerosis), and the second drug candidate T20K also has potential in further indications (e.g. inflammatory bowel disease). However, these areas are currently not the main focus of the company and we regard them as upside to our valuation.

During the forecasting process, we adjusted our sales projections and resulting cash flows for estimated success probabilities to obtain risk-adjusted expected values. We base our probability coefficients on statistical sector studies, such as DiMasi et al., and on our own estimates. In this instance, we have derived an 8% probability of success for the drug candidate which is close to entering phase I (T20K) and a 35% success probability for the drug candidate in phase II (Rabeximod) clinical development. We consider Rabeximod to be currently the most important value driver for the company.

Additionally, using First Berlin methodology, which takes into account company-specific risk factors, we have derived a cost of equity (COE) of 21.5% for Cyxone. Based on a debt ratio of 0.0%, we arrive at a WACC of 21.5%, which we have used to discount projected cash flows. Including projected net cash of SEK96.9m and a present value of SEK83.2m for milestone payments, we value Cyxone at SEK709.2m (USD79.7m), which implies a fair value of SEK13.50 (USD1.52) per share on a fully diluted basis. For the treatment cost, market size and potential sales projections in our valuation model, we have applied an exchange rate of 8.90 SEK per USD. Using our ten-factor risk analysis, we have set a Speculative risk rating for Cyxone. The main risk factors that we have identified are development, regulatory, competition and financing.

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

Compound	Project[1)]	Present Value (SEKM)	Patient Pop (K)	Treatment Cost (SEK)	Market Size (SEKM)	Market Share (%)	Peak Sales (SEKM)	PACME Margin[2)] (%)	Discount Factor (%)	Patent Life[3)] (years)	Time to Market (years)
Rabeximod	RA	SEK 483.9M	470K	106,800	50,196.0M	9%	8,461.5M	16%	21.5%	9	5
T20K	MS	SEK 218.3M	850K	213,600	181,560.0M	5%	12,711.4M	18%	21.5%	9	7
PACME PV		SEK 702.1M			231,756.0M		21,172.8M				
Costs PV[4)]		SEK 173.1M									
NPV		SEK 529.1M									
Milestones PV		SEK 83.2M									
Net cash (pro-forma)		SEK 96.9M									
Fair Value		SEK 709.2M									
Share Count (fully diluted)		52,544K									
Price Target		SEK 13.50									

Source: First Berlin Equity Research

In our view, Cyxone's valuation based on our sum-of-the-parts model is conservative, since we have seen in- and out-licensing deals on drugs up to phase II trials within the rheumatoid arthritis field or early stage in multiple sclerosis worth much more than this figure. Based on our calculations, the historical median value paid by pharmaceutical

companies to license arthritis or multiple sclerosis drugs up to phase II stage was approx. USD450m (SEK4.0bn) per drug. In table 2 we have summarised select arthritis and multiple sclerosis licensing deals conducted in the last decade where financial information has been disclosed.

Table 2: Selected RA and MS deals in the last decade

Licensee/licensor	Drug candidates/ targets	Description	Year	Development stage	Indication	Total deal value USDm
Merck / Exelixis	XL-499	Kinase	2011	Pre-clinical	RA	Up to 251 (12m upfront)
Amgen/Xercor	XmAb5871	Mab targeting CD19 and CD32b	2011	Pre-clinical	RA	Up to 500m
Roche/ Toyama Chemical	T-5224	AP-1 inhibitor	2007	Phase I	RA	Up to 370
Astra Zeneca/ Rigel Pharma	R788	Prodrug syk inhibitor	2010	Phase II	RA	1,200 (100m upfront)
Dr Reddy Labs/ XenoPort	XP23829	Tepilamide fumarate	2016	Pre-clinical	RRMS	Up to 440 (47.5m upfront)
Sanofi/ Principia Biopharma	PRN2246	BTK inhibitor -oral	2017	Phase I	MS	Up to 765m (40m upfront)
Novartis/ GSK	Azerra (ofatumumab)	CD20 inhibitor (similar to Rituxan)	2015	Phase II	RRMS	1,043 (300m upfront)
Servier/ GeNeuro.	GNbAC1	Promotes rejuvenation of myelin	2014	Phase II	RRMS	455 (47m upfront)

Source: First Berlin Equity Research, Companies

PRODUCTS – DETAILED ANALYSIS

Estimation of price, sales potential and product value

Rabeximod against Rheumatoid arthritis (RA) Rabeximod is an oral drug candidate that has shown attractive efficacy in the treatment of RA in combination with the first-line therapy methotrexate (MTX). Based on disease prevalence statistics (see disease chapter of this report), we estimate the total number of subjects suffering from moderate to severe RA in the US, Europe and Japan at 3.0m. Approximately 800k patients are treated with MTX of which 470k do not respond to treatment, which in our view represents the target population for Rabeximod. We have conservatively assumed an average ex-factory drug price per year of USD12,000 (SEK106,800). We note that comparable injectable treatments have a price in the range USD21k-35k per year. Moreover, newer oral drugs such as JAK-inhibitor Xeljanz are selling for about USD 25k-30k per year. Our assumed price applies a significant discount to competing drugs' prices and takes into account Rabeximod's lower production costs. This should enable the product to penetrate the market faster.

Due to ageing of the population, we have assumed that this segment will increase at a CAGR of 4% by 2040. We expect Cyxone to achieve a penetration rate of 9%, leading to peak sales of USD951m (SEK8.5bn) by 2034. We note that market projections on competing oral drugs such as Updacitinib and Filgotinib see peak sales in the range of USD1.4bn and 2.6bn (see competitive environment chapter of this report) despite strong side effects.

However, we prefer to stay cautious in our estimate, as Cyxone is behind its RA oral drugs competitors and the positive efficacy/safety profile still has to be confirmed in late stage development. We project a potential approval and market launch in 2023.

Table 3: Assumptions rheumatoid arthritis

Rabeximod	Present Value	Patient Pop	Treatment Cost	Market Size	Market CAGR	Market Share	Peak Sales	PACME Margin	Discount Factor	Patent Life
Parameters	$54M	470K	$12,000	$5,640M	4%	9%	$951M	16%	21.5%	9

Source: First Berlin Equity Research

We have assumed that Cyxone will out license the drug following successful phase II trials to a pharmaceutical partner, leading to an upfront payment of USD10m (SEK 89m) in 2020 and a gross royalty rate of 18% of sales. The partner will conduct phase III development and commercialization. We have assumed that the pharmaceutical partner will bear the marketing expenses, and that Cyxone's royalties will roughly equate to its profit on the product. Taking the 10% of profit to which the originator OxyPharma is entitled into consideration, we arrived at a net PACME royalty rate of 16%.

T20K against Multiple sclerosis (MS) T20K is a late-stage preclinical drug candidate against MS. Based on prevalence statistics (see disease chapter of this report), we estimate that about 1.0m subjects suffer from MS in the US, Europe and Japan. About 85% of this population, which equates to 850k subjects, suffers from relapsing remitting MS (RRMS), which is the main target of T20K. We have therefore assumed that the potential market will mostly consist of RRMS patients. Thus, we estimate this market will grow at a CAGR of 2% until 2040.

We have estimated an average ex-factory price for the drug's one year treatment of USD24k in its target markets. As a reference, Roche launched its oral drug Ocrevus in 2017at a list price of USD65k in the US, which implies an approx. 20% discount to peers' oral drugs Gilenya (USD90k), Tecfidera (USD83k), Aubagio (USD80k). Our assumption takes the typical 30% wholesaler margin as well as a roughly 45% discount to Ocrevus into account.

Given that the drug candidate is in late pre-clinical stage and the initiation of phase I is imminent, we have included the project in our valuation model. We project a potential approval and market launch in 2026. Based on an anticipated penetration rate of 5%, we expect Cyxone to achieve peak sales of USD1.4bn (SEK12.7bn) by 2035. We believe our estimate is conservative, considering that peers' drugs such as Tecfidera and the recently launched Ocrevus are projected to achieve peak sales in excess of USD4bn (Source: Pharma intelligence, 2018).

Table 4: Assumptions multiple sclerosis

T20K	Present Value	Patient Pop	Treatment Cost	Market Size	Market CAGR	Market Share	Peak Sales	PACME Margin	Discount Factor	Patent Life
Parameters	$25M	850K	$24,000	$20,400M	2%	5%	$1,428M	18%	21.5%	9

Source: First Berlin Equity Research

We have assumed that Cyxone will license the drug candidate after phase II trials, in order to maximize the licensing conditions and minimize investors' dilution. As a result we have projected that the upfront payment from the potential licensing pharmaceutical partner for the drug candidate will amount to USD10m (SEK 89m) in 2022. We have also assumed a royalty rate of 18% upon commercialization.

COMPANY PROFILE

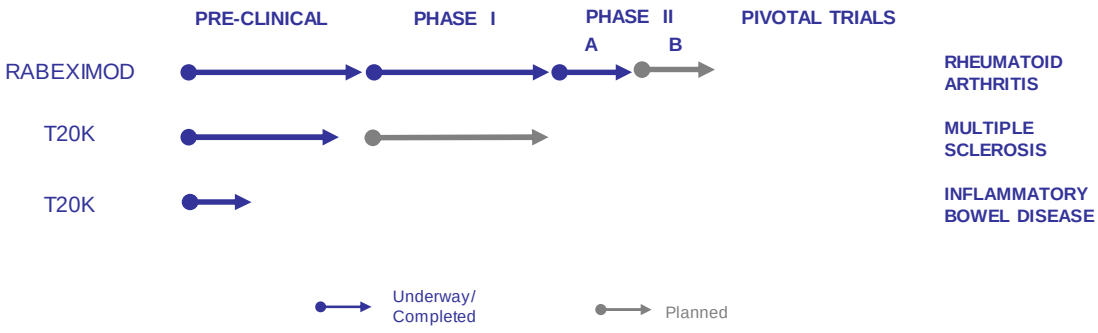
OVERVIEW

Swedish biotech company developing therapeutics against autoimmune and inflammation diseases Founded in 2015 and headquartered in Malmö, Sweden, Cyxone AB is a clinical stage biotech company with a product pipeline focused on severe autoimmune diseases such as Rheumatoid Arthritis (RA) and Multiple Sclerosis (MS). The company owns a patent-protected technology as well as novel molecules which play a relevant role in a damaged immune system and the inflammation process. The technology enables the generation of drug candidates based on a type of natural plant protein called Cyclotides. The Cyclotide-technology and the company's pre-clinical drug candidate T20K against MS are the result of almost a decade of research collaboration between the Medical University of Vienna and the University Clinic in Freiburg. The Cyclotide expertise was expanded through a cooperation with the University of Queensland, who are also pioneers in the field.

Backed by the investment fund Accequa AB, the company acquired the exclusive license rights to the Cyclotide-technology and the first Cyclotide-based generated drug candidate T20K in 2015. Cyxone has also taken over responsibility for the development of T20K as well as the development of Cyclotide-technology to generate other future potential drug candidates. T20K is in late-stage pre-clinical development for MS. Patient enrolment for a phase I trial is planned before the end of the year. Preclinical data for T20K in MS look promising. The product has shown clear immune suppression activity without the typical undesired side effects.

In June 2017, the company expanded its R&D pipeline through the acquisition of the Phase II drug candidate Rabeximod against RA from the originator company OxyPharma AB. Cyxone issued 1.9m shares, which at the then share price of SEK5.3 equated to approx. SEK10.1m (USD 1.1m) plus potential royalties of 10% on future net earnings generated with the drug. The acquired lead drug candidate Rabeximod achieved proof of principle against RA in a phase IIa study conducted in 2009. A phase IIb efficacy study of the product is set to start in the near future and preparations are underway. Rabeximod achieved strong data in the phase IIa study including 224 patients, delivering statistically significant therapeutic effect in week 16. Unfortunately, the trial design stipulated review of the trial data at week 12, which is why the programme missed the primary endpoint despite showing efficacy during the follow-up period. A further phase IIb efficacy trial is required. In our view, these results provide a sound basis for further development. Cyxone intends to conduct a clinical phase IIb-study with Rabeximod including 24 weeks' treatment with the same dose that previously showed significant effects on RA.

