Formycon

Pharma & biotech

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FY20 results – core progress on key projects

Formycon progressed all key projects in 2020. FYB201 (partnered with Bioeq) is a Lucentis biosimilar to treat neovascular age-related macular degeneration (nAMD). After scaling up manufacturing in 2020, Bioeq aims to resubmit a BLA to the FDA in H121 with a subsequent EMA filing. FYB202 (a Stelara biosimilar) in a joint venture with Aristo Pharma started its Phase III for psoriasis. FYB203 (an Eylea biosimilar partnered with Klinge) is in Phase III. FYB207 is a novel COVID-19 therapy that neutralises SARS-CoV-2 virus and might start trials in late 2021. Formycon ended 2020 with a strengthened €42.2m cash position (2019: €22.4m). FY20 revenue was €34.2m (FY19: €33.3m), while the loss was €5.9m (FY19: loss €2.3m).

FYB201 and FYB203 target $11.9bn nAMD market

Formycon forecasts a very valuable nAMD market for biosimilars and has two advanced projects. For Lucentis biosimilars, Bioeq, plans to resubmit a US BLA in mid-2021 after completing its manufacturing scale up. A subsequent EMA filing is planned. The Lucentis biosimilar market may have two other entrants. Lucentis 2020 sales fell 10% to about US$3.5bn (from $3.9bn in 2019). Formycon's Eylea biosimilar FYB203 is licensed to Klinge Biopharma. It started Phase III in August 2020. Sales of Eylea in 2020 were up 5% at $7.9bn (2019: $7.5bn). Potential competition has increased with both Samsung Bioepis and Amgen in Phase III. Roche has a new premium product in late development.

A shining opportunity funded through a JV

Formycon has made significant progress on FYB202 (a Stelara biosimilar for Crohn's disease, ulcerative colitis and psoriasis) through a joint venture deal with Aristo Pharma; Formycon owns 24.9%. Stelara 2020 sales were $7.7bn (2019: $6.4bn). It has a different mode of action from Humira so should be protected from the fierce competition as anti-TNF biosimilars are launched. Phase III started in November 2020. Formycon funds its share of the costs and then shares the potentially lucrative profits. Stelara patents expire in 2023 (US) and 2024 (EU). There is a strong field of competitors including Samsun Bioepis and Amgen.

Valuation: Strong portfolio plus novel COVID therapy

Formycon's current market cap is €673m, giving an EV of about €638m (€285m in September 2020). Restarting the regulatory review of FYB201 and the ongoing FYB202 and FYB203 Phase III studies support the market value. Progress on FYB206 and especially the promising COVID-19 therapy FYB207 should provide further upside. Formycon raised €25.8m of equity in Q420 so is well capitalised with strong partner revenues largely funding underlying costs of €40.9m.

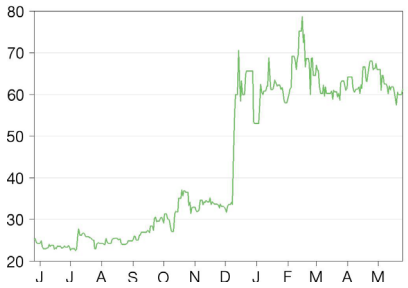
Historical and consensus estimates

Year end	Revenue (€m)	PBT (€m)	EPS (€)	DPS (€)	P/E (x)	Yield (%)
12/19	33.3	(2.3)	(0.23)	0.0	N/A	N/A
12/20	34.2	(5.9)	(0.58)	0.0	N/A	N/A
12/21e	40.8	(7.7)	(0.81)	0.0	N/A	N/A
12/22e	53.5	4.1	(0.43)	0.0	N/A	N/A

Source: Refinitiv consensus estimates, Formycon reports

Price	€61.2
Market cap	€673m

Share price graph



Share details

Code	FYB
Listing	Deutsche Börse Scale
Shares in issue	11m
Cash at end-December 2020	€42.2m

Business description

Formycon is a biotechnology company focused on biosimilars. Its lead product is FYB201, a Lucentis biosimilar awaiting FDA resubmission. FYB202, a Phase III biosimilar candidate of Stelara, is in a joint venture with Aristo Pharma. FYB203 is an Eylea biosimilar also in Phase III. There is a novel SARS-CoV-2 neutralising therapy in preclinical.

Bull

- Leading biosimilars company addressing markets worth $19.6bn in 2020.
- Two partnered products plus JV deal giving strong revenues and limiting cash use.
- Novel COVID-19 therapy could enter Phase I/IIa in Q421 and might become a key treatment.

