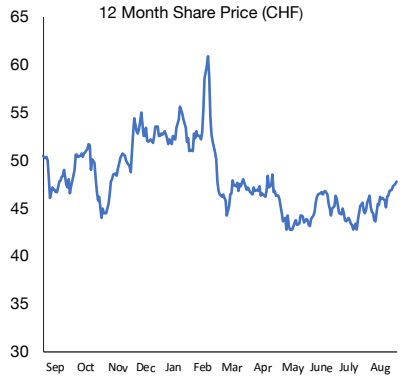
Basilea Pharmaceutica

1 September 2021

Share Price (CHF)	**47.8**
CP Fair Value (CHF)	**120**
Market Cap (CHFm)	618
Cash (CHFm)	165
EV (CHFm)	703
Country	Switzerland
Code	BSLN
Index	SIX



Source: Calvine Partners Research

Firing on all fronts

Basilea's expertise in oncology is clearly growing, benefiting from a strategy to identify those patients best suited to respond across the oncology pipeline. In its lead programme, Basilea is endeavouring to position its FGFR inhibitor derazantinib optimally versus its peers erdafitinib, pemigatinib and infigratinib. Bile duct cancer has served as an important proof of concept indication for the class generally with derazantinib's activity (as measured by PFS) highly competitive. Differentiation for derazantinib should come in the form of better tolerability and broader activity outside of FGFR2 fusions (mutations and amplifications). With the approval of erdafitinib in urothelial cancer, the race to market in other FGFR driven tumours is ongoing. From derazantinib's perspective, it is the additional potential activity against CSF1R, promising to boost the activity of the checkpoint inhibitors (CKIs), which offers an important differentiator. In gastric cancer, the opportunity for derazantinib is still wide open. Basilea has recently sought to further capitalise on derazantinib's better tolerability profile with a dose intensification strategy. Data on the combination with CKI atezolizumab start later this year (FGFRi refractory patients), with the results of the dose intensification in urothelial cancer in 2022. Positive data here should lead to a much greater appreciation of derazantinib in a highly competitive drug class.

Lisavanbulin looking good

Basilea has invested heavily in establishing a meaningful and relevant oncology franchise. Lisavanbulin represents an important programme targeting the mitotic spindle. Unlike older MTAs, lisavanbulin is orally available and can cross the blood-brain barrier, allowing it to target the major unmet need of glioblastoma. Although still early days, such has been the scale of the benefit observed in some glioblastoma patients, that we await with considerable enthusiasm the result of the ongoing Phase 2 trial, which will provide evidence regarding whether a novel biomarker (EB1) can help identify patients who would benefit from lisavanbulin treatment. The suitability of EB1 as a biomarker is also important when considering the applicability of lisavanbulin to other intractable cancers. Lisavanbulin is not included in our forecasts or valuation, but we look forward to additional supportive data.

Anti-infectives still important

The anti-infectives franchise at Basilea is long-standing and remains dominated by the antifungal Cresemba sold through partners and distributors. Growth has been impressive as the immunocompromised patient population increases and guidelines are updated with further geographies targeted, suggesting continued growth. The key for 5th generation cephalosporin, ceftobiprole, is US approval which requires a positive bacteraemia result as well as a commercial partner. Hopefully, 2022 will deliver on both fronts. (For Risks, see Page 12).

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2021 represents an important transition period for Basilea

Targeted approach should reduce attrition

Investment behind the oncology portfolio has delivered impressive results for both Basilea's FGFR inhibitor derazantinib as well as the mitotic spindle 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.

Market positioning is the key

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 modest-sized bile duct cancer indication, Basilea must ensure a strong commercial proposition in this and other cancer settings, given that targeted therapies are suitable only for a portion of the patient population. 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.

Data supporting differentiation encouraging

As a result, the clinical programme has sought to capitalise on the various different attributes of derazantinib compared to its peers, including a better toxicity profile, recognising that each of these molecules has subtly different kinase inhibition profiles. Basilea has recently undertaken a dose intensification strategy with derazantinib in both urothelial and gastric cancer to boost its already competitive clinical profile.