Figure 1: Snapshot of the clinical stage R&D pipeline focusing on autoimmune diseases



Source: First Berlin Equity Research, Cyxone AB

Extremely lean organisation Cyxone is still a young and small company. Therefore, the founders have implemented a resource-efficient virtual structure that utilizes personnel resources on demand, including the experienced management team. The company currently has only two employees on the payroll. The remaining staff works on a freelance basis and R&D work is largely outsourced.

Strategy focused on lead drug candidates The development strategy is to develop lead drug candidates such as Rabeximod, T20K and other Cyclotides through phase I or phase II. Thereafter, the company will out-license the commercial rights to pharmaceutical companies who should finance the cost intensive phase III clinical trials. The company intends to lower risks and R&D spending as well as to benefit from the expertise, financial resources, marketing muscle and experience of the pharmaceutical partner. In this report we focus on the lead drug candidates Rabeximod and T20K in the two main indications, RA and MS, which are the main value drivers of the company.

First North listing on April 2016 opens doors for access to new funds In order to further finance pipeline development, the company decided to go public on the First North Exchange in Sweden, which is a division of Nasdaq Nordic and an alternative stock exchange for smaller companies in Europe. Cyxone placed 5.0m shares at SEK5.00, raising SEK25.0m (USD2.8m) and equating to a pre-money valuation for the company of SEK40.0m (USD4.5m). The placement included 5.0m warrants in two tranches, T01 and T02, 97% of which were converted in 2017 into 4.9m shares raising gross proceeds of SEK24.3m (USD2.7m).

Capital increase raising gross proceeds of SEK44.3m to finance Rabeximod's phase IIb trial successfully closed On 26 October the company closed a placement of 17.7m shares at a price SEK2.50, equating to gross proceeds of SEK44.3m (USD5.0m). The shares have an equal number of warrants attached, which entitle the holder to subscribe to new shares in the period 2-11 September 2019 at a 25% discount to the weighted average price of the shares in the period 19-30 August 2019. The subscription price can not be less than SEK3.75 or higher than SEK7.50 per share. If the warrants are converted, the company can potentially raise further funds in the range SEK66.5m-SEK133.1 in September 2019.

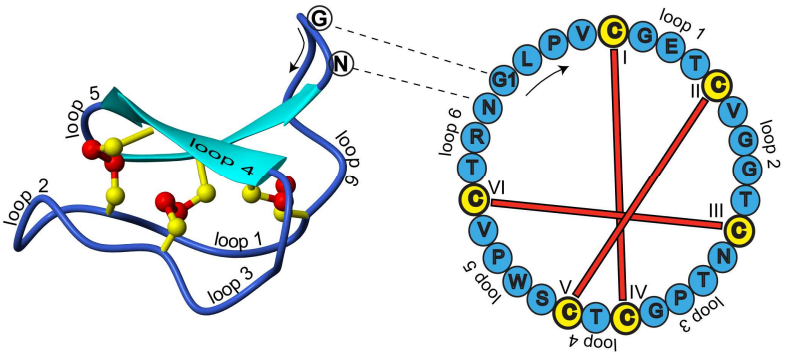
THE "CYCLOTIDE" TECHNOLOGY PROVIDES COMPETITIVE ADVANTAGE

Cyxone's proprietary technology enables the company to generate a novel highly efficient class of molecules called Cyclotides which show promising therapeutic potential. Cyclotides are plant-derived circular peptides which contain a cyclic cystine-knotted structure. In general, peptides are recognized for being highly selective, efficacious and relatively safe and well-tolerated. As a result, there is an increased interest in peptides in pharmaceutical R&D. Over 150 therapeutic peptides are currently being evaluated in clinical trials (Jolene L. lau et al., 2018). However, enthusiasm for therapeutic peptides has been tempered by certain limitations of peptides, such as chemical and physical instability, short plasma half-life and negligible oral bioavailability. Oral delivery is often viewed as a highly attractive feature for supporting patient compliance, particularly in chronic indications.

Cyclotides possess remarkable structural features solving the key limiting problems of standard peptides thus far. Their unique circular backbone structure and knotted arrangement makes them exceptionally stable to chemical, thermal and biological degradation compared to other peptides of similar size. This stability even makes them suitable for oral administration (Colgrave et al., 2004).

The circular Cyclotide chain usually consists of 30 amino acids including six conserved cysteines. Because of their relatively small size, they are easily produced by chemical synthesis. This translates into a large benefit allowing the achievement of low production costs (especially in comparison to highly complex and costly biological drugs, the production of which is difficult to scale). Additionally, the inter-cysteine sequences can tolerate a wide range of residue substitutions and chemical modifications (e.g. unnatural amino acids and PEGylation) to improve their pharmacological properties (Clark et al., 2006). Cyclotides' stability, flexibility and ability to cross the cell membrane mean that these molecules can be exploited as a vector to develop new stable peptide-base drugs (Krishnappa et al., 2010). Cyxone could therefore use the Cyclotide technology to generate novel mutant Cyclotide-based drug candidates with superior therapeutic activity in diverse targeted diseases.

Figure 2: Cyclotide structure and sequence



Source: First Berlin Equity Research, University of Queensland

The discovery of the first natural Cyclotide kalata B1 was based on its presence in tea extract of the Rubiaceae species Oldenlandia affinis used in African indigenous medicine to accelerate childbirth (Gran et al., 1970). In the meantime, a wide range of relevant pharmaceutical applications have been found in screening studies of natural Cyclotides (Craik et al., 2012, 2013; Henriques and Craik, 2015). Cyclotides have for example shown therapeutic properties in the following indications: anti-HIV (Wang et. al., 2008), cytotoxicity to lymphoma cell lines (Svangard et al., 2004), immunosuppressive activity in autoimmune diseases (Thellet al., 2014) and anti-multiple sclerosis activity using intravenous delivery (Wanget al., 2014).

Further studies based on Kalata B1 mutated Cyclotides have shown therapeutic potential in cancer therapy, targeting the vascular endothelial growth factor-A receptor VEGF-R2 (Gunasekera et al., 2008); in chronic pain therapy, targeting the bradykinin B1 receptor (Wong et al., 2012), as well as in the context of cardiovascular disease targeting thrombin (Getz et al., 2011), and in obesity (Eliasenet al., 2012). The wide range of therapeutic applications of mutated Cyclotides underscore the huge potential of the Cyclotide technology. Recently Gruber et al. reported that T20K, Cyxone's Cyclotide mutated from kalata B1, showed efficacy in a mouse model of multiple sclerosis when administered orally (Thell et al., 2016).

We note that most studies conducted so far were based on Kalata B1 and some mutations of this molecule. But there is a large number of Cyclotides to be investigated. In a recent study, Gruber and colleagues identified 164 Cyclotides in Viola tricolour alone, which led them to estimate the total number of Cyclotides in the Violaceae to be 150,000 (Hellinger et al., 2015). Although the exact number of Cyclotides is difficult to estimate, it appears that it will certainly be in the tens of thousands (Weidmann et al, 2016).

COMPANY HISTORY

Table 5: Key milestones in company's history

Time	Corporate events
2009-2014	Researchers at the Medical University of Vienna and the University Clinic in Freiburg conducted research in the field of Cyclotides, leading to the discovery of the company's drug candidate T20K. The research groups have well established close collaboration with a Cyclotide-focused research group in Queensland, Australia. Together, these teams are at the forefront of Cyclotide research.
2014-2015	Cyxone's founders recognized the potential of the Cyclotide technology under the research leadership of Associate Professor Christian Gruber. Negotiations to acquire the Cyclotide technology started in 2014. An agreement to obtain exclusive license rights for patent applications for Cyclotides and T20K was closed in 2015 with the biotech specialized investment fund Accequa AB.
2015	Cyxone was founded in Malmö, Sweden as Cyxone AB. Accequa became the main shareholder and transferred the rights of the Cyclotide technology and T20K to Cyxone.
2016	Cyxone carried out a listing of the company on the First North Exchange in Sweden and conducted a capital increase that secured the company new funding of SEK25 million before issue costs. These funds will enable the development of the T20K program through phase I. Following completion of assessment of the potential of the lead Cyclotide candidate T20K, the company decided to purchase the entire family of patents protecting the product from the Medical University of Vienna.
June 2017	Cyxone closed the acquisition agreement for the RA phase II drug candidate Rabeximod with the originator OxyPharma. The company agreed to issue 1.9m shares to OxyPharma as well as potential royalties of 10% on Rabeximod net earnings in case of successful registration and commercialization of the product. The company secured an option to determine the timing of transaction closure and share transfer to gain time for further analysis of the product.
February and October 2017	The company raised net proceeds of SEK23.1m stemming from the conversion of warrants from the capital increase in 2016.
April 2018	The Cyclotide discoverers Carsten Gründemann and Christian W. Gruber of the University of Vienna and Kjell G. Stenberg, CEO of Cyxone, published a joint article in the renowned International Journal of Peptide Research and Therapeutics, demonstrating the potential of Cyclotides and T20K for treatment of autoimmune diseases in animal models.
June 2018	Cyxone completed the acquisition of Rabeximod and issued 1.9m shares (increasing the number of shares outstanding from 17.8m to 19.7m).
October 2018	Cyxone placed 17.7m shares raising gross proceeds of SEK44.3m (USD5.0m). Based on an equal number of attached warrants, the company can potentially raise further funds in the range SEK66.5m-SEK133.1 in September 2019. This amount represents a 25% discount to the average share price during the period 19-30 August 2019.

Source: First Berlin Equity Research, Cyxone AB

THE LEAD DRUG CANDIDATE RABEXIMOD SHOWS PROMISE IN RHEUMATOID ARTHRITIS (RA)

PRE-CLINICAL DATA SUGGEST NOVEL MECHANISM OF ACTION IN RA

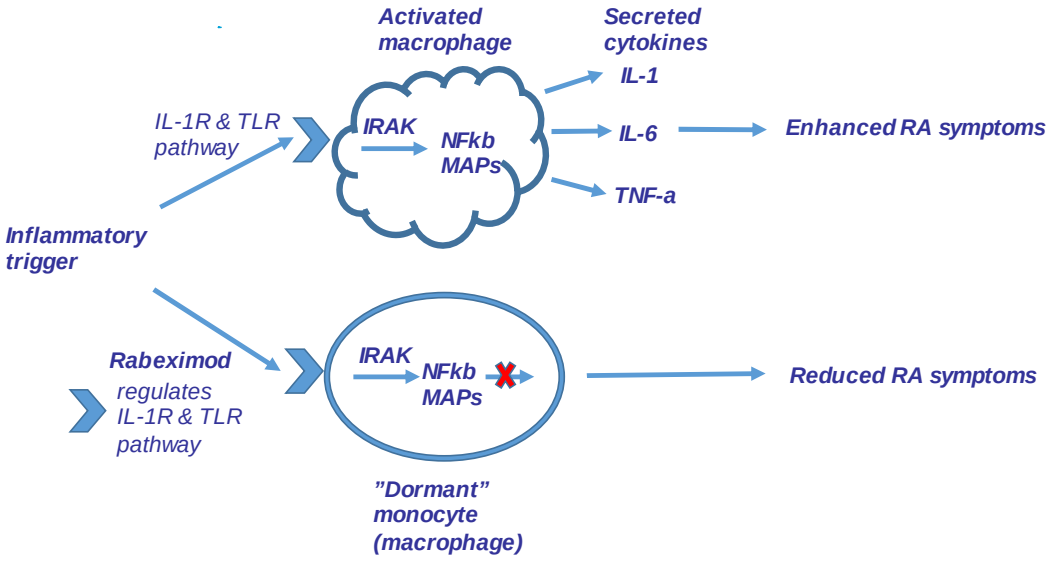
Rabeximod's mode of action is not fully understood. Pre-clinical studies suggest it may act by inhibiting activation of macrophages and cytokines that cause RA symptoms Cyxone's lead product candidate Rabeximod, also known as Rob 803, is a quinoxaline analogue belonging to the class of acetamides (small molecule). Unlike most typical drugs, Rabeximod was originally studied and developed in animal models of chronic inflammatory diseases such as rheumatoid arthritis (RA) and multiple sclerosis (MS) rather than against a specific target. As a result, the precise mechanism of action and specific binding sites of the product are not fully established. However, many in vitro and in vivo studies have suggested Rabeximod inhibits the inflammatory process by blocking the activation of inflammatory cells called macrophages. Macrophage cells exist in several different subpopulations with various functions, such as destroying surrounding tissue, directing healing responses, presenting antigens to T-cells and triggering an immune mediated inflammatory response.