Bear

- No EMA guidance for intraocular biosimilars.
- US biosimilar market still maturing.
- Tough biosimilar competition emerging for all three key products.

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Edison profile page

Financials: FY20 results review

Formycon reported 2020 revenues of €34.2m as development payments vs €33.3m in 2019. The net loss was €5.9m (vs a loss of €2.3m in 2019). Cash was €42.2m (2019: €22.4m).

The FYB202 project is run through a joint venture company which requires investment (FYB 202 GmbH & Co. KG, undisclosed financials). There was no 2020 investment in the JV. The last investment was €4.7m in 2019. The JV has a balance sheet value of €20.7m. As this project is in Phase III, a further cash investment is possible and can be funded from cash reserves.

Formycon raised €25.75m gross at €25.75 per share by issuing 1m shares in October 2020. Formycon's share capital increased to €11m comprising €1 par value shares.

The underlying 2020 operating outflow was €5.1m. There was €0.65m of capital investment and a small interest charge of €0.1m. After the €25.75m cash raised, year-end 2020 cash and cash equivalents increased to €42.25m from €22.35m as of 31 December 2019.

Exhibit 1: Financial summary Formycon Group

Year-end 31 December (€m)	2020	2019
Income statement		
Revenue	34.23	33.26
Profit before tax (as reported)	(5.92)	(2.27)
Net income (as reported)	(5.93)	(2.29)
EPS* (€)	(0.58)	(0.23)
Dividend per share (€)	0.00	0.00
Balance sheet		
Total non-current assets	24.66	25.00
Total current assets	50.94	28.56
Total assets	75.60	53.56
Equity	68.04	48.21
Liabilities	5.42	3.47
Provisions	2.14	1.88
Total liabilities	75.60	53.56
Cash flow statement		
Net cash from operating activities	(5.10)	(1.48)
Net cash from investing activities	(0.65)	(5.71)
Net cash from financing activities	26.64	17.24
Net cash flow	19.89	10.05
Cash & cash equivalent end of year	42.25	22.35

Source: Formycon accounts. Note: *10m shares in 2019, 10.25m average shares in 2020.

Three key projects

Formycon's pipeline is shown in Exhibit 2. For more detail on underlying regulatory issues and details of Formycon's structure and alliances, see our May 2020 note.

Exhibit 2: Formycon pipeline

Project	Partner/JV	Target	2020 market		Status	Next milestone	Notes
			US	RoW			
FYB201	Bioeq/ Coherus	Lucentis (nAMD)	$1.9bn	$1.6bn	Pre-regulatory	■ FDA resubmission mid-2021. ■ EMA H2 2021 ■ European partner deal	Re-entering regulatory phase after commercial scale up
FYB202	JV with Aristo Pharma	Stelara (inflammation)	$5.24bn	$2.47bn	Phase III	Data Q3/4 2022	Market opens from Sept 2023. Formycon owns 24.9%
FYB203	Klinge Biopharma	Eylea (nAMD)	$4.95bn	$2.96bn	Phase III	Data Q4 2021	Market opens from 2024 if patent extensions apply
FYB206	N/A	N/A			Preclinical	NA	Undisclosed major opportunity
FYB207	N/A	SARS-CoV-2 (COVID-19)			Preclinical	Phase I/IIa from Q421	Uncertain as depends on persistent COVID-19 rates

Source: Edison Investment Research based on Formycon announcements, sales from other company announcements and ClinicalTrials.gov

Formycon's project is FYB201, a biosimilar to Lucentis and licensed to Bioeq, based in Zug. FYB202, a Stelara biosimilar, entered Phase III in November 2019. The Eylea biosimilar, FYB203, entered Phase III in August 2020. A further project is undisclosed beyond a name: FYB206. FYB207, a preclinical project developed strongly over 2020, is a fusion protein to neutralise SARS CoV-2 virus. This is a potential general therapy for treatment of COVID-19 patients.

The three main projects with identified targets are each in a deal or joint venture. Although we cite the reference product sales for each project, the in-market biosimilar price will be typically lower by about 15–20% initially and possibly 30–50% if competition is fierce. One element in these markets is that switching rates from established reference products to slightly cheaper biosimilars have often been slow. Some competitor clinical trials now appear to be generating data to resolve this issue.

