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Basilea Pharmaceutica

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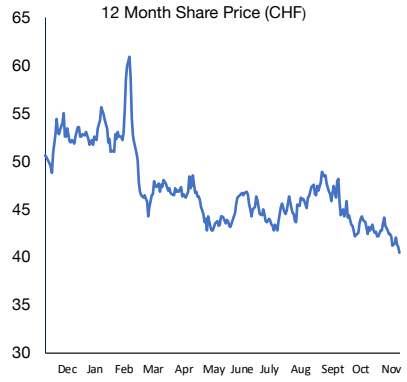
Share Price (CHF)	**40.4**
CP Fair Value (CHF)	**120**
Market Cap (CHFm)	523
Cash (CHFm)	164
EV (CHFm)	586
Country	Switzerland
Code	BSLN
Index	SIX



Source: Calvine Partners Research

Can derazantinib be class leading?

The emergence of the FGFR inhibitor class has brought some truly remarkable data with early approvals in difficult to treat FGFR driven cancers, including urothelial and bile duct cancers. With both of these also programmes for derazantinib, Basilea has adapted its development strategy to find a suitable pathway to secure regulatory approval and ensure its commercial success. The most obvious change has been incorporating a dose intensification strategy for both urothelial and gastric cancer indications. While efficacy data have been more encouraging as they have matured, existing safety data suggest that a higher dose should be manageable and provide the best possibility of derazantinib generating a class leading response compared to other competing FGFR inhibitors. At the same time, our enthusiasm for derazantinib is due to its additional ability to target CSF1R. CSF1R plays an important role in maintaining an immunosuppressive tumour microenvironment. As a result, this additional property should boost the activity of the checkpoint inhibitors (CKIs), particularly in those cancers (such as urothelial and gastric cancers), where their efficacy is more limited.

Multiple studies underway

Despite some early disappointing data combining FGFRi with immunotherapy (BISCAY) in urothelial cancer (UC), there are several studies underway evaluating the combination of erdafitinib (NORSE), rogaratinib (FORT-2) and pemigatinib (FIGHT-205) with different CKIs. Data from the ongoing Phase 2 NORSE study provides some encouragement in this regard, with the combination generating a significantly higher response than erdafitinib alone. In FORT-2, data have been helpful, with patients receiving the combination benefiting independent of PD-L1 expression levels or FGFR alteration status. Reassuringly, the toxicity profile generally reflects that of the FGFRi alone. For derazantinib, Basilea has sought to maximise the possibility of success through increasing the dose and capitalising on the additional activity against CSF1R in both FIDES-02 (UC) and FIDES-03 (gastric cancer). Much of the data will read out in 2022 with an insight into (FGFR) refractory patients anticipated in H1 2022 (although this is a difficult patient group and at the lower dose). Gastric cancer represents another challenge, but data elsewhere (bemarituzumab), as well as derazantinib preclinical data, have provided reassurance. Again, the ability to change the immunosuppressive microenvironment should be crucial in delivering a positive result in FIDES-03. Finally, we suspect that derazantinib's additional activity against CSF1R should reduce the potential for resistance to develop. All told, we are approaching a crucial time for the fortunes of derazantinib, with data providing an insight into the potential for class leadership starting in H1 2022.

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Important transition period ahead

Targeted approach should reduce attrition

Investment behind the oncology portfolio has delivered impressive results for both Basilea's FGFR inhibitor derazantinib and the mitotic spindle assembly checkpoint controller lisavanbulin. Both programmes employ a targeted approach seeking to identify those patients who will benefit most from treatment. As a result, clinical trials should be smaller and the risk of failure lower. At the same time, each therapy targets only a subset of total available patients, so market positioning is critical to maximising sales potential.

Evolving clinical programmes

This is clearly the case with derazantinib, where Basilea is following in the footsteps of Pemazyre (pemigatinib; Incyte) and Truseltiq (infigratinib; Bridgebio) in bile duct cancer and Balversa (erdafitinib; J&J) in bladder cancer. With two selective FGFR inhibitors approved in the already modestly sized bile duct cancer indication, Basilea must ensure a strong commercial proposition in this and other cancer settings. The US bile duct cancer indication, for example, comprises only circa 20,000 patients, of whom 15-20% harbour an FGFR genetic aberration and are suitable for (FGFR) targeted therapy.

Dose intensification strategy justified by MTD data

As a result, the evolving clinical programme at Basilea has sought to capitalise on the various different attributes of derazantinib compared to its peers. Each has different kinase inhibition profiles, and derazantinib appears to have a cleaner toxicity profile. A manageable safety profile has allowed Basilea to explore a dose intensification strategy with derazantinib, in both urothelial and gastric cancer, to boost its already competitive clinical profile. If successful, we expect Basilea to explore this higher dose in other relevant cancers.