Macrophage cells are considered to play a pivotal role in the inflammatory process of RA leading to tissue destruction and clinical symptoms. The macrophage is a key cell in immune presentation of antigens and contributes considerably to both the initiating phase of the inflammation as well as the perpetuation of the inflammatory process (Kinne et al., 2000). Macrophages produce a number of inflammatory cytokines (e.g. TNFα, IL-1, IL-6, MIP-1α, MIP-1β), which are cytotoxic and also contribute to cartilage and bone destruction (Ma Y et al., 2005). The degree of macrophage infiltration and activation not only correlates with joint pain and the general inflammatory status of the patient, but also with the radiological progression of permanent joint damage (Mulherin et al., 1996; Takk et al., 1997).

In vitro study: Rabeximod blocks activation of inflammatory macrophages In order to further understand Rabeximod's mode of action, a research team from the Karolinska Institute in Stockholm investigated the influence of Rabeximod on human cell lines by using peripheral blood mononuclear cells (PBMCs) from anonymous blood donors. The researchers isolated monocytes from the cells and exposed them in a cell culture to Rabeximod in order to follow up their behaviour (i.e. differentiation). Importantly, the in vitro data showed that Rabeximod suppresses the differentiation of monocytes into pro-inflammatory macrophages and impairs the production of certain types of pro-inflammatory cytokines (Giusti et al., 2009). Particularly, the addition of Rabeximod to the cultures reduced the release of inflammatory cytokines IL-1, IL-6 and TNF-α (Hutqvist et al., 2008).

As can be seen in figure 3 overleaf, Rabeximod blocks the activation of inflammatory macrophages. Inflammatory macrophages are stimulated through the IL1 receptor family and the TLR receptors. Rabeximod seems to block this pathway after receptor activation. As a result, Rabeximod affects the production of a number of inflammatory cytokines secreted in response to the activation of the IL1R/TLR pathway. It is therefore likely that Rabeximod acts upstream of cytokine secretion. The study suggests that the product blocks several mechanisms in the inflammation process with beneficial effects also in patients unresponsive to target-directed drugs such as TNF-α blockers.

Figure 3: Rabeximod may block activation of macrophages for inflammation



Source: First Berlin Equity Research, Cyxone AB, Disease models investigated by OxyPharma

These findings validate Cyxone's therapeutic approach in pursuing the inactivation of inflammatory macrophages and not targeting only one of the inflammatory cytokines. We therefore believe Cyxone's drug candidate approach may prove superior to its peers' targeted strategy.

In vivo study established Rabeximod's ability to reduce disease severity in autoimmune disorders such as RA and MS Several animal studies investigated Rabeximod's ability to treat autoimmune diseases such as collagen-induced arthritis, collagen antibody induced arthritis and experimental autoimmune encephalomyelitis (MS) which are all mice and rat models with a proven track record of predictability for efficacy in humans. Rabeximod proved to be effective in a rat model of collagen-induced arthritis (Westman et al. 2008) and has demonstrated a similar clinical benefit as an anti-TNF- drug in a mouse model of collagen antibody-induced arthritis (Hultqvist et al. 2009).

Rabeximod's treatment had protective effects both at the initiation (preventing the disease) and also in relapsing phases of arthritis (reducing disease severity) The in vivo studies determined a dose of 40 mg/kg to deliver the best preventive effect with an arthritis-reducing capacity similar to Enbrel, the most widely used TNF-α blocking agent for treatment of RA. Overall, the in vivo studies also demonstrated the anti-inflammatory effect of Rabeximod similar to the potent corticosteroid drug Dexamethasone which is also widely used for RA treatment. Interestingly, the preclinical studies showed a pronounced effect of Rabeximod in the emerging inflammatory phase of the autoimmune disease as well as in the more advanced stages.

PHASE I AND PHASE IIA DATA IN MODERATE TO SEVERE RA SHOWED POSITIVE RESULTS

Phase I clinical trials in healthy volunteers showed that the product is well tolerated and has a favourable pharmacokinetic profile To date, one first-in-human, single-centred, randomized, placebo controlled phase I clinical trial has been completed. This first study assessed safety, tolerability, pharmacokinetics and pharmacodynamics of rising oral doses of Rabeximod in 87 healthy male volunteers. The purpose was to examine their

response to ascending doses of the product. Rabeximod was well-tolerated after a single dose of up to 400 mg/kg, a loading dose of up to 200 mg/kg and a 50 mg/kg maintenance dose, without producing significant side effects. Seven out of 24 subjects who participated in the multiple dose stage experienced phototoxic reactions at the 660/100 mg dose level. However, symptoms disappeared at the end of the study.

Phase IIa clinical trial with 224 patients completed by originator OxyPharma In August 2009, Rabeximod's originator OxyPharma completed a European multi-centred (33 centres across 9 countries), double blinded, phase IIa clinical trial evaluating the safety and preliminary efficacy of the product in 224 patients with moderate or severe active RA in combination with methotrexate (MTX). MTX is the first line standard of care treatment for RA patients in this particular stage of the disease. Rabeximod was administered orally, once daily in three different doses: 6.25mg, 15.0mg and 37.5mg. The primary endpoint of the study was to evaluate the efficacy of Rabeximod over 12 weeks in combination with a stable dose of MTX in RA patients, with clinical follow-up visits through week 16. Efficacy was defined in accordance with American College of Rheumatology 20 or ACR20, which measures a >20% disease improvement based on the number of swollen and tender joints, plus three out of the following five criteria: patient global assessment, physician global assessment, patient pain assessment, patient self-assessed disability by mHAQ (Health Assessment Questionnaire) and C-reactive protein (CRP).

Figure 4: Phase II study design to evaluate efficacy and safety of oral Rabeximod in combination with methotrexate (MTX) for RA

Source: First Berlin Equity Research, Cyxone AB

The phase IIa study showed statistically significant superior efficacy for the combination Rabeximod/MTX in RA, but missed the primary endpoint due to design parameters The phase IIa study was well-designed and included input from leading experts from the RA field. However, it was based on the general view in the early 2000s that clinical studies should be conducted with a time horizon of 12 weeks (at present the timeframe varies from 12-24 weeks). While the typical time frame of 12 weeks is enough for other drugs, Rabeximod requires slightly longer to unfold its full potential. As can be seen in table 6 overleaf, Rabeximod's optimal dose of 15mg showed a clear increasing trend of ACR20 efficacy over time. This dose achieved the highest efficacy of 53.3% of patients benefiting from the treatment during the follow up period at week 16 with the statistically significant level of $p<0.0198$, against 28.6% efficacy with placebo. However, the positive results were achieved outside the 12 weeks time frame stipulated for the primary endpoint. The efficacy of Rabeximod versus placebo was not statistically significant during the designated 12 week period. The study was therefore formally recorded as having not achieved its primary endpoint. A further phase II efficacy study became necessary to continue development. Based on OxyPharma's limited financial resources and the challenging competitive environment back in 2009, when Pfizer's drug candidate Xeljanz was showing promising results for RA, the originator company decided to discontinue development. While Xeljanz has been approved, its negative side-effect profile accompanied

by a black box warning limits its therapeutic potential (see chapter on competitive environment analysis) and creates a market opportunity for Rabeximod and other drugs.

Table 6: Overview of Rabeximod's ACR20 efficacy rates in phase IIa study for RA in combination with MTX

Efficacy ACR20%	Rabeximod 15mg	Placebo
Week 4	15.1% .	19.6%
Week 8	41.3%	30.4%
Week 12 - Primary endpoint for efficacy	45.9%*	33.3%
Week 16 - Follow up period	53.3% **Significant (p<0.0198)**	28.6%

**The study did not meet the primary endpoint of showing statistically significant superior efficacy compared to placebo at week 12. However, it demonstrated statistically significant superior efficacy at week 16 (follow-up period).*

Source: First Berlin Equity Research, Cyxone AB

Analysis of further parameters reinforces positive efficacy profile of the optimal 15mg Rabeximod dose at week 16 The Disease Activity Scores (DAS scores) improved at all doses, reaching statistical significance with the optimal dose of 15 mg ($p<0.0415$) at week 16. Also the response in accordance to the European League Against Rheumatism (EULAR) guidance increased in patients treated with Rabeximod, achieving statistical significance with the optimal 15 mg dose ($p<0.0371$) at week 16. Other secondary endpoints such as mean swollen and tender joint count, subject and physician global assessment of disease activity (VAS), joint pain, HAQ-DI and acute phase reactants (CRP and ESR) showed significant improvement. Morning stiffness was also improved and approached statistical significance at week 16 ($p<0.0549$).

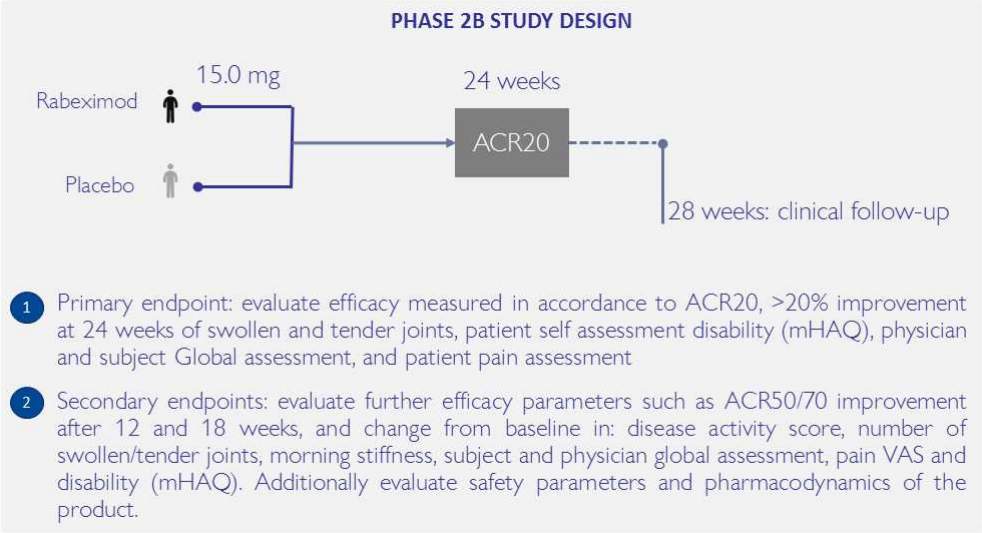
The overall safety profile of Rabeximod was also positive The product was well tolerated in all three doses studied and did not generate severe adverse events. Non-serious adverse events were more common in the Rabeximod than in the placebo group (34.5% for Rabeximod - mainly in the 37.5 mg cohort - against 11.1% for placebo). The most common adverse event was associated with skin and subcutaneous tissue. The incidence observed was 45.5% for the 37.5 mg group, 19.0% for the 15 mg group and 12.1% for the 6.25 mg group, compared to 1.9% for the placebo group.

Rabeximod could become a "novel" treatment with a positive efficacy and safety profile for RA. Based on work in cell lines, animal models and human phase I-II trials, Cyxone has demonstrated that the product showed promising efficacy without adding significant side effects.

PLANNED PHASE IIB TRIAL OF RABEXIMOD IN MODERATE TO SEVERE RA

A confirmation phase IIb trial Cyxone intends to conduct a phase IIb study of Rabeximod in moderate to severe RA patients. This planned multi-centre, double blinded, placebo controlled phase IIb trial in Europe will include approximately 200-250 patients in total. Considering that the phase IIa study failed due to short duration, the company has decided to conduct the trial over a period of 24 weeks (6 months). In preparation for the phase IIb trial, the company will additionally carry out an animal study in rats and dogs to investigate toxicity during long term treatment, which may last 6-9 months. Cyxone expects to enrol the first patient in this phase II trial towards mid-2019. First top-line data will likely be published in H2/20. We give an overview of the main parameters for the phase IIb trial in figure 5 overleaf.