FYB201: Seeing a competitive space for Lucentis

Lucentis (ranibizumab, Roche, US, and Novartis, EU) is a humanised monoclonal antibody fragment. It binds vascular endothelial growth factor-A (VEGF-A) preventing the growth of blood vessels across the retina. It is given by intravitreal injection. Lucentis had 2020 US sales of $1.9bn, a decline of 7%. In the EU, sales were CHF1.4bn ($1.6bn), a 16% decline. This indicates global sales of about $3.5bn relative to 2019 sales of $3.9bn. Eylea increased sales in the period (see below). Lucentis patents expired in 2020 in the US and will expire in 2022 in Europe.

FYB201 is fully licensed to Bioeq. Bioeq comprises a joint venture between Polpharma (a Polish pharmaceutical company) and Santo. The clinical studies for FYB201 were run by a Bioeq subsidiary, Bioeq GmbH, based in Germany. In 2019, Bioeq licensed the US sales rights to Coherus, a US biosimilar specialist. Out-licensing to a European marketing partner has not yet been completed but we would expect an announcement this year.

Coherus is developing and in-licensing a variety of products. It has one approved and marketed product so far (UDENYCA (pegfilgrastim-cbqv) for oncology), which generated $476m in sales in 2020. Coherus will share 50–55% of gross profits on US sales of FYB201 with Bioeq. Formycon management has indicated tiered royalties (up to double digit) on net sales.

The Phase III study, COLUMBUS-AMD (NCT02611778), reported its primary endpoint in May 2018, which confirmed comparable efficacy between FYB201 and Lucentis in patients with nAMD (included in wet AMD).

The project suffered a setback in early 2020 as the BLA, filed by Bioeq in Q419, was withdrawn. The reason was a reconfiguration of the manufacturing plant by the contractor. The regulatory strategy has been revised and the decision taken to scale up the manufacturing process. The resubmitted BLA will therefore be for the product based on the commercial scale process. This is planned to be submitted to the FDA by mid-2021. We assume that an EMA filing will be made subsequently so FYB201 could be available soon after the European patent expiry.

Competitors in nAMD include:

- Samsung Bioepis (Korea, sales via Biogen) filed its ranibizumab biosimilar of SB11 with the FDA in November 2020, so this is likely to be the first product onto the US market with strong marketing backing. The EMA filing was made in October 2020. Trial results on 18 May showed equivalence. Biogen holds exclusive rights for both SB11 and the Eylea biosimilar SB15.
- Xbrane (Sweden) is partnered with STADA, a privately-owned German-based generics and OTC company that sells (some) in-licensed biosimilars. The global Phase III (NCT03805100, XPLORE) of Xlucane (ranibizumab biosimilar) completed recruitment in November 2020 and results are expected in mid-2021. The product might be launched after regulatory review from H222. STADA and Xbrane have partnered with Bausch + Lomb in the US with its specialist eye-care franchise making this a strong competitor. Xlucane appears likely to be the third product to reach the US market.

- Roche has a novel antibody, faricimab, in Phase III that targets both VEGF-A and angiopoietin-2 (Ang-2). Data released in February 2021 showed that three-quarters of patients receiving faricimab could be treated every three months or longer in the first year. This could be a premium product.
- Novartis gained FDA approval in late 2019 for Beovu (brolucizumab) and approval in the EU in February 2020. It claims a long dosing interval of up to every 12 weeks. However, there have been post-approval safety issues raised and these limited 2020 sales to $190m.

A market complication will be biosimilar versions of Avastin. Avastin is a cancer therapy (stopping blood vessel growth into tumours) and has the same biochemical action as Lucentis. Avastin is sometimes used off-label for nAMD, as it is cheaper; it is not approved for use in the eye.

FYB203: Eylea, a tough battleground.

FYB203 is a project to develop an Eylea (aflibercept) biosimilar. Regeneron had 2020 Eylea sales of $7.9bn (up 5% from $7.5bn), split into US sales of $4.9bn with European sales at $3bn.

Eylea is injected into the eye, like Lucentis, but has a different mode of action as Eylea binds to both VEGF-A and placental growth factor; Lucentis binds only VEGF-A. Formycon has a global licensing deal with Klinge Biopharma GmbH and gains sales-related royalties.

The Eylea maintenance dose interval is every eight weeks, double that of Lucentis, although Formycon notes that clinical surveys show that the use patterns are similar. US Eylea patents start to expire in 2020, but there seem to be patent extensions (Sharma et al., 2018) that should prevent biosimilar competition in the US until 2024. European patents expire in 2025. In addition, Eylea formulation patents do not expire until 2027–28. Formycon has filed patents for an alternative formulation that has shown preclinical intraocular bioequivalence.