Still potential for a best-in-class label

Inevitably, given the speed with which targeted and specific FGFR inhibitors have gained regulatory approval, there are concerns that derazantinib may be left behind. Further, there are several other competing FGFR inhibitors in clinical development, suggesting that the market may become more crowded in future. Given these concerns, the clinical programme pursued by Basilea for derazantinib seeks to capitalise on its differentiated profile to secure a best-in-class label in challenging cancer settings.

FGFR inhibitors in development	Company	Kinase profile	Status
Pemazyre (pemigatinib)	Incyte	FGFR1-3	Approved iCCA ORR35.5%, median duration of response 9.1 months, median PFS 6.9 months, OS not mature. Clinical proof of concept ongoing in solid cancers. FIGHT 201: metastatic or unresectable bladder cancer. FIGHT-302 potential 1st line in iCCA. Primary completion 2022. Phase 2 (FIGHT-205) comparing Keytruda plus Pemazyre vs Pemazyre vs SoC in metastatic/unresectable UC. Phase 2 (FIGHT-207) ongoing evaluating Pemazyre mono in various FGFR driven tumour types - 3 cohorts dependent on type of FGFR alteration.
Balversa (erdafitinib)	J&J	FGFR1-3	Approved UC. Phase 3 ongoing comparing erdafitinib to chemotherapy and Keytruda Phase 2 603TiP study evaluating in advanced or metastatic solid tumours (exc UC) with FGFR mutations or fusions. Enrolling 280 patients (240 broad panel cohort and 40 exploratory cohort), primary endpoint ORR. Phase 2 NORSE study ongoing evaluating combination with cetrelimab in cisplatiin ineligible mUC 68% vs 33% monotherapy.
Truseltiq (infigratinib)	QED Therapeutics	FGFR1-3	Approved in iCCA. ORR of 23.1% and DoR 5 months. Median PFS 7.3 months. UC ORR of 31% in 1st line and 24% in 2nd line and later. Patients with upper tract UC had ORR of 50%. PROOF302 ongoing in adjuvant UC. Phase 2 (PROPEL-2) in achondroplasia ongoing.
AZD4547	AstraZeneca	FGFR1-3	Positive preclinical data in breast cancer. Development discontinued 2019.
DEBIO1347	Debiopharma	FGFR1-3	Phase 2 basket study (FUZE) ongoing in iCCA, UC and other solid tumours (exc. primary brain tumours).
PRN1371	Principia Biopharm	FGFR1-4	Development discontinued in Jan 2020 to focus on immune mediated diseases
futibatinib	TAIHO Pharma	FGFR1-4	Positive interim data from Phase 2 FEONIX-CCA2 study in May 2020. ORR 37.2%, median PFS 7.2 months. Combination with Pembrolizumab in Phase 2 advanced metastatic UC.
rogaratinib	Bayer	FGFR1-4	Mixed data from Phase II/III trial in UC (FORT-1). ORR of 19.5% obtained for the rogaratinib arm vs 19.3% for the chemotherapy arm. Disease control rate was 49.4% vs 55.7% and PFS was 2.7m vs 2.9ms. FORT-2 in combination with Tecentriq in patients with UC is ongoing.
derazantinib	Basilea	FGFR1-3	PoC data in iCCA in patients with FGFR2 gene fusions ORR of 21%, median DoR 6.4 months and DCR of 76%. PFS 8.0 months. FIDES-01, FIDES-02 & FIDES-03 ongoing in iCCA (monotherapy), UC (mono & combination with Tecentriq) and gastric (mono & combination with ramucirumab and paclitaxel; combination with atezolizumab).
bemarituzumab	Amgen	FGFR2b	Phase 2 FIGHT trial generated positive data in FGFR2b+ve HER2 -ve gastric cancer. Median OS of 19.2 months vs 13.5 months for chemo alone. In patients with >10% FGFR2b median OS was 25.4 months vs 11.1 months chemo alone.

Source: Calvine Partners Research

The safety profile is clearly helpful

From a safety perspective, derazantinib appears to possess a more manageable toxicity profile compared to many of its peers resulting in reduced rates of retinal side effects, stomatitis, hand-foot syndrome and nail toxicity. With a more benign safety profile, risks associated with increasing the daily dose to 400mg from 300mg should be manageable, particularly in monotherapy. Confidence in derazantinib's profile can also be seen with the decision to employ the higher dose in combination with the anti PD-L1 atezolizumab (Tecentriq) in both UC and gastric cancer.

Use of higher dose just in time for UC and gastric cancer…

The early-stage nature of the urothelial and, in particular, the gastric cancer indications has allowed Basilea to explore its dose intensification strategy with minimal impact on expected timing. We will have to wait until 2022 before we get a glimpse into the impact of the higher derazantinib dose; however, before that, combination data will be available in H1 2022 in FGFR refractory patients albeit at the lower 300mg dose.