Figure 5: Overview of the planned phase IIb trial to evaluate the efficacy and safety of orally administered Rabeximod in combination with MTX



Source: First Berlin Equity Research, Cyxone AB

The company believes a positive outcome of this trial would be sufficient to support the conduct of a registration pivotal double-blind, randomized trial of Rabeximod in combination with MTX against placebo.

Cyxone intends to negotiate a potential collaboration agreement following successful phase IIb results The company is aiming to collaborate with a large pharmaceutical company willing to finance the expensive phase III trials. Assuming a positive outcome in the phase IIb trial, the company will then likely conduct a single pivotal double-blind, placebo-controlled phase III trial with the selected pharmaceutical partner both in Europe and the United States. The primary endpoint is likely to be ACR20 efficacy. A trial of this scope can easily cost >USD30m. We therefore believe an agreement with a deep-pocketed pharmaceutical development partner would be a reasonable path.

RHEUMATOID ARTHRITIS (RA)

RA IS A DISEASE WITH HIGH UNMET MEDICAL NEED

Description of RA Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes progressive articular damage and results in a wide range of systemic symptoms due to the associated inflammation. RA most commonly affects the joints of the hands, feet, wrists, elbows, knees and ankles. However, over time, RA can also affect the cardiovascular system (e.g. heart or blood vessels), the respiratory system (e.g. lungs) and other main body organs such as the kidneys, eyes, and skin.

In response to the RA disease, the body's immune system mistakenly attacks the joints. In this process the associated inflammation causes the synovium - the tissue that lines the inside of joints - to thicken, resulting in swelling and pain at the joints sites. Over time, there is loss of cartilage, joints can become loose, unstable, painful and lose their mobility and normal form. Joint damage and joint deformity cannot be reversed. Since this damage can take place at an early stage, doctors recommend early diagnosis and aggressive treatment to control RA. If not treated adequately, RA can be a disabling and painful condition, which can lead to substantial loss of function and mobility (Source: Mayo clinic).

Prevalence of RA Prevalence of RA is estimated at around 1% of the world's population and affects approx. 1-2% of the western world population (Alamanos et al., 2006, Chopra et al., 2008). The disease is 2-3 times more common in women than in men (rheumatology.org, 2016) with peak onset of the disease in the ages between 20 and 40. Based on statistics from 2005-2010, prevalence in adults in the US was 1.3m. In the US, the direct cost of RA was estimated at approximately USD13,500 per affected person per year, and indirect costs could range between USD1,000 - 33,000 per affected person per year (Kvien TK, 2004). The cause of RA is still unknown, but there is a strong genetic component. According to Scott et.al., 50% of the risk for development of RA is attributable to genetic factors. Also, the risk of developing RA is higher in individuals who have the HLA-DRB1*04 gene types. >80% of RA patients carry this gene (Choy et al., 2012).

Diagnosis and classification The diagnosis of RA is made upon the appearance of symptoms and is based primarily on physical examination by the physician, followed by radiographs (X-rays) and diagnostic tests. These tests are based on markers such as the antibody rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs). The most common ACPA tests are the anti-CCP (cyclic citrullinated peptide) test and the anti-MCV assay (antibodies against mutated citrullinated Vimentin). The disease can be classified by physicians in accordance with certain parameters defined by the American College of Rheumatology (ACR, updated in 2010) and the European League Against Rheumatism (EULAR). The classification criteria establish a point value between 0 and 10. Every patient with a point total of 6 or higher is classified as an RA patient, provided there is inflammation of the synovial membrane in at least one joint and there is no other plausible reason for the inflammation. However, the classification process is laborious and therefore currently mostly used for research purposes (Sources: Arthritis Foundation US, NRAS UK).

RA biology: B cells may play an important role in the RA inflammation process B-cells, which are part of the body's immune system, play a pivotal role in the inflammation process in RA. B cells produce pro-inflammatory cytokines, such as tumour necrosis factor (TNF)-alpha and interleukin (IL)-6. TNF-alpha can activate macrophages and amplify the pro-inflammatory signal, resulting in an enhanced production of IL-1, IL-6 and additional TNF-alpha, contributing to the inflammatory damage (Bugatti et al., 2014). In addition, activated B-cells would usually express the protein CD20. As a result, modern disease modifying medication would usually target some part of the B-cell inflammation pathway.

TREATMENT OF RA AND COMPETITIVE ENVIRONMENT

Treatment and main products Treatment for RA is tailored to the specific symptoms and disease severity. Traditionally, the first-line therapy for early stages of RA has included non-steroidal anti-inflammatory drugs (NSAIDs) to relieve pain and inflammation. However, NSAIDs have problems with dose-limiting side effects such as headache, stomach problems, higher blood pressure, kidney injury, decreased platelet function and the possibility of renal damage or gastrointestinal bleeding (Fujita et al., 2013; Murray and Brater, 1993). As a result, physicians recommend administering NSAIDs at the lowest dose and for the shortest time possible. In some cases, corticosteroids have also been used to quickly stop inflammation that threatens the joints or internal organs (Rainford et al., 2007). Nevertheless, corticosteroids show limitations in the case of long-term administration, inducing severe side effects such as bone damage, diabetes, hypertension, weight gain and eye disorders (Ethgen et al., 2013; Curtis et al., 2006).

While NSAIDs treat symptoms of RA, they are not able to stop progress of the disease (Tabas and Glas, 2013). In order to slow or stop the progression of the disease and damage to the joints, alongside NSAIDs physicians prescribe conventional disease-modifying anti-rheumatic drugs (conventional DMARDs), biologic agents targeting inflammatory cytokines (biologic DMARDs) or small molecules targeting the JAK enzymes (newer DMARDs).

Conventional DMARDs are a variety of older, small molecule drugs with different chemical structures and modes of action. The most commonly used DMARDs for the treatment of RA include methotrexate (MTX), leflunomide, hydroxychloroquine (HC) and sulfasalazine. Further existing DMARDs which are less frequently used include: gold salt, azathioprine, cyclophosphamide, minocycline and penicillamine (Kim et al., 2013). Since the first administration of MTX in RA in the early 1960s, the drug has been used as first-line treatment basically due to its superior efficacy and side effect profile compared to other existing DMARDs. At present, MTX remains the first-line therapy for RA patients (Visser et al., 2009; Favalli et al., 2014). However, RA is a complex disease and a considerable proportion of patients, which can be as high as 70-80%, do not respond to MTX (Moreland et.al., 2012). For these patients, a combination of MTX as anchor drug with other conventional or biologic DMARDs is a recommended option (van Vollenhoven et al., 2014).

Biologic DMARDs are considered a second-line treatment for patients who have an inadequate response to conventional DMARDs. Biologics are large molecules (e.g. monoclonal antibodies) which must be injected or infused. They usually target so called inflammatory cytokines, which play an important role in the inflammation process. TNF-α, IL-1, and IL-6 appear to be among the most relevant pro-inflammatory cytokines in RA. TNF-α is considered to be the master pro-inflammatory cytokine. Therefore, the use of biologic therapies is dominated by the TNF-α blockers adalimumab (Humira), etanercept (Enbrel), and infliximab (Remicade), golimumab (Simponi), and certolizumab pegol (Cimzia). However, up to 40% of patients do not respond to anti-TNF treatment (Roda et al., 2016). Furthermore, there are potential serious side effects associated with TNF blockers, such as serious infections (e.g. tuberculosis or pneumonia) and lymphoma - although RA patients in general have a higher risk of lymphoma compared with the general population (Antoni and Braun, 2002; Bongartz et al., 2006). Further biologic DMARD alternatives include products such as the T-cell co-stimulatory blocker abatacept (Orencia), the CD20-protein blocker rituximab (Rituxan), the Interleukin-6 (IL-6) inhibitor tocilizumab (Actemra), and the Interleukin-1 (IL-1) inhibitor anakinra (Kineret).

A significant advance in RA treatment is the availability of the first highly efficacious oral drug tofacitinib (Xeljanz). This product is an inhibitor of the enzyme janus kinase 3 (JAK3) and received approval in 2012 in the US and 2017 in Europe. The proportion of patients achieving ACR20 and ACR50 efficacy in the Xeljanz clinical trials was comparable to that

seen in clinical trials of TNF-α blockers. While the product showed very good efficacy, the side effect profile generated concerns. As a result the drug approval included a black box warning (FDA's strictest notification of health risks associated with a drug) for serious infections such as tuberculosis and for several cancer types such as lung and breast cancer, gastric, colorectal, renal cell and prostate cancer. In June 2018, the second JAK-inhibitor, baricitinib (Olumiant) received approval in the US. For the approved lower dose, the product did not show superior efficacy compared to TNF-blockers. Further, the approval also included a black box warning for serious infections and potentially deadly blood clots.

Blockbuster DMARDs and the TNF-α blockers top the list of most prescribed drugs for RA Currently, the RA market of moderate to severe patients is dominated by the conventional DMARDs and the TNF-α blockers drugs which are also prescribed for other therapies beyond RA. AbbVie's and Pfizer's blockbusters Humira and Enbrel are the leaders achieving worldwide sales of USD18.9bn and USD8.2bn in 2017.

Outlook treatment development: promising IL-6 and JAK-inhibiting drug candidates dominate the late stage pipeline development In the period 2012-2017, 209 phase I-III trials were initiated or were planned. Unfortunately, the novel mechanism of actions and targets such as inhibiting IL-12, IL-17, IL-20, IL-21, IL23, Flt-3, PI3, histamine H4 receptor and MMP9 (ustekinumab, sekunimab, ABT-122, fletikumab, NNC-114-0005, guselkumab, fostamatinib, duvelisib, toreforant and andecaliximab) proved mostly unsuccessful and suffered setbacks due to a lack of safety or efficacy (Source: Pharma Intelligence, 2017). We have summarized the drug candidates in late stage development for RA in the table below.

Table 7: Therapies in development or recently approved for moderate to severe RA

Company	Drug candidate	Mechanism	Development stage / measure	Comments
Sanofi/ Regeneron	sarilumab/ Kevzara	IL-6 inhibitor	Approved in May/June 2017 in the US/EU / looked for DAS28 and ACR20 (week 24)	Boxed warning recommending testing for tuberculosis before treatment
GSK/ JNJ	sirukumab	IL-6 inhibitor	Phase III /looked for ACR 20 (week 16) and DAS28 / ACR50 (week 24)	Development discontinued after FDA refused approval based on safety concerns and request of further trials
R-Pharma/ UCB	olokizumab	IL-6 inhibitor	Phase III - looking for ACR20 (week 12)	The trial is expected to be completed in 2019
Elly Lilly	baricitinib/ Olumiant - oral	JAK1/2 inhibitor	Approved in the EU. Approved in the US with a black box warning / looked for ACR20 (weeks 12&24)	Black box warning due to risk of deadly blood clots. First one-daily formulation in the market
AbbVie	upadicitinib - oral	JAK1 inhibitor	Phase III looking for ACR20 / DAS28 (week 12) Phase III results reported in June 2018 met the primary endpoints	Positive phase III results, however safety profile did not show obvious improvement compared to other JAKs
Gilead/ Galapagos	filgotinib - oral	JAK1 inhibitor	Phase III / looking for ACR20 (week 12 & 24) Phase III results reported in May 2018 met the primary endpoints.	Positive phase III results, two further ongoing phase III trials are set to deliver results in 2019. The safety profile seems similar to the other JAK's
Astellas	Peficitinib - oral	JAK1/3 inhibitor	Phase II / looking for ACR20 (week 12)	Phase III set to start in Sept 2018

Source: First Berlin Equity Research, Datamonitor 2017, ClinicalTrials.gov

At present, there is a lot of activity in the IL-6 inhibitor pathway which looks like a promising approach. Candidates from this class have achieved good efficacy (DAS 20>60%). Sanofi/Regeneron's product sarilumab gained approval in 2017 (although with a black box warning) evaluating ACR20 and DAS28 at week 24. It is the second in the class to receive approval following Genentech's lead drug tocilizumab/ Actemra. However, IL-6 inhibitors are expected to achieve a very small market share compared to TNF-α blockers, as has been the case with tocilizumab/Actemra which has been on the market since 2010 (source: Datamonitor healthcare's forecast for RA, 2017). Following the discontinuation of GSK's sirukumab development, we have identified one remaining IL-6 inhibitor, olokizumab from R-Pharma/UCB, in phase III development.