Good safety profile in a fairly benign class

We sense that there are concerns that derazantinib, as a fast follower, would struggle to gain market share against incumbent therapies unless it offers an added benefit. The safety profile is clearly important, and here derazantinib fares well with reduced retinal side effects, stomatitis, hand-foot syndrome and nail toxicity compared to its peers. Additionally, there is the issue of class (adverse) effects potentially affecting uptake of these targeted therapies in general. Although the shared problem of hyperphosphataemia represents the most frequent side effect, it can be managed through dosing and phosphate lowering therapy. While these remain relatively early days, awareness of the FGFR class is growing, and sales progress of approved therapies has been encouraging.

From an efficacy perspective, it is challenging to make comparisons without the benefit of direct head-to-head

Data in iCCA reassuring

studies. However, comparisons will inevitably be made on published data. In this regard, we concede 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 7.8 months in FGFR2 gene fusion iCCA patients.

Variable	Derazantinib[1] FIDES-01 Cohort 1	Infigratinib[2] (QED)	Pemigatinib[3] (Incyte) FIGHT-202	Futibatinib[4] (Taiho) FOENIX-CCA2
N	103	108	108	103
Objective response rate	**21%**	**23%**	**37%**	**42%**
Disease control rate	**75 %**	**84%**	**82%**	**83%**
Median Progression-free survival	**7.8 months**	**7.3 months**	**7.0 months**	**9.0 months**

Broader applicability across iCCA

Importantly, the profile of derazantinib in the proof of principle iCCA indication has also been fleshed out, with some encouraging data in those patients with gene mutations and amplifications. Experience historically with other FGFR inhibitors such as pemigatinib or infigratinib suggests that FGFR inhibitors appear to work well in those harbouring FGFR2 fusions, but less so for mutations and amplifications. Supportive data in these patients seems unique to derazantinib and suggests potentially broader applicability across FGFR driven tumours than FGFR gene fusions. Only about 15% of patients harbour FGFR2 gene fusions in bile duct cancer, so activity in other aberrations would be welcome. We await further data in this patient population (topline results H1 2022) as Basilea completes its optimisation of derazantinib's profile ahead of a regulatory submission in iCCA.

Derazantinib Pooled[5]	Pemigatinib[6] (Incyte) FIGHT-202
23*	20
7%*	**0%**
79%*	**40%**
7.2 months	**2.1 months**

Still room for improvement in urothelial cancer

With the approvals of erdafitinib, pemigatinib and now infigratinib, awareness of the potential of the FGFR inhibitor class has grown. Indeed, we view the growing competitive environment as a positive endorsement of the approach generally in FGFR driven tumours. Outside of the small but needy bile duct cancer opportunity, the introduction of erdafitinib in urothelial cancer represented a significant approval. While the treatment of urothelial cancer has benefited from immunotherapy, it is relevant only to a minority of patients and has been adversely affected by regulatory caution surrounding its use.

Approval of CKIs and FGFRi therapies transformational

Although combination therapy has been explored in bladder cancer, this has yet to bear fruit, either as combination immunotherapy or chemotherapy. Basilea believes that derazantinib's additional activity against CSF1R could well be a differentiating feature.

Ability to target CSF1R and FGFR is likely important to boost CKI activity

The activity against CSF1R appears to be relevant to re-programming tumour-associated macrophages (TAMs). In addition to their beneficial roles, TAMs can also be central to the much more insidious process of tumour metastasis. The transition from a normal function in immune surveillance to a pro-tumourigenic role is termed macrophage polarisation. Several signals and growth factors catalyse this change to a polarised immunosuppressive state, and arguably the best characterised is colony-stimulating factor 1 (CSF1).

Still much to learn about CSF-1/CSF1R inhibition

The milieu of cells that represent the tumour microenvironment frequently serves as a barrier to immune activity. It is one of the critical reasons immunotherapy may have limited clinical efficacy in certain immunologically cold cancers. CSF1/CSF1R inhibition as a therapeutic approach represents a novel class of immunomodulatory immunotherapeutic; confirmed, we believe, with the approval of Turalio (pexidartinib) for TGCT (tenosynovial giant cell tumour).

Nectin-4 is also an important target more broadly in UC

Options for the treatment of advanced bladder cancer have improved markedly not just with the approval of erdafitinib but also with the approval of the antibody drug conjugate Padcev (enfortumab vedotin), which binds to Nectin-4 on the surface of bladder cancer cells. The availability of different approaches suggests significant merit in exploring combinations, particularly given the high likelihood of resistance arising.

Despite the competitive landscape intensifying in bladder cancer, this is a significantly larger opportunity than iCCA.