…not relevant for iCCA but PFS data supportive

Unfortunately, the biliary cancer indication was too far progressed to explore dose intensification. However, we suspect that the commercial reward here will be modest anyway despite potential differentiation with respect to a broader range of FGFR aberrations (in addition to gene fusions). Positive data in these patients appears unique to derazantinib (so far) and suggest potentially broader applicability across FGFR driven tumours than FGFR gene fusions. In bile duct cancer, only about 15% of patients harbour FGFR2 gene fusions, so activity in other aberrations would be welcome. We await further data in this patient population (topline results H1 2022) as Basilea optimises derazantinib's profile.

Urothelial cancer: the proof is in the pudding

Only monotherapy data so far and only in iCCA

From an efficacy perspective, we only have data for derazantinib in monotherapy in biliary cancer. While we recognise the limitations with respect to cross-trial comparisons, it appears that on measures such as ORR and DCR, other FGFR inhibitors perhaps look more impressive. Still, from our perspective, it is important to note that on the more patient relevant PFS endpoint, derazantinib looks highly competitive with a median PFS of 8.0 months in FGFR2 gene fusion iCCA patients. This compares to 7.3 months for infigratinib, 7.0 months for pemigatinib and 9.0 months for futibatinib.

Higher dose adds to monotherapy potential but combination the key

Given the highly competitive market emerging for FGFR inhibitors combined with the more limited patient population available for targeted therapies, we believe it will be the combination data that will best define the market positioning and commercial success of derazantinib. The combination with the checkpoint inhibitors (CKIs) seeks to capitalise on derazantinib's additional ability to inhibit CSF1R, which should help transform immunologically cold cancers into ones more tractable to checkpoint inhibition.

Additional activity against CSF1R adds promise

The milieu of cells that represent the tumour microenvironment frequently serve as a barrier to immune activity and is one of the critical reasons why immunotherapy alone may have limited clinical efficacy in certain immunologically cold cancers. Thus, CSF-1/CSF1R inhibition as an approach represents a novel class of immunomodulatory therapeutic confirmed, we believe, with the approval of Turalio (pexidartinib) for TGCT (tenosynovial giant cell tumour).

Urothelial cancer still represents an unmet need, but competition growing

Urothelial cancer benefiting already from FGFRi

Urothelial carcinoma represents the second cancer setting for derazantinib. It is the most common and frequent form of bladder cancer, representing more than 90% of all bladder cancers. Approximately 20% of patients diagnosed with metastatic urothelial carcinoma (mUC) have an FGFR genetic alteration. The five-year survival rate for patients with Stage IV metastatic bladder cancer is only 6%, suggesting a significant unmet need.

…but remains a significant unmet need

Despite the competitive landscape intensifying in bladder cancer, this is a significantly larger opportunity than iCCA. With approximately 84,000 new cases in the US alone, bladder cancer is a relatively common cancer and is complex to treat. While approximately 70% are low-grade superficial tumours, they have a high propensity to recur post-resection and adjuvant chemotherapy. As a result, treatment is often lifelong and consequently expensive. We have seen conflicting numbers for the number of patients harbouring FGFR mutations, with a consensus of 15-20% for all FGFR alterations. For patients harbouring an FGFR3 mutation, the number appears to be closer to 12%. As an indicator of market potential, we note at the time of erdafitinib approval; originator J&J suggested that it should reach blockbuster status (>$1bn in sales).

Erdafitinib received accelerated approval

Erdafitinib was approved for the treatment of adults with locally advanced or mUC with FGFR3 or FGFR2 genetic alterations, and has progressed during or following at least one line of platinum-containing chemotherapy. Since the approval, J&J has expended significant resources to evaluate the potential of erdafitinib in various cancer settings.

CKIs work only in a small minority

Combination with the CKIs has been an obvious target, particularly for those with cisplatin-ineligible locally advanced or mUC. In the first-line setting, carboplatin-based regimens are not well tolerated and deliver modest ORR, combined with limited durability. Checkpoint inhibitors may give characteristically durable responses, but only a minority of those treated achieve a response (ORR 24-29%).

So far, combining existing FGFRis with checkpoint inhibitors has resulted in conflicting data. First up, the BISCAY study evaluated the anti PD-L1 durvalumab (Imfinzi) combination with various targeted agents, including the FGFRi AZD4547 in urothelial cancer. Response rates to the combinations were generally modest (ranging from 9%-36%), and as a result, did

Early combination data were disappointing

not achieve the efficacy criteria to warrant further development. Additionally, the addition of targeted therapy to durvalumab did not increase the duration of response or PFS. At six months, PFS rates ranged from 20% to 43%, while at one year, OS rates ranged from 42% to 56% across the study arms.