New oral JAK-inhibitors can potentially become a game changer in MR therapy, if they manage to deliver a better safety profile Given that oral medication promotes patient compliance, JAK-inhibitors have good chances of gaining significant market share. While usually achieving a good level of efficacy (i.e. ACR20 in the range 60%-75%) so far, the negative side effect profile reflected in black box warnings has been a key limiting factor in the success of this class of drugs (e.g. Pfizer's Xeljanz and Elly Lilly's Olumiant). Abbvie's upadicitinib safety profile has been also linked with thrombosis risk due to decline of platelets. Recently published data from the three SELECT phase III trials have slightly lowered these concerns. Nevertheless, we believe this product does not show significant safety superiority compared with peers. It remains open how well Gilead/Galapagos' filgotinib or Astellas' eficitib manage to deliver an improved efficacy/safety profile. Gilead/Galapagos reported solid results from the first of three phase III studies a few months ago which showed efficacy and safety comparable to peers. However, final data from the two remaining phase III trials are still pending and due in 2019. Maintaining a low rate of serious infections and malignancies is crucial to success in this highly crowded market. Nevertheless, at present market expectations of the next wave of JAK-inhibitors are high and consensus projections from Evaluate Pharma see blockbuster sales potential for lead drugs such as Abbvie's Updactinib (USD 2.6bn by 2024) and Gilead's Filgotinib (USD 1.4bn by 2024).

Biosimilars will challenge the dominance of branded TNF-α blockers, triggering price pressure in the market There are currently 24 biosimilar programmes which are in phase III development or have gained approval targeting the leading three TNF-α blockers and the CD-20 inhibitor Rituxan (Source: Pharma Intelligence 2017). Humira will likely face the strongest competition with 10 biosimilars approved or in development. However, the other three products will also see 4-5 biosimilars each challenging their position. We therefore believe competition in these segments will be fierce, putting pressure on price for these drugs. We summarize the biosimilar competitive position for these products in the table below.

Table 8: Patent situation of the lead TNF-α blockers and CD-20 inhibitors

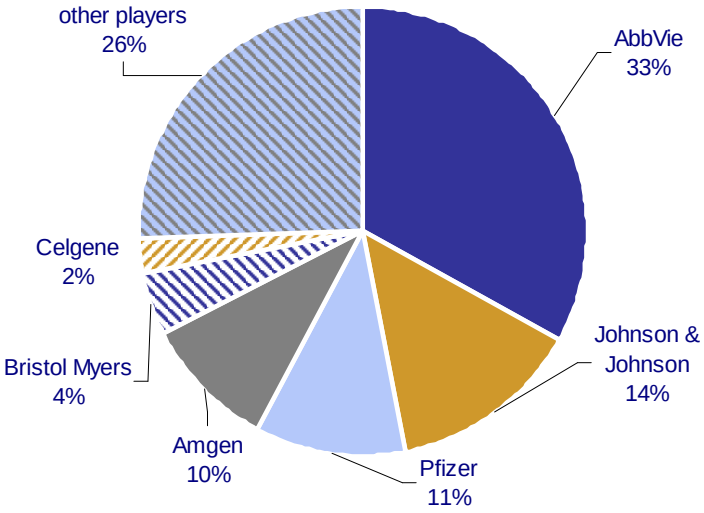
Reference drug	Patent expiration	Biosimilars approved & launched	Biosimilars development completed	Biosimilars in process	TOTAL
Enbrel / etanercept	July 5, 2015	2	1	1	4
Humira /adalimumab	December 31, 2016	3	5	2	10
Remicade /infliximab	September 4, 2018	2	1	2	5
Rituxan / rituximab	2015	2	1	2	5
TOTAL		**9**	**8**	**7**	**24**

Source: First Berlin Equity Research, Pharma Intelligence 2017, Gary Branning: Competition heats up in RA 2016

Despite therapeutic options, high unmet medical need generates opportunities for new therapies that address current shortcomings The RA market could see a strong dynamic in coming years as JAK and IL-6 inhibitors as well as new biogeneric options reach the market. However, RA is a complex disease to treat, and at least one third of patients remain or become unresponsive to treatment (Hyrich et al., 2007). Oral drugs with a superior efficacy and safety profile are in high demand. As a result we see good chances for new oral products with a novel mode of action such as Rabeximod.

Large pharmaceutical and biotech companies control the RA market The global RA market is dominated by large pharma and biotech companies that have been continuously expanding their presence in this market for years. According to Evaluate Pharma, this market is highly consolidated with the top six players accounting for nearly 75% of the market share. AbbVie is the dominant player with sales of USD 17.4bn and a market share of 33%. Based on a sound MS product portfolio and promising pipeline in late stage development, this company is poised to maintain its leading position out to 2024. Johnson & Johnson, Pfizer, Amgen, Bristol Myers and Celgene are also among the top six players. We think Pfizer is likely to outpace Johnson & Johnson thanks to positive long term data from its JAK-inhibitor, Xeljanz. Johnson & Johnson is suffering strong erosion of its core drug Remicade due to biosimilar competition. Further relevant players are Roche, UCB, Eli Lilly and Gilead Biosciences. Eli Lilly and Gilead in particular are new entrants in the field poised to gain significant market share with their JAK-inhibitors Olumiant and filgotinib. These two drugs are estimated to achieve sales in the range USD1.4-1.5bn by 2024.

Figure 6: Key RA players in 2017



Source: First Berlin Equity Research, Evaluate Pharma Ltd 2018

RA market to grow moderately in the period 2017-2025 The global RA drugs market was valued at USD20.3bn in 2016, and is expected to reach USD30.4bn by 2025, expanding at a CAGR of 4.6% in the period (Source: Grand View Research, 2018). The moderate growth rate is chiefly due to the price erosion caused by the anticipated entry of biosimilars.

T20K: A PLANT-DERIVED DRUG CANDIDATE FOR TREATMENT OF MS

PRE-CLINICAL DATA SHOW PROMISING PROFILE FOR THE TREATMENT OF MS

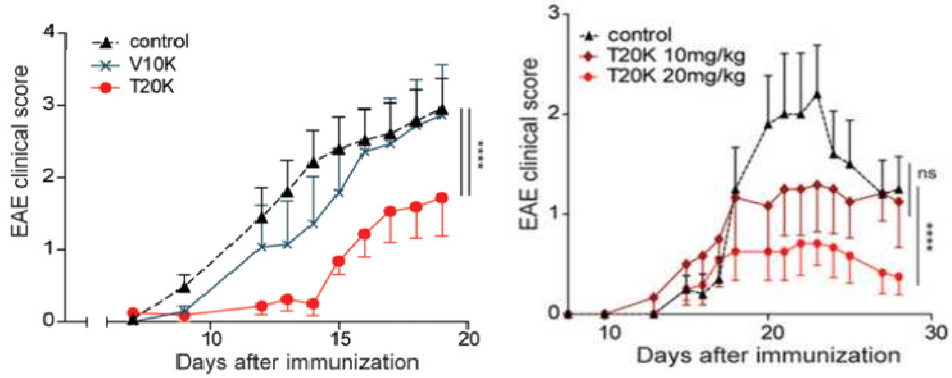
Profile and suggested mode of action T20K kalata B1 (short T20K) is a synthesized circular peptide (Cyclotide) which can be administered orally for the treatment of MS. The drug candidate is currently undergoing late stage pre-clinical development. As shown in an in vitro model in human cells, this compound appears to act by inhibiting T-cell proliferation through down-regulation of the growth factor IL-2 as well as surface expression of the protein CD25 (Gründemann et al., 2013). The cytokine IL-2 plays a pivotal role in T-lymphocyte activation and proliferation. Enhanced T-cell activation is a major cause of autoimmune disorders such as MS and can lead to persistent inflammation, which can trigger tissue and organ damage (Thell et al., 2016).

Strong data in academic mouse study conducted by Thell et al. demonstrated attractive efficacy profile of the oral T20K, which has the potential to substantially reduce symptoms of MS The first in vivo study in mice receiving T20K orally showed that the compound produced a significant delay in disease onset and also lowered disease symptoms. T20K substantially reduced disease progression without adverse effects. Analysis of ex-vivo mice cells also confirmed that the compound inhibited lymphocyte proliferation and reduced pro-inflammatory cytokines, in particular IL-2. These attributes make T20K a unique therapeutic approach for the treatment of MS. The academic animal study on T20K was conducted by Thell et al. as a joint collaboration of the University of Vienna, the University of Queensland and the University of Freiburg and was published in the US journal PNAS in 2016. The study of T20K used the mouse model Experimental Autoimmune Encephalomyelitis (EAE), whereby scientists induce brain inflammation in the mouse. EAE represents the state of the art in vivo assay to investigate MS.

In a first step, the scientists tested parenteral application (i.p.) of T20K, 7 days in advance of induction of the disease, with a dose of 10mg/kg. The results were encouraging, as mice treated with T20K showed a significant delay in disease onset as well as only minor symptoms. Untreated mice saw no reduction in EAE symptoms and suffered severe bilateral paralysis and weight loss (see figure 7 overleaf). These attributes could be advantageous in relapsing remitting MS, which is one of the most common types of MS. After the decline of the first symptoms, treatment with T20K could potentially protect the patient from disease relapses and consequently from further disabilities. Analysis of survival rates confirmed that T20K produces a long lasting therapeutic effect. In addition, daily treatment with lower doses seemed to be very efficient in the prevention of disease progression.

In a second step, the investigators treated mice with two different oral doses of T20K: 10 mg/kg (same dose as i.p. injections), and 20 mg/kg. Results showed that T20K improved the disease in a dose-dependent manner compared to untreated mice from the control group. The higher oral dose of 20 mg/kg showed significantly superior efficacy compared to the lower dose and the untreated mice (see figure 7 overleaf). These results suggest that oral treatment require a higher dose compared to i.p. treatment, which may be due to low bioavailability of T20K which is also the case with other peptides. Further, the safety analysis for both oral doses confirmed a lack of adverse effects with no liver or intestinal tract toxicity. Administration of up to three oral doses of T20K showed a positive safety profile.

Figure 7: Efficacy of T20K on day 7 for single i.p. administration at 10 mg/kg (left) and for oral administration in two doses of 10mg and 20mg (right)



Source: Cyxone AB

In a third step, the investigators conducted a head-to-head comparison of oral T20K with the oral drug fingolimod, a compound blocking the IL-6 protein which was recently approved to prevent MS progression. First, both compounds were administered a single dose of 20mg/kg 7 days in advance of the onset of the disease. T20K showed a statistically significant reduction of disease progression ($p < 0.001$) while the peer drug showed no protective effects. Further, investigators tested administration of both compounds with 20 mg/kg three times in 3-days intervals. T20K and fingolimod showed similar efficacy results measured as reduction in disease progression. The safety profile of both compounds was also similar, with no differences in adverse effects.

Cyxone conducted further in vivo studies to verify results of the academic study Cyxone repeated the murine tests which confirmed the results of the academic study in Vienna and Freiburg. Further, in order to strengthen the animal data package in preparation for the clinical trials in humans, the company carried out further studies on T20K. Experiments with intravenous (i.v.), intraperitoneal (i.p.) and oral (p.o.) applications were investigated in order to establish the relationship between administered doses, amounts of T20K in blood and tissues and their effects in animals. The safety results were encouraging. Single administration of T20K to healthy animals did not produce toxic effects up to the doses of 15 mg/kg (i.v.), 75 mg/kg (i.p.) and 250 mg/kg (p.o.). These safety levels are well above the level required to produce efficacy. Pharmacokinetic studies were also positive. These tests showed that in the case of systemic administration (oral), the compound clears rapidly from the blood which is why there was only negligible free T20K circulating in the bloodstream. Importantly, T20K seems to migrate to and stay in body tissue that regulates inflammation: the spleen and the intestines (immunoregulating organs). These properties make the compound unique, considering that pharmacological effects of drugs are often determined by the quantity of free substance present in the blood.