The Bioeq Phase III (MAGELLAN-AMD, NCT04522167, sponsored by Bioeq) started in August 2020 and is scheduled to complete its primary endpoint in August 2021 so we might expect an announcement in Q421. The primary endpoint is the change in visual acuity at eight weeks. The trial will recruit 400 patients and has a straightforward design with a biosimilar arm and an Eylea comparator arm. There is no switch over.

The visible competitive products in development have increased over the last 12 months. There are two strong players: Samsung Bioepis (with Biogen) and Amgen.

- Samsung Bioepis (partnered with Biogen) has a Phase III, NCT04450329, that may have reached its primary endpoint in April 2021. The trial has a direct SB15 arm and an Eylea arm. After 32 weeks, patients in the Eylea arm are randomised to either stay on Eylea or switch to SB15. This appears to be a way of gaining switching data.
- Amgen Biosimilars is running a Phase III (NCT04270747) with ABP 938. This is a 566-patient study of complex design as it tests switching. One arm receives ABP 938 for 48 weeks. The second arm receives Eylea for 16 weeks. They are then re-randomised into two sub arms. The first switches to ABP 938. The second sub arm stays on Eylea 48.
- Momenta Pharmaceuticals is developing the Eylea biosimilar, M710/ MYL-1701P. Momenta was acquired in Q420 by Jansen. A Phase III trial (NCT03610646) in 355 patients was due to report by Q420. A 70-patient extension study is ongoing in diabetic macular odema (NCT04674800). Data from this study is due in Q222.
- Alteogen (South Korea) listed a Phase I trial (NCT04058535) for ALT-L9. There has been no update since 2019, but media reports state that it completed in early 2021.
- Sam Chun Dang Pharm (China) is developing SCD411 in a Phase III (NCT04480463). This is a 560-patient, straightforward two-arm study. It should read out the primary endpoint (eight-week visual acuity) in Q122. We assume that Sam Chun Dang Pharm will partner SCD411 if it is to be sold outside China.

FYB202: Chasing a major immunology market

Formycon is developing a biosimilar, FYB202, to Stelara (ustekinumab, Jansen), the second biggest anti-inflammatory product after Humira. The biosimilar market for anti-inflammatory therapies is likely to be competitive with the patent expiries Humira (adalimumab, an anti-TNF monoclonal), mainly used for rheumatoid arthritis, but also Crohn's disease, ulcerative colitis and psoriatic arthritis. Stelara has a different mode of action to anti-TNF therapies as it binds a different set of inflammatory messenger proteins.

Stelara is an antibody that binds interleukin-12 (IL-12) and IL-23. These potent cytokines drive the immune response so neutralising them controls autoimmune diseases such as Crohn's disease and psoriasis. Ustekinumab is not used for rheumatoid arthritis (a massive market) but is effective for psoriatic arthritis (Veale and Fearon, 2015). It is also now indicated for Crohn's disease and ulcerative colitis and these appear to be driving the sales growth. Sales in 2020 rose strongly by 20% to $7.7bn from $6.4bn in 2019.

FYB202 is licensed to privately owned Aristo Pharma through a joint venture vehicle, FYB 202 GmbH & Co KG. Formycon holds 24.9% (Aristo owns 75.1%) and will therefore fund this proportion of the clinical and development costs and receive that share of profits. Phase III started in November 2020. This 'VESPUCCI' trial, NCT04595409, is recruiting 392 psoriasis patients in a blinded comparison trial against Stelara. The primary endpoint should be reached from September 2021 with full data by May 2022. This should enable a regulatory filing in H222 and launch in 2023. Stelara has its main US patent expiry in September 2023 in the US and in January 2024 in Europe.

Competitors with biosimilars in development are increasing in number as the patent expiry looms. Interestingly, several of these companies are running three-arm studies, one arm being their candidate product and the other two comparing US and EU manufactured Stelara. Presumably some differences in the two manufacturing sites has raised some marketing concerns. This does not seem an issue for Amgen.

- Samsung Bioepis started a 201-patient Phase I (NCT04772274) of SB17, its Stelara biosimilar, in February 2021. This should report in September 2021 enabling, we assume, a 2022 Phase III. This is a three-arm study comparing US and EU manufactured Stelara.
- BioFactura Australia, working with Avance, also has a Phase I comparing its biosimilar (BFI-751) with the US and EU versions of Stelara. This 228-patient study (NCT04843631) is due to end in January 2022.
- Amgen Biosimilars is developing ABP 654. Its 352-patient psoriasis Phase III (NCT04761627) is due to report data from March 2023. This has both continuous dose arms and an arm where patients will switch between Stelara and ABP 654 on a 16-week rotation.
- Icelandic biosimilars specialist Alvotech is starting a 294-patient Phase I (NCT04744363) trial of a Stelara biosimilar. This is partnered with Fuji for Japan and STADA in Europe. The trial again compares the US and EU forms of Stelara. It should read out in February 2022.
- Australian NeuClone was in Phase I; the trial was due to end in late 2019; no data is available.