….but this hasn't dampened enthusiasm

Despite this disappointing outturn, efforts to evaluate different combinations have been ongoing, perhaps reflecting the different kinase inhibition profiles offered by the various FGFRi's and the general desire to investigate combinations that boosted the performance of the CKIs. In addition, other patient selection criteria were deemed potentially important in improving success, including PD-L1 status and tumour mutational burden.

Recently reported data more encouraging

Updated data from the Phase 1b/2 NORSE trial were presented recently at ESMO, evaluating the combination of erdafitinib with the (investigational) anti PD-1 cetrelimab in UC patients who were cisplatin ineligible. Data were very encouraging, with an ORR of 68% (n=19) for the combination, compared to erdafitinib alone (33%). In those receiving the combination, 21% experienced complete responses, and 47% were partial responses. The safety profile of the combination was in line with erdafitinib monotherapy with hyperphosphataemia the most frequent treatment-emergent adverse event. While this is encouraging and appears to demonstrate that the combination of an FGFRi and a CKI can deliver better results, we await outcomes data with respect to PFS and OS. That said, the study's objective was to demonstrate that treatment with an FGFRi could alter the tumour microenvironment to make it more tractable to PD-1 based intervention.

With the Phase 2 part of NORSE ongoing, we look forward to further data release to provide further insights into the prospect of the combination offering new treatment options for metastatic patients ineligible for cisplatin therapy. At 50%, this remains a sizeable proportion of the bladder cancer treatment market.

FORT=2 suggested broader benefit

Additional encouragement for this approach has been delivered by early data from the combination of rogaratinib and atezolizumab. Data presented from the FORT-2 study at ASCO 2021 were also notable to the extent that 79% of the 14 patients with a response had low or negative PD-L1 expression, while further analysis of 16 patients with low or no PD-L1 expression and no FGFR3 mutation or fusion also showed some benefit. These data suggest that the

combination delivered benefit irrespective of PD-L1 expression levels or indeed FGFR alteration status.

FIDES-02 combination data start later this year

Basilea has designed the FIDES-02 Phase 1/2 study to recruit cisplatin-ineligible patients or those who failed on first-line therapy (or prior treatment with FGFR inhibitors). The trial comprises three open-label studies in urothelial cancer with an FGFR gene alteration to assess the activity of derazantinib alone or in combination with Tecentriq. In FIDES-02, we will have direct evidence of the synergistic activity of derazantinib and Tecentriq. In FGFR refractory patients (receiving the 300mg dose), interim data will begin to emerge in H1 2022, providing insight into the combination. More importantly, the cohorts receiving the higher 400mg dose will also report in 2022.

Additional activity against CSF1R suggestive of class leading response

The preliminary results of the NORSE study, in particular, are highly encouraging for the ongoing Phase 2 FIDES-02 study. Hopefully, with the additional activity against CSF1R, the likelihood of a positive outcome should be greater than erdafitinib+cetrelimab. The positive result of NORSE, however, is at odds with the disappointing result from BISCAY. Various explanations have been offered, including the difference between study populations (refractory versus cisplatin-ineligible).

Monotherapy data to fall back on

From a risk management perspective, even if the combination arm fails to show a benefit over derazantinib alone, we are hopeful the monotherapy arm particularly given the dose intensification. Also, it will be interesting to see whether derazantinib shows activity in those patients who have previously failed on other FGFR inhibitors. However, as we have highlighted already, this is at the lower 300mg dose.

Treatment options in UC improving

Basilea cognisant of evolving competitive landscape

Bladder cancer treatment options have improved considerably in recent years, not just with the approval of erdafitinib but also with the approval of the antibody conjugate enfortumab vedotin (Padcev) for mUC patients failing platinum-containing chemotherapy or are cisplatin ineligible. Although enfortumab may not represent direct competition given that it targets nectin-4 and has broad applicability in UC, efficacy data have been compelling and raised the efficacy bar in this setting. Further, efforts to evaluate the combination of enfortumab with CKIs are ongoing, with the most recent update further establishing its credentials here.

Positive data evaluating the combination of enfortumab with the CKI pembrolizumab (Keytruda) have been reported with the most recent update at ASCO 2021 after two years (24.9

Enfortumab can boost CKI activity

months) of follow up for the Phase 2 study EV-103. ORR was 73.3%, including 17.8% CR and an ORR of 57.1% (8/14) in patients with liver metastasis. A very impressive 93% of assessable patients experienced a reduction in tumour size, while the median PFS was 12.3 months and the OS rate was 56.3% (median PFS not reached).

Breakthrough therapy designation helpful

Based on the data generated by the combination, the FDA had previously granted breakthrough therapy designation to enfortumab vedotin + pembrolizumab for the treatment of patients with first-line cisplatin-ineligible locally advanced or mUC in February 2020. Thus, these are exciting times for the future potential of enfortumab in urothelial cancer.