Final toxicity animal studies are underway and results are expected soon, enrolment of patients for the phase I study is expected to start before year end As a next step, the company will expand toxicity studies of T20K to more animals (mice and dogs) to provide more comprehensive long term data. This dose-escalating study to confirm a maximum tolerated dose (MTD) as well as a safe starting dose for first-in-human clinical trials has been initiated and results are expected during the next weeks. The clinical trial application (CTA) for the first in-human investigational new drug (IND) application will follow shortly after. The company intends to initiate the phase I trial before the end of the year.

T20K's phase I study will start with intravenous injection (i.v.) first and switch to oral administration upon demonstration of the compound's free level in blood T20K's very low levels in the blood and straight migration to the immunoregulating organs are positive features for the compound's safety and efficacy profile. However, the company is

also required by the regulatory authorities to demonstrate a safe level of free T20K in the blood in humans. This investigation will be conducted using the i.v. application to identify a safe, free blood level of T20K. The trial will also examine the compound's efficacy after i.v. injection. Development activity will then switch to oral administration of T20K.

MULTIPLE SCLEROSIS (MS)

AN AUTOIMMUNE DISEASE THAT CAN LEAD TO DISABILTY

Description of MS Multiple sclerosis (MS) is an autoimmune disease characterized by an inflammatory process of the central nervous system (CNS). The CNS comprises the brain, spinal cord and optic nerves. In MS, the immune system attacks the protective sheath called myelin that covers and insulates nerve fibres, the nerve fibres themselves, as well as the specialized cells that produce myelin. As a result of the damage produced, communication problems between the brain and the rest of the body emerge. Eventually, the disease can cause the nerves to deteriorate or become permanently damaged. The damaged areas develop scar tissue which gives the disease its name – multiple areas of scarring or multiple sclerosis. The cause of MS is unknown (Source: Mayo clinic.org).

Symptoms and types of MS Symptoms of MS differ widely and depend on the amount of nerve damage and which nerves are affected. Therefore, symptoms reflect whether acute myelin damage (which can fully or partially resolve) or chronic myelin damage including neuron injury (which is generally irreversible) or both have taken place. Symptoms may include numbness or weakness in one or more limbs, partial or complete loss of vision, prolonged double vision, fatigue, depression and anxiety as well as dizziness. In severe cases patients may lose the ability to walk independently or at all. MS is classified in three types based on the predominance of the symptom episodes. Around 85% of people suffering from multiple sclerosis have Relapsing-Remitting Multiple Sclerosis (RRMS). They usually show first signs of the disease in their early 20s. In the course of the disease weeks, months, or years of recovery (called remissions) are interspersed with attacks with symptoms (called relapses). Depending on the severity of the disease and the damage caused, about 50% of RRMS patients will move on to the more severe disease type of MS called secondary progressive (SPMS) generally decades after first clinical onset. About 10% of MS cases have a primary progressive (PPMS) course where the disease gradually progresses directly from onset. In this case there are no pauses or periods of recovery. We have summarized the MS types in the table below.

Table 8: Overview of main types of MS

MAIN TYPES OF MS	Characteristics
Relapsing – Remitting MS (RRMS)	• **85% of MS population** • Self-limited attacks (>24hrs) with periods of remission (>1 month) • Acute attacks over days/weeks • Usually accompanied by periods of partial or complete recovery over several weeks
Secondary Progressive MS (SPMS)	• **50% of RRMS cases** • Progressive disease, independent of relapses • Ultimately attack rate is reduced with remissions, and plateaus • Steady deterioration in function
Primary Progressive MS (PPMS)	• **15% of MS population** • >1year disease progression with occasional plateaus and temporary improvements • Steady decline in function from the beginning without acute attacks

Source: First Berlin Equity Research, The International Multiple Sclerosis Study (IMPrESS) from Kanavos et al., 2016

Prevalence of MS The national MS society in the US estimates that there are more than 2.3 million people with MS worldwide with approximately 1.0m in the United States (more than double the previous estimate) and 450k in Europe (recent estimates also suggest higher prevalence in Europe). MS typically manifests itself in early adulthood. The average age of onset of first symptoms is 29 years (Kanavos et al., 2016 - Impress). Women are affected at least three times more than men (Bove et al., 2014).

Diagnosis of MS At present, there are no specific symptoms or laboratory tests to determine if a person has MS. As a result, upon appearance of some symptoms that may point towards MS, several procedures are carried out to rule out other possible causes or diseases. These procedures include a careful analysis of medical history, a neurologic exam (e.g. assessment of cranial nerve function, coordination and strength, nerve sensation, reflexes, presence of Lhermitte's sign) and various tests including magnetic resonance imaging (MRI), evoked potentials (EP) and Cerebrospinal fluid (CSF) (Source: National Multiple Sclerosis Society, US).

Inflammation and CNS damage in MS At present, much of the CNS damage in MS is believed to result from an immune-mediated process. Although several cell types within the CNS may contribute to the production of pro-inflammatory cytokines and chemokines, T cells have been identified as playing a key role in the inflammatory process leading to myelin damage. In MS patients, certain T cell populations (i.e. CD4+ T-cells and T-Helper type 17) may secret cytokines and chemokines which allow the T-cells to cross the blood-brain barrier (BBB) and cause inflammation in the central nervous system (CNS), triggering disease progression. Once in the CNS, additional T cell activation takes place which initiates a damaging inflammatory cascade of events within the CNS. As a result, further inflammatory cells are activated, such as macrophages and B cells, which produce antibodies and pro-inflammatory cytokines that additionally damage myelin and other neuronal structures (Tuosto, 2015).

TREATMENT OF MS AND COMPETITIVE ENVIRONMENT

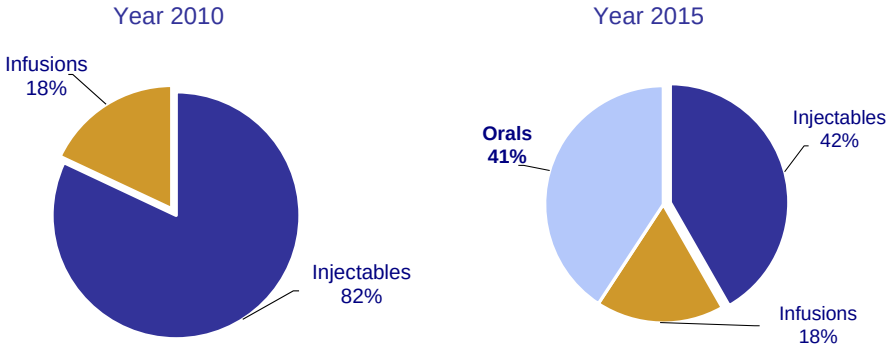
Treatment for MS: disease modifying injectable drugs ABCR + Tysabri established as mainstream first-line therapies Based on the scientific understanding of the key role that T cells play in MS, the main therapies for the disease are directed to the T-cells or their secreted inflammatory chemokines. The first-line treatment of MS is based on disease modifying drugs (DMDs). The main therapeutic goals of DMDs are to act earlier, against inflammation and reduce clinical relapses. Traditionally, there were five main DMDs used in RRMS, which included injectable drugs such as interferon beta (IFN-β) and glatiramer acetate (GA). These mainstream DMDs are frequently referred to as ABCR (Avonex, Betaseron, Copaxone, Rebif). The mechanism of action of these compounds is still poorly understood. Studies suggest that they exert some effects on T lymphocytes. These therapies often fail to exhibit sufficient clinical effectiveness and have only little effect on progressive phases of the disease. A substantial proportion of MS patients (7%-49%) do not respond to treatment with IFN-β1 (Rio et al., 2006). Typical side effects are flu-like symptoms, injection site reaction and elevated liver enzymes.

In 2004 the potent monoclonal antibody natalizumab/Tysabri entered the market as second-line treatment with an i.v. infusion and positive clinical benefits. The drug offered a new alternative to the traditional injectable DMDs, particularly for highly active RRMS patients. The product also showed stronger side effects such as a brain infection called multifocal leukoencephalopathy. In the period until 2016, the injectable drug Copaxone was the most successful DMD, achieving sales slightly above USD4.0bn.

Oral therapies bring new dynamic to the MS market The next wave of innovation took place in the period 2010-2014, when three oral drugs reached the market as first-line

treatments, additionally filling the gap in oral administration: 1) fingolimod/Gilenya, 2) teriflunomide/Aubagio, 3) dimethyl flumarate/Tecfidera. Generally, these drugs were more potent than those used in traditional first-line therapy, but they also showed more severe adverse side effects. Gilenya has label restrictions and monitoring requirements. Aubagio carries a black box warning and also requires constant monitoring. Tecfidera was initially the most successful of these drugs with a high volume of physicians' prescriptions upon market launch in 2013/2014. In 2015, safety concerns led to a patient monitoring requirement, hampering the strong market uptake slightly. Tecfidera achieved sales of approx. USD 4bn in 2016 and keeps growing although more moderately. Oral therapies proved successful despite safety shortcomings and took approx. 40-45% market share (EU and US) hitting injectable drugs which saw their share decline from approx. 80-90% in 2010 to 40-45% in 2015 (Source: Ipsos healthcare MS monitor, 2016).

Figure 8: Worldwide MS therapies by type of administration in 2010 and 2015



Source: First Berlin Equity Research, Ipsos healthcare MS monitor 2016

In 2014, the i.v. infusion alemtuzumab/Lemtrada entered the market. However, due to safety concerns and negative labelling in the US, the product did not achieve large market penetration. We give an overview of the main MS therapies in the table below.

Table 9: Overview of main first- and second-line treatment for MS

Company	Drug	Molecule	Mode of action	Approved
Biogen	Avonex	IFN-β1a – injection	Immunomodulation	First-line for RRMS
Merck & Co	Rebif	IFN-β1a – injection	Immunomodulation	First-line for RRMS
Bayer/ Novartis	Betaseron/ Extavia	IFN-β1b – injection	Immunomodulation	First-line for RRMS
Teva	Copaxone	glatiramer acetate – injection	Immunomodulation	First-line for RRMS
Biogen	Tysabri	natalizumab – intra venous infusion	Blocking migration of immune cells to the CNS	Second-line for RRMS, first-line for highly active RRMS
Merck KGaA	Mavenclad	cladribine – oral	Immunomodulation	Second line for RRMS
Novartis	Gilenya	fingolimod – oral	Blocking egress of T and B cells from lymph nodes	First-line in the US / second-line in the EU for RRMS
Sanofi-Genzyme	Aubagio	teriflunomide – oral	Prevents T cells from dividing, reducing their number	First line for RRMS
Biogen	Tecfidera	dimethyl fumarate – oral	Neuroprotective and anti inflammatory effects	First line for RRMS
Sanofi-Genzyme	Lemtrada	alemtuzumab – intra venous infusion	Immunomodulation	First line, used as second-line in the EU / third-line in the US for RRMS
Roche	Ocrevus	ocrelizumab – intra venous infusion	Anti CD20 marker on B cells, immunosuppression	First line for RRMS and PPMS

Source: First Berlin Equity Research, Tuosto, 2015, Dörr et al., 2015, Ipsos Healthcxare MS monitor 2016, respective companies

Ocrevus is perceived as a breakthrough therapy showing superior efficacy for RRMS, becoming the first drug approved for PPMS The latest highlight in MS therapy development took place in 2017 with the approval and market launch of ocrelizumab/Ocrevus. This drug received approval as a first-line treatment for RRMS and also became the first therapy approved for PPMS. Key opinion leaders see the product as a game changer and are endorsing it based on the superior efficacy (compared to Rebif and placebo) achieved in clinical trials. The product is forecast to achieve the highest sales in the MS market approaching USD5bn by 2023 (Source: Global Data Healthcare, 2018).

Outlook for therapies in development: oral drug candidates dominate the industry's late stage pipeline Currently, oral drug candidates prevail in the industry's late stage MS pipelines, with a focus set on offering an improved efficacy/safety profile relative to the approved treatments Gilenya (3 products) and Tecfidera (1 product). Data published so far on the majority of phase III drug candidates look encouraging, which may add new alternatives for patients not responding to the available therapies or suffering from severe side effects. One drug candidate, laquinimod/Nerventra, proved unsuccessful and suffered setbacks in 2017 in RRMS and PPMS due to a lack of safety or efficacy, leading to a cancelation of the development programme in MS. We have summarized the drug candidates in late stage development for MS in the table below.