Clearing SARS-CoV-2, a new project

Formycon has announced a preclinical COVID-19 project to produce a fusion protein against the SARS-CoV-2 virus to clear virus quickly from the blood. Other similar ideas use monoclonal antibodies, for example Regeneron uses a mix of two monoclonal antibodies. The Formycon approach uses the natural target of the SARS-CoV-2 virus: the spike protein angiotensin-converting enzyme 2 (ACE2).[1]

[1] ACE1 releases a small peptide that causes blood vessels to contract. This, plus ACE2, which expands blood vessels so reducing pressure, keeps the blood pressure in balance..

ACE2 is on the surface of cells in some organs like the heart and kidneys and normally cleaves a precursor protein to release a small peptide hormone. This causes blood vessels to dilate. If SARS-CoV-2 spike protein binds the ACE2 catalytic pocket, the virus become anchored to a cell and can then enter the cell and replicate driving infection.

FYB207 takes the binding pocket of ACE2 and attaches it (by gene engineering) to the constant region of immunoglobulin. The constant region allows the fusion protein to be taken up and destroyed by other cells. As the natural ACE2 binding region is used, SARS-CoV-2 cannot evolve not to bind it as it would then not be able to enter cells and reproduce. It is an ingenious system but at this preclinical stage, there is no data.

Regeneron's antibody mixture, REGN-COV2, is an intravenous infusion of a combination of two monoclonal antibodies (REGN10933 and REGN10987) that bind virus and block the infectivity of SARS-CoV-2. The Phase III efficacy reported in March 2021 showed that in high-risk non-hospitalised patients it significantly reduced the risk of hospitalisation or death by 70% compared to placebo. Data on hospitalised patients is being acquired. The weakness of the antibody approach is that is can be rendered less effective by viral mutations, which spread rapidly.

FYB207 might be a better product than antibody mixtures. Clinical Phase I / IIa trials are expected by Formycon to start in Q421. The dose will also be crucial as a lower effective dose could be much cheaper. A trial would also need to observe any effects on blood pressure. The key advantage is that FYB207 might be effective irrespective of viral mutations. In commercial terms, vaccination should curb high infection rates but if, like flu, SARS-CoV-2 remains a perennial background disease, there will be significant numbers of vulnerable people. A fast, effective and strain independent therapy should therefore have an important long-term role.

Valuation: Clear pipeline and solid financial position

Formycon's market cap is €673m with about €7.6m of liabilities. Adding liabilities and subtracting €42.2m cash gives an EV of about €638m (compared to €285m in September 2020). Formycon has a robust financial position with high development revenues covering most costs, cash for investment (plus €7m in receivables) and a pipeline targeting major global markets.

Commercially, the Samsung Bioepis-Biogen alliance may be the first into the US Eylea biosimilar market with SB11. FYB201 might be second, with Xbrane's Xlucane third in late 2022. In Europe, the 2022 patent expiry means that all three may launch in a similar timeframe.

A more lucrative market is likely to be for Eylea biosimilars. Two strong players, Samsung Bioepis and Amgen, are moving quickly. Within a few years, the new Roche product, faricimab, could become well established and take the ultra-long injection interval premium slot; we note that injection intervals are in reality determined by the physician and the patient response.

The Stelara opportunity is the biggest market and still showing strong growth. Having the FYB202 Phase III underway shows excellent progress. The main current competitor is Amgen in Phase III. Samsung Bioepis is not too far behind as it will complete Phase I in late 2021.

It is harder to assess the potential for FYB207. It is clearly a very innovative product and there will remain a need for effective therapies to rapidly clear SARS-CoV-2 viral loads. FYB207 could become a key weapon in the therapeutic arsenal. The long-term market will be affected by mutation rates and vaccination effectiveness; hence, it is difficult to project the market at this time.

The main uncertainties are on exact product launch dates, competition and the ability of partners to market effectively in complex global markets. We believe that Formycon should become one of the leading biosimilar companies as its portfolio develops and projects mature. For maximum value potential, Formycon intends to take more financial risk and to fund projects itself.

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