Gastric cancer beckons for derazantinib

Outlook for gastric cancer bleak

Gastric cancer could be a significant market opportunity for derazantinib given the lack of competition and the poor outlook for patients. Although improvements in *H. pylori* diagnosis and eradication have significantly reduced its prevalence, there are still approximately 1m cases of gastric cancer diagnosed globally every year, although many of these are in Asia where Basilea does not have full commercial rights to derazantinib. Rights to derazantinib for China, Hong Kong, Taiwan and Macau are held by Sinovant. Nevertheless, this is an important setting in the West, with circa 27,000 new cases in the US per year resulting in 11,000 deaths. While the 5-year survival rate may look relatively decent at 31%, this hides the very low survival rate once metastatic (18% Stage IIIC compared to 89% for Stage IA).

No FGFRi approved, CKI's lacklustre

First-line therapy in patients with advanced gastric cancer comprises nivolumab with fluoropyrimidine or platinum-based chemotherapy, with agents such as docetaxel, paclitaxel and irinotecan used following progression. CKIs have found a role in the treatment of advanced gastric cancer delivering durable responses. Other approaches have been evaluated. Second-line ramucirumab (Cyramza) therapy, for example, has been associated with a survival benefit and was the first FDA approved agent in this setting in 2014.

Efforts are ongoing to boost CKI

At the same time, although the CKIs have been shown to generate durable responses, this has been in a small minority of gastric cancer patients, with response rates in pre-treated patients ranging between 11%-24%. Furthermore, even in those patients who have experienced durable responses, resistance usually develops. Nevertheless, the CKIs remain an important therapeutic option; however, identifying those patients who will benefit most remains therapeutically challenging.

Some patients benefiting from targeted agents

Various strategies are underway to enrich patient populations, with one of the most successful being to improve the immunogenicity of the tumour microenvironment in gastric cancer. Following a targeted approach has proven to be fruitful elsewhere in gastric cancer. For example, in May 2021, we saw the accelerated approval of the CKI pembrolizumab (Keytruda), combined with the specific anti-HER2 therapy trastuzumab (Herceptin) and chemotherapy, for first-line treatment of patients with locally advanced unresectable or metastatic HER2 positive gastric or gastroesophageal junction adenocarcinoma.

FGFR targeting shows promise

FGFR represents another important target in gastric cancer, with approximately 10%-15% of patients harbouring an FGFR alteration. Consequently, these patients represent an obvious target for FGFR inhibition. Derazantinib is being explored in the gastric cancer setting, evaluating in monotherapy at the increased dose of 400mg, in combination with atezolizumab, and, in a separate cohort, the combination with ramucirumab and paclitaxel.

Bemarituzumab data is very promising

One of the more reassuring aspects of FIDES-01 & 02 has been the wealth of existing clinical data elsewhere, although this has perhaps proven problematic commercially. On the other hand, gastric cancer may be higher risk, but the commercial opportunity is clear. Additionally, there are reasons to be optimistic, particularly given the performance of the FGFR2b targeted antibody bemarituzumab. Results of the 155-patient FIGHT trial comparing bemarituzumab plus chemotherapy against just chemotherapy as a first-line treatment for FGFR2b-positive, non-HER2-positive, gastric cancer patients were overtly positive. Updated data presented at ASCO in June 2021 showed that treatment (follow up at 12.5 months) resulted in overall survival (OS) of 19.2 months versus 13.5 months for chemotherapy alone. Even more impressively, in an exploratory pre-specified subgroup analysis, patients with >10% of tumours overexpressing FGFR2b experienced a median OS of 25.4 months versus 11.1 months for chemotherapy alone.

Derazantinib preclinical data supportive

More recently, Basilea has reported preclinical results from derazantinib in several preclinical models of gastric cancer. Encouragingly for derazantinib, preclinical data presented at the ACR-NCI-EORTC (ANE) virtual International Conference on Molecular Targets and Cancer Therapeutics further support the role of derazantinib in gastric cancer and, in particular, its additional activity against CSF1R.

CSF1R activity boosts response

Data presented at the conference suggested synergistic anti-tumour effects with paclitaxel, building on the previous preclinical data reported in monotherapy. The data presented were from several gastric cancer models, including *in-vivo* tumour models representing different FGFR aberrations. Data in more prevalent FGFR gene fusion models reported complete regression. Importantly, where higher levels of immunosuppressive M2-tumor-associated macrophages were involved, the combination with paclitaxel and derazantinib generated a more profound response. These data bode well for the forthcoming FIDES-03 data, which evaluate derazantinib in combination with paclitaxel (and atezolizumab) in gastric cancer. Positive results should help further inform the differentiated profile of derazantinib versus its FGFRi competitors.

Although we have not included the gastric cancer opportunity in our financial model, our research suggests that even a modest 25% share of the 15% of patients who harbour an FGFR alteration would represent a $200m opportunity in the US and Europe alone. When combined with $400m for a potential 20% share of the UC market and $40m for the iCCA indication, all on an unrisked basis, the financial reward for Basilea (and a potential partner) could be highly lucrative.