Table 10: Therapies in development for MS

Company	Drug candidate	Mechanism – administration	Development stage / target	Comments
Novartis	siponimod	preventing T cells from entering the CNS, same class as approved drug singolimod/ Gilenya – oral	Phase III completed/ targeting SPMS	Positive phase III results, primary endpoints achieved, filing in 2018 in the US and EU
Actelion	ponesimod	preventing T cells from entering the CNS, same class as approved drug singolimod/ Gilenya– oral	Phase III underway/ targeting RRMS	Phase III comparison with approved drugs Aubagio and Tecfidera
Celgene	ozanimod	preventing T cells from entering the CNS, same class as approved drug fingolimod/ Gilenya – oral	Phase III and filing completed/targeting RRMS	The product has a positive efficacy and better safety profile than Gilenya. Due to regulatory delays, it won't launch until late 2019/early 2020
AB Science	masitinib	anti tyrosine kninase – oral	Phase III underway Targeting SPMS and PPMS	Final results expected in Q2/19
Biogen/ Alkermes	ALKS8700	monomethyl fumarate prodrug, similar to Biogen's approved drug Tecfidera – oral extended release	Two phase III studies (1st open label, 2nd comparison with Tecfidera) underway/ targeting RRMS	Interim results from open label study presented in early 2018 showed positive efficacy and safety data
Teva/ Active Biotech	laquinimod/ Nerventra	Not fully clear, is likely to lower pro inflammatory cells – oral	Phase III in RRMS and phase II in PPMS failed in 2017	Companies discontinued development in MS

Source: First Berlin Equity Research, Radick et al., 2015, companies

Total MS market to grow at a CAGR of 6.3% to 2025 The global MS drugs market was valued at USD16.1bn in 2016, and is expected to reach USD27.3bn by 2025, expanding at a CAGR of 6.3% in the period. Moreover, the market for oral medications is expected to grow at an even stronger rate (Source: Credence Research, 2017). We anticipate demand for drugs with improved efficacy/safety profile will remain high. The increasing base of patients

suffering MS as well as rising demand for novel, more potent drugs are the main growth drivers. The MS market is becoming crowded, but there is still high unmet medical need. Despite the increasingly competitive environment, there is still significant room for new oral drugs showing an improved efficacy/safety profile. In particular, existing drugs' efficacy in advanced SPMS is still poor and accompanied by strong side effects.

New entrants such as Biogen and Roche/Genentech will challenge the dominance of established players Traditionally, the market has been dominated by four main players. Biogen, Merck/Serono, Teva and Bayer Healthcare based on their commercialized injectable DMDs. New entrants such as Biogen (Tecfidera) and Roche-Genentech (Ocrevus) are highly likely to become new market leaders.

FINANCIAL HISTORY AND OUTLOOK

Cyxone's financial statements are prepared in accordance with the Swedish Annual Accounts Act and the general recommendations of the Swedish Accounting Standards Board, BFNAR 2012:1 Annual reports and consolidated accounts (K3). There are some historical events or relevant information to consider in order to better understand the company's reported figures. The most relevant are:

I) The company was established in the summer of 2015, and operations started in the autumn of 2015. The company's first financial year was extended, and ran from 13 July 2015 to 31 December 2016 (it is reported in our financial statement as FY/16),

II) The company capitalises development costs which are accounted for in the balance sheet as a long term asset. According to K3 accounting recommendations from 2016, a reserve corresponding to capitalised development costs is made to company's equity.

FINANCIAL HISTORY

Income Statement H1/18

Cyxone's financial statement is typical of an early stage R&D biotech company. The company is generating no revenues and is loss-making. As such, Cyxone generated no revenue in both H1/18 and H1/17. The company's EBIT came in at SEK-6.5m in H1/18, a widening of the loss by 60% y/y (H1/17: SEK-4.1m). The widening of the loss was due mainly to increasing external costs amounting to SEK5.6m in H1/18 (H1/17: SEK2.9m) such as consulting fees for the preparation of the capital increase. Cyxone reported a net loss of SEK6.5m (H1/17: SEK-4.1m), which equates to SEK-0.37 per share (H1/17: SEK-0.27).

Table 11: Income Statement H1/18 and H1/17 (selected items)

All figures in SEK '000	H1/18	H1/17	*Delta*
Revenue	**0**	**0**	***n.m.***
Personnel costs	855	1,176	*-27%*
Other external costs	5,649	2,879	*96%*
Depreciation & amortization	11	11	*0%*
EBIT	**-6,515**	**-4,066**	***60%***
Net income / loss	-6,503	-4,075	*60%*
EPS	-0.37	-0.27	*37%*

Source: Cyxone AB

Balance Sheet H1/18

At the end of H1/18, Cyxone's equity position decreased to SEK30.6m from SEK37.1m at the end of FY/17. The company's equity position is strong, corresponding to an equity ratio (ER) of 93.0% (FY/17 ER: 90.4%). The company's cash position decreased to SEK17.8m (FY/17: SEK33.4m). As is typical of a biotech company, Cyxone is highly dependent on raising new funds to finance operations, further pipeline development and expansion measures. On 3 July 2018, after the closing of the H1/18 reporting period, Cyxone increased its share count by approx 1.9m shares to 19.7m in order to pay for the completion of the acquisition of the lead drug candidate Rabeximod. Furthermore, on 26 October 2018, in order to finance phase IIb development of Rabeximod, the company placed 17.7m shares raising gross proceeds of SEK44.3m. As a result, shares outstanding increased from 17.8m at the end of H1/18 to 37.5m currently.

Table 12: Balance Sheet H1/18 and FY/17 (selected items)

All figures in SEK '000	H1/18	FY/17	*Delta*
Liquid funds	17,817	33,357	*-47%*
Capitalised development costs	13,638	6,554	*108%*
Patents, licenses & other intangibles	1,267	1,011	*25%*
Total Assets	32,991	41,064	*-20%*
Equity	30,629	37,132	*-18%*
Equity ratio	93%	90%	*3 pp*

Source: Cyxone AB

Cash Flows H1/18

In H1/18, cash flow from operating activities came in at SEK-8.2m (H1/17: SEK-3.3m) and cash flow from investing activities which largely proceeds from capitalized development expenses amounted to SEK7.4m (H1/17: SEK1.6m) with the increase being due to increased development activity on T20K. Cash flow from financing activities amounted to SEK0.0m in H1/18 (H1/17: SEK11.4m). We note the company conducted a capital increase in H1/17 through conversion of a first tranche of warrants (T01) raising net proceeds of SEK11.4m in order to finance the development of T20K. The second warrants tranche T02 was converted in H2/17 raising a further SEK11.7m to complete the total net amount of SEK23.1m required to finance T20K through phase I. Thus net cash flow in H1/18 came in at SEK-15.5m (H1/17: SEK6.5m).

Table 13: Cash flow statement H1/18 and H1/17 (selected items)

All figures in SEK '000	H1/18	H1/17	*Delta*
Operating cash flow	**-8,189**	**-3,302**	***148%***
Cashflow from investing	**-7,351**	**-1,597**	*360%*
Cash flow from financing	0	11,415	*-100%*
Net cash flow	**-15,540**	**6,516**	*-338%*

Source: Cyxone AB

FINANCIAL OUTLOOK

Considering that Cyxone's development pipeline is still at an early stage, we do not anticipate revenues until the potential market launch of the lead programme Rabeximod takes place towards 2023E.

With regard to upfront and milestone payments, it is difficult to predict the conditions under which Cyxone 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 through a combination of raising funds from investors and upfront payments from licensing to pharmaceutical partners. We also assume that Rabeximod's phase IIb trial will deliver positive data. We project that the out-licensing of Rabeximod will lead to upfront payments in 2020E of SEK89m (USD10m) and future royalties. The partner will conduct the expensive phase III development and receive distribution rights in the RA indication. We expect that Cyxone will complete phase II trials of T20K in MS, in order to maximise royalty conditions. Following successful phase II trials, we anticipate Cyxone will outlicense the product, receiving an upfront payment in 2022 of SEK89m (USD10m) and royalties upon commercialization. We expect the partner to conduct the phase III trials and commercialize the drug upon approval.

Our 2018 projections are the baseline for our projections going forward. Considering the company's increased activity with T20K, we project OPEX to rise from SEK8.8m in FY/17 to SEK13.9m in 2018E and SEK18.3 in 2019E. We project that the company will achieve positive EBIT in 2020E and 2022E thanks to licensing upfront payments on Rabeximod and T20K. We expect the company to generate first revenues and achieve a sustainable break-even in 2023E due to the marketing of Rabeximod in RA. Going forward, we model revenue and net earnings until 2040E. We have taken typical industry development timeframes into consideration.

Table 14: Revenue, EBIT, net income forecasts (selected items)

in SEK'000	2016	2017	2018E	2019E	2020E	2021E
Sales	21	0	0	0	0	0
Upfront & milestone payment	0	0	0	0	89,000	0
OPEX	-4,180	-8,824	-13,922	-18,285	-23,105	-29,274
EBIT	-4,159	-8,824	-13,922	-18,285	65,895	-29,274
Net income	-4,162	-8,824	-13,905	-18,263	65,931	-29,241

Source: First Berlin Equity Research

We forecast no financial debt on Cyxone's balance sheet by 2018E year end and going forward. Considering that Cyxone capitalises development expenses, we project a strongly increasing capitalised development costs position in the balance sheet. Our R&D curve assumes that the company will spend SEK100.0m in research and development in the period 2018E-2021E. In our view this budget is sufficient to complete phase II clinical trials for Rabeximod and finance the T20K development until 2021E.

Table 14: Balance sheet forecasts (selected items)

in SEK'000	2016	2017	2018E	2019E	2020E	2021E
Liquid funds	21,598	33,357	33,956	52,923	91,034	35,998
Capitalised development costs	753	6,554	26,554	52,554	80,554	106,554
Patents, licenses & other intang.	844	1,011	1,387	1,778	2,305	2,948
Total Assets	23,561	41,064	62,124	107,505	174,167	145,802
Equity	22,831	37,132	59,184	103,757	169,688	140,447
Equity ratio	97%	90%	95%	97%	97%	96%

Source: First Berlin Equity Research

Our cash flow forecast includes Cyxone's recent placement to finance the phase IIb development of Rabeximod, leading to gross proceeds of SEK44.3m in Q4/18E. We also project warrants conversion in FY/19E at SEK3.75 (25% discount to SEK5.00), which represents the lower end of the share price range for the conversion. Based on this assumption, we estimate that Cyxone will raise gross proceeds of SEK66.5m leading to a positive financing cash flow. Further we anticipate Cyxone will outlicense Rabeximod in 2020E, leading to an upfront payment of SEK89m from the pharmaceutical partner and a first operating cash flow positive year.

Table 14: Cash flow forecasts (selected items)

in SEK'000	2016	2017	2018E	2019E	2020E	2021E
Operating cash flow	-3,796	-5,376	-14,960	-17,444	66,694	-28,303
Cash flow from investing	-1,599	-5,990	-20,398	-26,426	-28,583	-26,733
Cash flow from financing	26,993	23,125	35,958	62,836	0	0
Net cash flow	21,598	11,759	599	18,966	38,111	-55,036

Source: First Berlin Equity Research

NEWSFLOW

In our view, Cyxone's stock price will be driven by news about its pipeline as well as by achievement of financial milestones. 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:

Pipeline & financing

2018

- Completion of the required animal and safety pre-clinical study of T20K, filing for IND, positive review of the regulator in Q4/18E.
- Initiation of enrolment for the first in human phase I trial of T20K in Q4/18E.

2019

- Enrolment of first patients for phase IIb studies of Rabeximod in combination with MTX in RA in Q2/19E.
- Publication of final safety data for the phase I trial of oral T20K as well as initial safety and efficacy data of the i.v. version of T20K in H2/19E.

Further, we expect regular updates of the company during the quarterly publication of financial figures. Publication of Q3/18 results is due on 21 November 2018.