Room for differentiated additions in bladder cancer

With approximately 84,000 new cases in the US alone, bladder cancer is a relatively common cancer. It is also 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 carrying an FGFR3 mutation, the number appears to be closer to 12%. At the time of Balversa approval, we note that originator J&J was touting blockbuster status with peak sales expectations over $1bn.

FIDES-02 will provide data on the combination starting 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. We have previously noted that 25% of patients in the Balversa study also received a CKI; however, its contribution to the result is unknown. In FIDES-02, we will have direct evidence of the synergistic activity of derazantinib and Tecentriq. In refractory patients (receiving the 300mg dose), these data will begin to emerge later this year, providing insight into the combination. More importantly, the cohorts receiving the 400mg derazantinib dose (dose intensification) will report in 2022.

Basilea looking at various opportunities to differentiate

From a risk management perspective, even if the combination arm fails to show a benefit over derazantinib alone, we are optimistic on the monotherapy arm, particularly given the dose intensification. Moreover, Balversa's approval has de-risked the overall approach. Also, it will be interesting to see whether derazantinib shows activity in those patients who have previously failed on other FGFR inhibitors. Perhaps a combination of the different kinase profile and a higher dose might increase the probability of a positive outcome.

Gastric cancer also targeted

Given the small size of the patient populations who suffer from an FGFR driven cancer, we might have anticipated the industry using basket studies to identify additional relevant cancers. Nevertheless, Basilea has identified gastric cancer as the 3rd FGFR cancer to merit its attention with derazantinib.

Large unmet need

FGFR is a recent target in gastric cancer, with approximately 10%-15% of patients harbouring an FGFR alteration (amplification, mutation and fusions). Consequently, these patients represent an obvious target for FGFR inhibition, and derazantinib has implemented the FIDES-03 study. At the same time, although the checkpoint inhibitor class has been

shown to generate durable and significant responses, this has been in a minority of gastric cancer patients. Consequently, FIDES-03 will also evaluate the combination of derazantinib and the PD-L1 inhibitor Tecentriq and, in a separate cohort, the combination with ramucirumab and paclitaxel.

Outlook poor for metastatic patients

Although the incidence of gastric cancer has decreased over the past 50 years, it remains a significant unmet need. One of the reasons for the reduction has been an improvement in *H. pylori* diagnosis and eradication. However, there are still approximately 1m cases diagnosed globally every year, with circa 27,000 new cases in the US, resulting in 11,000 deaths. It is the 5th most common cancer and the 3rd leading cause of cancer death. While the 5-year survival rate may look relatively good at 31%, this hides the very low survival rate once metastatic (18% Stage IIIC compared to 89% for Stage IA).

Bemarituzumab experience provides encouragement

Gastric cancer presents a wide-open opportunity for FGFR inhibition. Unfortunately, there is not an already approved proxy for gastric cancer in the same way that there is for biliary and bladder cancer (with Balversa or Pemazyre). However, there is encouragement, and potential competition from the evaluation of the FGFR2b targeted antibody bemarituzumab. The 155-patient FIGHT trial compared bemarituzumab plus chemotherapy against just chemotherapy as a first-line treatment for FGFR2b-positive, non-HER2-positive, gastric cancer patients. Updated data presented in June 2021 showed that treatment (follow up at 12.5 months) delivered a clinically relevant improvement in overall survival. Gastric cancer patients receiving the combination experienced 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.

These data appear to have been sufficient to persuade Amgen of the merits of bemarituzumab as it completed its acquisition of Five Prime Therapeutics for $1.9bn in March 2021.

Financial model doesn't reflect potential in gastric cancer

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 urothelial cancer 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.

Basilea is following the science

Essentially, Basilea appears to have followed a well-planned clinical evaluation of derazantinib, taking into account the intensifying competitive environment. The iCCA and urothelial cancer indications should represent a low-risk route to market in monotherapy, given positive results and approval elsewhere. The adjustment to the FIDES-02 and FIDES-03 dosing may have added uncertainty for now. Still, 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.