Uncertainty should be removed next year

Essentially, Basilea appears to have followed a well-planned clinical evaluation of derazantinib, taking into account the intensifying competitive environment. Although the dose intensification in FIDES-02 and FIDES-03 may have added uncertainty, for now, Basilea is following the science and the data support dose intensification, which could provide a meaningful additional benefit in bladder as well as gastric cancer.

However, given the competitive situation, expectations remain rightly modest for now until the broader utility of derazantinib becomes clearer. Ultimately, our belief remains that the combination data will be required to fully capitalise on the potential of derazantinib, leading to greater market appreciation and the delivery of a suitable commercial partner.

Risks

Basilea's currently marketed products are out-licensed to third parties, suggesting little influence over sales performance. Nevertheless, execution on key product Cresemba has been through highly appropriate partners (particularly Astellas and Pfizer).

While the antibiotic Zevtera is already marketed outside of the USA for the treatment of CAP and HAP (excluding VAP), we see the more significant market opportunity in the *Staph aureus* bacteraemia indication. While previous clinical data support this approach, there is uncertainty associated with this difficult-to-treat patient population, which has been reflected in our probability adjustment. Approval of ceftobiprole in the US requires a positive outcome for both the (lower risk) ABSSSI indication (already achieved) as well as the bacteraemia indication.

The oncology programmes are also unpartnered. This is a highly competitive field, but we note Basilea's endeavours to differentiate derazantinib, and we would highlight the combination with the checkpoint inhibitors as a starting point. The recent introduction of a dose intensification strategy should help differentiation but adds further uncertainty. Data on lisavanbulin may be in a small number of patients, but the effects have been remarkable in two patients with long-lasting clinical benefit. The relevance of the novel biomarker EB1 will be important in identifying appropriate patients in glioblastoma and other cancers. For now, lisavanbulin sits outside our forecasts, so it represents upside to our financial model and valuation.

Our financial forecasts suggest Basilea will experience several years of losses. With our expectation of a 2023 ceftobiprole launch, our projections do not incorporate an upfront payment that the company would receive from a commercial partnership. Consequently, we are forecasting a negative cash position but recognise that there are many puts and takes. Additionally, we have effectively taxed the company on its first year of profits despite significant tax losses, which will significantly reduce the tax burden in the near term.

Financial Model and Summary

Strong partners capitalising on Cresemba's potential

The base anti-infectives business at Basilea continues to deliver good growth with the international roll out of Cresemba continuing. We should also not forget about the potential for antibiotic ceftobiprole to deliver future US revenues in the more meaningful *Staph aureus* bacteraemia indication, should ERADICATE give a positive result.

FGFR programme the key pipeline asset for now

However, the investment case for Basilea is intricately linked to the outlook for the emerging oncology franchise and, for now, derazantinib in particular. There is positive news from the class in general, given the excellent clinical data generated in FGFR driven tumours by various selective and highly targeted FGFR inhibitors. These promise to transform the treatment options for patients with previously intractable tumours such as bladder and bile duct cancer. Additionally, although still early days, these targeted agents appear to be delivering good commercial traction. At its recent results meeting, Incyte reported pemigatinib revenues of $18m in Q2 202, with growth driven by duration of therapy use in the 2nd line setting.

Basilea is fortunate to have been able to implement dose intensification

From derazantinib's perspective, this is a fast-moving field, and Basilea has needed to adapt clinical development plans as new data have emerged and therapies have received accelerated approval. The more limited nature of available market size for highly targeted therapies is an important issue, and so new entrants have to offer a highly differentiated proposition if they are to provide a sensible economic return.

Supportive data emerging for FGFRi/CKI combination

Fortunately, each of the FGFRi's possess different kinase inhibition profiles, with this manifesting itself in a more benign safety profile for derazantinib compared to its peers. We have always viewed the bile duct cancer indication as a modest opportunity for derazantinib. While broader applicability with other FGFR aberrations in addition to gene fusions would likely aid commercial potential, we believe that it is the potential to boost the activity of the checkpoint inhibitor (anti PD-1/PD-L1) class that will provide differentiation and lead to regulatory filings in bladder and ultimately gastric cancer. Recent data elsewhere has supported the FGFRi/CKI combination, despite some earlier disappointments. We look forward to data from derazantinib, which will hopefully confirm that the additional activity against CSF1R will provide a more effective approach than other approved FGFR inhibitors.