SHAREHOLDERS & STOCK INFORMATION

Stock Information	
ISIN	SE0007815428
WKN	A2AHCN
Bloomberg ticker	CYXO SS
No. of issued shares	37,457,517
Country	Sweden
Sector	Healthcare
Subsector	Biotechnology

Source: Nasdaq First North, First Berlin Equity Research

Shareholder Structure	
Accequa AB	30.2%
OxyPharma AB	9.7%
Avanza Pension	3.5%
Nordnet Pensionsförsäkring	3.2%
Hosni Adam Omeirat	1.1%
Stephan Käll	1.0%
Kjell Stenberg	1.0%
Others	50.3%

Source: Cyxone AB (prior to the capital increase implemented on 26 October 2018)

MANAGEMENT

MANAGEMENT BOARD

Kjell Stenberg, PhD, is the CEO of Cyxone. He joined the company in 2015. Mr. Stenberg brings over 42 years of experience in biotechnology and pharmaceutical business development to Cyxone. Prior to joining Cyxone, Mr. Stenberg served as Chief Operating Officer of Medwell Capital Corp. (also known as BioMS Medical Corp.) developing a new drug in phase III studies for MS. In 2008, BioMS entered into a partnership with Eli Lilly which was awarded the Licensing Deal of the Year by Scrips. Previously, Dr. Stenberg served as CEO of Combio A/S. From 1975 to 2000, Dr. Stenberg served as Senior Researcher and Manager at Astra/AstraZeneca, where he was instrumental in bringing various drugs to market in the capacity of Director of Research or Director of Development. He is Chairman of the listed biotech company Aptahem AB and board member of Novation Pharmaceuticals and Galecto Biotech.

Ola Skanung, joined Cyxone in 2015 as CFO. Mr Skanung brings many years of experience as CFO and working with start-ups and growth projects within the private as well as with state and regional development actors. Beside his position at Cyxone, he works as part time CFO for two Swedish listed biotech companies, Aptahem AB and Gabather AB. From 2012 to 2015 he served as CFO with a focus on raising funds and finding collaboration partners for Ideon AB, Sweden's first and largest science park. From 2005 to 2010 he also held the CFO position at Inovationsbron AB, an organization commissioned by the Swedish government to create new businesses out of research and innovation. Before joining Inovationsbron, Mr Skanung served in a variety of Finance and Controlling roles with technology companies such as UpGrade Communication AB, SDC Sweden AB, Beijer Petroleum AB and Sydbensin AB. Mr Skanung holds a B Sc in business administration and entrepreneurship and additional exams in financial law and change management from the Universities of Växjö, Malmö and Lund, Sweden.

SUPERVISORY BOARD

Bert Junno, PhD, is Chairman of Cyxone's Supervisory Board. He co-founded Gabather AB and has been its CEO and a board member since 2014. He is also a co-founder of the life science companies WntResearch AB (public), Galecto Biotech AB, Aptahem AB (public) and Cyxone AB. He serves on the advisory board of the Swedish patent office since 2010. Mr. Junno has previous management and board level experience from several European and US based companies in the fields of electronics, biotech and IT. Bert Junno holds a PhD in Semiconductor Physics and Technology and a M.Sc. in Physics from Lund University.

Theresa Comiskey Olsen, Attorney at Law (USA), is a Partner at Langseth Law Firm in Oslo, Norway. Ms Olsen has been with Langseth since January 2016 after starting her own practice with focus on legal transactions in the Life Sciences/Biotech field. Prior to starting her practice in 2008, she was General Counsel of Nycomed, which has since been acquired by Takeda. Ms Olsen continues to grow her practice at Langseth with a focus on legal transactions in the Life Sciences/Biotech field. She holds a B.A. from the University of Pennsylvania and her J.D. from University of Detroit Mercy School of Law.

Saad Gilani is a Managing Director at Yorkville Advisors Global and has been with the firm since 2005. As Head of the Healthcare Group, he has led financing transactions in a variety of life science companies focused on biotechnology, molecular diagnostics and medical devices in the US and in Europe. Mr Gilani is a member of the firm's Investment Committee. He also sits on the supervisory board of Temple Therapeutics BV based in The Netherlands. Prior to joining Yorkville Advisors Global, Mr Gilani worked at Keyence Corporation for 11

years where he held various management roles within the Engineering and Marketing groups. He earned a BSc in Electrical Engineering from Rutgers College of Engineering and received his MBA from Rutgers University in NJ, where he specialized in finance.

Mikael Lindstam, PhD, has been engaged in several start-up companies and development programs that have generated investments of more than SEK100m. Dr. Lindstam has been part of the development of Galecto Biotech AB and Gabather AB from Forskarpatent's portfolio including a number of license deals and IP-divestments. Dr. Lindstam is cúrrently the CEO of Aptahem AB, a company developing aptamers for stroke and other diseases. Dr. Lindstam has a PhD in organic chemistry and long experience of marketing, entrepreneurship and management.

SCIENTIFIC ADVISORY BOARD

Christian Gruber, PhD, is chairman of the scientific advisory board. He is a research group leader and Assistant Professor at the Medical University of Vienna (Austria), and an ARC Future Fellow at The University of Queensland (Australia). He studied Biochemistry at the University of Tübingen (Germany) and Molecular Biotechnology at the Queensland University of Technology (Australia), and he has received a PhD in Molecular Biosciences from the University of Queensland. For his achievements he has received several scientific awards, e.g. the 2013 Heribert Konzett Award of the Austrian Pharmacological Society, the 2014 Young Investigator Silver Award of the International Union of Basic and Clinical Pharmacology, and the 2014 Dr. Willmar Schwabe Award of the Society for Medicinal Plant and Natural Product Research. The research focus of his team is the study of the biological function and pharmacological mechanism of nature-based peptides isolated from plants and invertebrates (e.g., peptide hormones, neuropeptides and peptide toxins), and the development of novel peptide therapeutics. He is board member and Austrian delegate to the European Peptide Society and member elect of the "Max-Bergmann-Kreis".

Carsten Gründemann, PhD, is a research group leader and Principal Investigator at the University Medical Center Freiburg (Germany). He studied Biochemistry at the University of Tübingen (Germany) and Biology at the University of Freiburg, and received his PhD in Experimental Immunology from the University of Tübingen (Germany). He received the "Excellence in Integrative Medicine Research Award 2013" from the European Society of Integrative Medicine (ESIM) for his achievements. The research focus of his team is to study the immunological functions and mechanisms of traditionally used plants and fungi.

INCOME STATEMENT

All figures in SEK '000	2016	2017	2018E	2019E	2020E	2021E
Revenue	**21**	**0**	**0**	**0**	**0**	**0**
Upfront & milestone payments	**0**	**0**	**0**	**0**	**89,000**	**0**
Total revenue	**21**	**0**	**0**	**0**	**89,000**	**0**
Personnel Costs	1,318	2,287	1,800	2,520	2,600	2,600
Other external costs	2,862	6,515	12,100	15,730	20,449	26,584
Depreciation & Amortization	0	22	22	35	56	90
Operating income (EBIT)	**-4,159**	**-8,824**	**-13,922**	**-18,285**	**65,895**	**-29,274**
Net financial result	-3	0	17	22	36	32
Pre-tax income (EBT)	**-4,162**	**-8,824**	**-13,905**	**-18,263**	**65,931**	**-29,241**
Income taxes	0	0	0	0	0	0
Net income / loss	**-4,162**	**-8,824**	**-13,905**	**-18,263**	**65,931**	**-29,241**
Diluted EPS	**-0.32**	**-0.50**	**-0.62**	**-0.43**	**1.37**	**-0.55**
Ratios						
EBIT-Margin on total revenue	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
EBITDA margin on total revenue	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Net Margin on total revenue	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Expenses as % of Revenues						
Personnel Costs	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Other external costs	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Y-Y Growth						
Total revenue	n.m.	-100.0%	n.a.	n.a.	n.a.	n.a.
Operating income	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.

BALANCE SHEET

All figures in SEK '000	2016	2017	2018E	2019E	2020E	2021E
Assets						
Current Assets, Total	**21,964**	**33,499**	**34,184**	**53,173**	**91,309**	**36,300**
Cash and Cash Equivalents	21,598	33,357	33,956	52,923	91,034	35,998
Accounts Receivable	366	142	227	250	275	302
Non-Current Assets, Total	**1,597**	**7,565**	**27,941**	**54,332**	**82,859**	**109,502**
Capitalised development costs	753	6,554	26,554	52,554	80,554	106,554
Other intangibles (patents, licenses)	844	1,011	1,387	1,778	2,305	2,948
Total Assets	**23,561**	**41,064**	**62,124**	**107,505**	**174,167**	**145,802**
Shareholders' Equity & Debt						
Current Liabilities, Total	**730**	**3,932**	**2,940**	**3,747**	**4,479**	**5,355**
Accounts Payable	398	3,079	1,600	1,920	2,304	2,765
Other current liabilities	332	853	1,340	1,827	2,175	2,590
Longterm Liabilities, Total	**0**	**0**	**0**	**0**	**0**	**0**
Shareholders Equity	**22,831**	**37,132**	**59,184**	**103,757**	**169,688**	**140,447**
Total Consolidated Equity and Debt	**23,561**	**41,064**	**62,124**	**107,505**	**174,167**	**145,802**
Ratios						
Current ratio (x)	30.09	8.52	11.63	14.19	20.39	6.78
Quick ratio (x)	30.09	8.52	11.63	14.19	20.39	6.78
Net gearing	n.a.	n.a.	n.a.	-51.0%	-53.6%	-25.6%
Book value per share (€)	1.77	2.09	2.63	2.43	3.53	2.63
Net debt	-21,598	-33,357	-33,956	-52,923	-91,034	-35,998
Equity ratio	96.9%	90.4%	95.3%	96.5%	97.4%	96.3%

CASH FLOW STATEMENT

All figures in SEK '000	2016	2017	2018E	2019E	2020E	2021E
Net income	**-4,162**	**-8,824**	**-13,905**	**-18,263**	**65,931**	**-29,241**
Interest, net	3	0	-17	-22	-36	-32
Tax provision	0	0	0	0	0	0
EBIT	**-4,159**	**-8,824**	**-13,922**	**-18,285**	**65,895**	**-29,274**
Depreciation and amortization	0	22	22	35	56	90
EBITDA	**-4,159**	**-8,802**	**-13,900**	**-18,250**	**65,951**	**-29,184**
Changes in Working Capital	366	3,426	-1,077	785	707	849
Cash interest net	-3	0	17	22	36	32
Other Adjustments	0	0	0	0	0	0
Operating cash flow	**-3,796**	**-5,376**	**-14,960**	**-17,444**	**66,694**	**-28,303**
CapEx	-1,599	-5,990	-20,398	-26,426	-28,583	-26,733
Free cash flow	**-5,395**	**-11,366**	**-35,358**	**-43,870**	**38,111**	**-55,036**
Cash flow from investing	**-1,599**	**-5,990**	**-20,398**	**-26,426**	**-28,583**	**-26,733**
Debt Financing, net	0	0	0	0	0	0
Equity Financing, net	26,993	23,125	35,958	62,836	0	0
Cash flow from financing	**26,993**	**23,125**	**35,958**	**62,836**	**0**	**0**
Net cash flows	**21,598**	**11,759**	**599**	**18,966**	**38,111**	**-55,036**
Cash, start of the year	0	21,598	33,357	33,956	52,923	91,034
Cash, end of the year	**21,598**	**33,357**	**33,956**	**52,923**	**91,034**	**35,998**

Y-Y Growth						
Operating Cashflow	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.
EBITDA/share	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

FIRST BERLIN RECOMMENDATION & PRICE TARGET HISTORY

Report No.:	Date of publication	Previous day closing price	Recommendation	Price target
Initial Report	Today	SEK 2.09	Buy	SEK 13.50

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Category		1	2
Current market capitalisation (in €)		0 - 2 billion	> 2 billion
Strong Buy[1]	An expected favourable price trend of:	> 50%	> 30%
Buy	An expected favourable price trend of:	> 25%	> 15%
Add	An expected favourable price trend of:	0% to 25%	0% to 15%
Reduce	An expected negative price trend of:	0% to -15%	0% to -10%
Sell	An expected negative price trend of:	< -15%	< -10%

[1] The expected price trend is in combination with sizable confidence in the quality and forecast security of management.

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- **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

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