Basilea was fortunate that timing allowed for the implementation of a dose intensification strategy as the

company seeks to fully investigate the potential for derazantinib in UC and gastric cancers. The competitive noise in UC is mounting given the introduction of enfortumab vedotin, which appears to have broad applicability in the treatment of cisplatin-ineligible patients. While none of the ongoing studies will provide a head-to-head comparison between different agents and combinations, it would be very reassuring should the combination of derazantinib (at the higher dose) with atezolizumab deliver therapeutic leadership in cisplatin-ineligible patients in FIDES-02. Although we will have a glimpse into the combination in H1 2022, we remain cautious given this study is in FGFR refractory patients and at the lower dose. As a result, we suspect that we will need to wait until data on the higher dose becomes available later in 2022.

Combination data in UC will be key to a regulatory filing

Without a competing FGFRi approved in gastric cancer, we view this programme as a higher risk than either bile duct or bladder cancer. As a result, we have not included any revenues from this indication in our financial model. Nevertheless, we have highlighted the positive clinical data from bemarituzumab and the more recent preclinical data generated by derazantinib. A positive result from FIDES-03 should lead to the inclusion of sales in our financial model, suggesting further upside to our DCF derived valuation.

We are particularly enthusiastic about the promise in gastric cancer

We suspect that a regulatory filing for derazantinib will require a positive outcome from FIDES-02. Positive data should also attract the attention of a potential commercial partner. Basilea may have followed the science in developing derazantinib, but the speed at which the competitive environment is changing and the need to fully exploit various cancer settings and combinations, suggest that a deeper-pocketed partner is required. As we have stated before, depending on the result from FIDES-02, a partner with an existing oncology franchise and, preferably, possession of a CKI would clearly be best placed to progress the development of derazantinib expeditiously.

Basilea Income Statement (CHF'000)

Basilea Income Statement (CHF'000)							
Year to December	2019A	2020A	2021E	2022E	2023E	2024E	2025E
Total revenue	**134381**	**127629**	**137196**	**130014**	**142039**	**177548**	**241218**
COGS	(18,868)	(24,054)	(25,381)	(20,802)	(18,465)	(23,081)	(31,358)
Gross profit	**115,513**	**103,575**	**111,815**	**109,212**	**123,574**	**154,467**	**209,860**
Gross margin	86.0%	81.2%	81.5%	84.0%	87.0%	87.0%	87.0%
R&D	(102,662)	(97,410)	(96,723)	(91,010)	(78,121)	(72,795)	(74,778)
SG&A	(30,051)	(29,422)	(31,555)	(29,903)	(34,089)	(35,510)	(41,007)
Total cost and operating expenses	(151,581)	(150,886)	(153,660)	(141,715)	(130,676)	(131,386)	(147,143)
Non-underlying items	0.00	15,035	0.00	0.00	0.00	0.00	0.00
Operating profit US GAAP	**(17,200)**	**(8,222)**	**(16,464)**	**(11,701)**	**11,363**	**46,163**	**94,075**
Finance income	28	104	0	161	167	165	32
Finance expense	(6,424)	(7,589)	(7,456)	(7,480)	(3,225)	(3,225)	(3,225)
Other financial income	1,583	2,057	0	0	0	0	0
Other financial expense	(369)	(1,017)	0	0	0	0	0
Underlying PBT	(22,382)	(29,702)	(23,920)	(19,020)	8,305	43,101	90,878
PBT IFRS	(22,382)	(14,667)	(23,920)	(19,020)	8,305	43,101	90,878
Loss before tax	(22,382)	(29,702)	(23,920)	(19,020)	8,305	43,101	90,878
Tax	(40)	(55)	(60)	(60)	(1,179)	(6,120)	(12,905)
Underlying net income	**(22,422)**	**(29,757)**	**(23,980)**	**(19,080)**	**7,126**	**36,980**	**77,973**
Net income US GAAP	**(22,422)**	**(14,722)**	**(23,980)**	**(19,080)**	**7,126**	**36,980**	**77,973**
EPS Basic (CHF)	(2.09)	(1.43)	(2.33)	(1.69)	0.63	3.28	6.91
EPS Diluted (CHF)	**(2.08)**	**(1.36)**	**(2.13)**	**(1.69)**	**0.63**	**3.28**	**6.91**

Source: Calvine Partners Research

Basilea Cash Flow Statement (CHF'000)

	2019E	2020A	2021E	2022E	2023E	2024E
Net profit/(loss)	(22,422)	(14,722)	(23,980)	(18,702)	7,126	36,972
Depreciation and amortization	1,639	1,190	900	957	1,020	1,088
Gain on disposal of assets, net	0	(15,035)	0	0	0	0
Stock-based compensation	3,048	3,525	0	0	0	0
Interest and accretion of debt issuance cost	758	1,670	800	534	0	0
Accounts receivable	(2,457)	(1,657)	(1,266)	277	(661)	(1,953)
Other receivables	8,909	(1,657)	0	0	0	0
Inventories	(4,142)	(2,618)	(6,095)	3,099	(2,003)	(5,916)
Accounts payable	378	6,394	29	(463)	(685)	(32)
Deferred revenue	(45,626)	(33,630)	(2,500)	0	0	0
Accruals and other current liabilities	693	(1,425)	0	0	0	0
Other operating cash flow items	(4,614)	4,639	(2,300)	0	0	0
Net cash provided by/used in operating activities	**(63,836)**	**(53,326)**	**(34,411)**	**(14,298)**	**4,796**	**30,159**
Cash flow from investing activities						
Payments for short-term investments	(20,000)	(81,023)	(10,000)	0	0	0
Maturities of short-term investments	50,000	30,000	91,023	15,507	0	0
Payments for long-term investments	(30,000)	0	0	0	0	0
Proceeds from sale of assets	0	18,325	0	0	0	0
Investments in tangible assets	(294)	(1,823)	(1,136)	(1,249)	(1,374)	(1,512)
Investment in intangible assets	(110)	(442)	(332)	(332)	(332)	(332)
Net cash used in/provided by investing activities	**(404)**	**(34,963)**	**79,555**	**13,925**	**(1,707)**	**(1,844)**
Cash flow financing activities						
Net proceeds from exercise of stock options	37	1,322	0	0	0	0
Repayment of Convertible loan	0	(53,634)	(12,625)	(138,015)	0	0
Issuance of Convertible bonds	0	93,892	0			
Purchase of treasury shares	1,272	3,487	(3,694)			
Issuance of new shares			42,241			
Net cash provided by financing activities	**1,309**	**45,067**	**25,922**	**(138,015)**	**0**	**0**
Effect of exchange rate changes on cash and cash equivalents	67	(758)	0	0	0	0
Net change in cash and cash equivalents	(62,864)	(43,980)	71,066	(138,387)	3,089	28,315
Cash and cash equivalents at beginning of period	173,908	111,044	67,064	138,130	(258)	2,831
Cash and cash equivalents at end of period	**111,044**	**67,064**	**138,130**	**(258)**	**2,831**	**31,147**

Source: Calvine Partners Research

Basilea Balance Sheet (CHF'000)

Year to December	2019A	2020A	2021E	2022E	2023E	2024E
Non-current assets						
Tangible assets, net	5,162	2,627	6,246	6,871	7,558	8,313
Intangible assets, net	372	672	672	672	672	672
Long-term investments	30,000	0	0	0	0	0
Other non-current assets	1,073	2,967	2,967	2,967	2,967	2,967
Total non-current assets	36,607	6,266	9,885	10,510	11,197	11,952
Current Assets						
Cash and cash equivalents	109,024	60,749	138,130	(258)	2,831	31,147
Short-term investments	22,020	106,530	15,507	0	0	0
Accounts receivable	6,242	8,710	7,428	7,151	7,812	9,765
Other receivables	22,053	23,684	23,684	23,684	23,684	23,684
Inventories	18,569	21,192	24,759	21,660	23,664	29,580
Other current assets	6,952	2,663	2,663	2,663	2,663	2,663
Total current assets	184,860	223,528	212,171	54,900	60,654	96,838
Total assets	**221,467**	**229,794**	**222,056**	**65,410**	**71,851**	**108,791**
Current liabilities						
Accounts payable	6,765	13,151	5,495	5,032	4,346	4,314
Deferred revenue	32,873	2,556	3,000	0	0	0
Accruals and other current liabilities	35,856	34,454	30,435	30,435	30,435	30,435
Total current liabilities	75,494	50,161	38,930	35,467	34,781	34,749
Non-current liabilities						
Convertible senior unsecured bonds	197,740	239,668	227,869	99,234	99,234	99,234
Deferred revenue, less of current portion	16,471	13,158	12,542	0	0	0
Other non-current liabilities	24,722	28,853	27,810	27,810	27,810	27,810
Total non-current liabilities	238,933	281,679	268,221	127,044	127,044	127,044
Total liabilities	**314,427**	**331,840**	**307,151**	**162,511**	**161,825**	**161,793**
Shareholders equity (deficit)						
Share capital	11,882	11,922	12,931	12,931	12,931	12,931
Additional paid-in capital	927,342	982,438	1,025,878	1,025,878	1,025,878	1,025,878
Accumulated other comprehensive loss	(24,555)	(27,252)	(27,252)	(27,252)	(27,252)	(27,252)
Treasury shares held by a subsidiary	(5,963)	(52,766)	(52,766)	(52,766)	(52,766)	(52,766)
Loss carried forward	(979,244)	(1,001,666)	(1,016,388)	(1,040,368)	(1,059,069)	(1,051,943)
Net loss for the year	(22,422)	(14,722)	(23,980)	(18,702)	7,126	36,972
Total shareholders' equity (deficit)	(92,960)	(102,046)	(81,577)	(100,278)	(93,152)	(56,180)
Total liabilities and equity (deficit)	**221,467**	**229,794**	**225,574**	**62,232**	**68,673**	**105,613**

Source: Calvine Partners Research

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