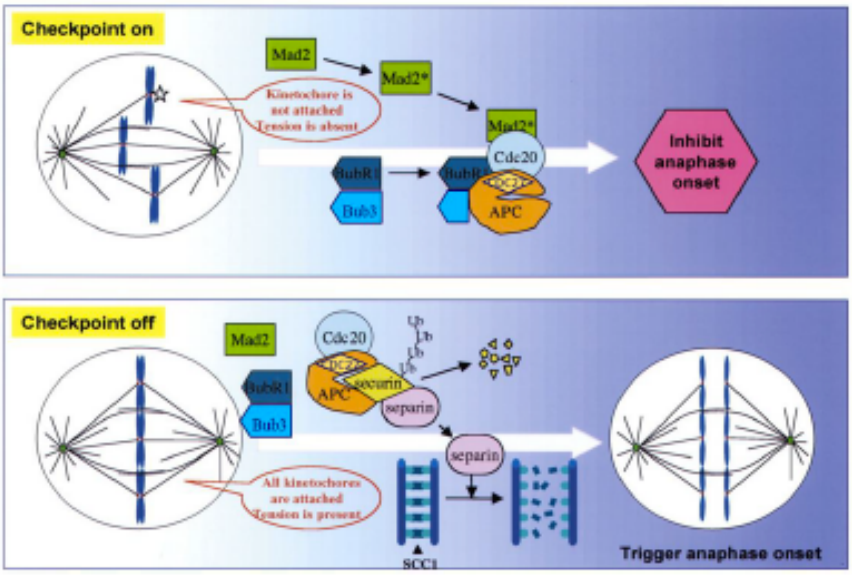
Much will be revealed over next 12 months

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.

Lisavanbulin shows considerable promise

Mitotic checkpoint a proven target

Lisavanbulin is a tumour checkpoint controller exerting its influence at the mitotic checkpoint or spindle assembly checkpoint (SAC). The mitotic checkpoint has long been an important target in cancer, since preventing cells (in this case, tumour cells) from passing through mitosis (somatic cell division) rapidly leads to apoptosis and cell death.



Adapted from Zhou J et al. J Cell Sci 2002;115:3547-3555

MTAs still an important chemotherapeutic choice

Microtubules have represented important targets for chemotherapy. Historically, many MTAs derived from natural sources. Development of newer synthetic (or semi-synthetic) microtubule agents has been slow but represent an obvious route for development, particularly as they can cross the blood-brain barrier.

Rapid resistance an issue though

Although MTAs have proven highly effective in multiple solid and haematological cancers, side effects have limited their use. Peripheral neuropathy, for example, affects as many as 80% of patients receiving taxanes. In addition, one of the most significant factors limiting the applicability of microtubule inhibitors has been the development of rapid resistance.

Lisavanbulin operates differently

Lisavanbulin (formerly BAL101553) is a (highly soluble) prodrug of BAL27862, retaining its potency in human tumour models, which are resistant to archetypal MTAs, including the taxanes and the vinca alkaloids. BAL27862 binds to the colchicine site with distinct effects on microtubule organisation via a unique mechanism of action, which is separate from that of other established MTAs.

Crossing the blood-brain barrier is a key attribute in glioblastoma

As a small molecule, another key feature of lisavanbulin is its ability to cross the blood-brain barrier - unlike many commercially available MTAs, which are natural compounds. Additionally, lisavanbulin appears to possess a dual mechanism of action, inhibiting not only growth and viability of the tumour but also the vasculature feeding the tumour

Lisavanbulin's activity against resistant tumours and its oral bioavailability represent differentiated features, while its ability to cross the blood-brain barrier is particularly relevant to the lead indication glioblastoma. Despite the introduction of radiotherapy and chemotherapies (1st line temozolomide; TMZ), glioblastoma is notable for its ability to develop resistance rapidly, leading to relapse and ultimately death. Additionally, the development of novel therapies has been littered with failure.

Relevance of EB1 critical for success – data later this year and next

The approach pursued by Basilea to improve the likelihood of success has been to identify a relevant biomarker to aid the identification of patients most likely to respond to lisavanbulin. The relevance of EB1 has been informed not only from preclinical data but also from clinical data in patients who have benefited from a strong and durable response (one with 80% tumour shrinkage). The relevance of EB1 is critical as Basilea seeks to lower the attrition rate with circa 5% of glioblastoma patients likely appropriate for therapy on this basis. While these are small numbers, other tumour types could also be tractable to this biomarker led approach. Research by Basilea

suggests that melanoma, breast, colorectal and lung, as well as rare tumours such as neuroblastoma and medulloblastoma, could also be relevant. Should the interim data at year-end 2021 prove positive using EB1, we would expect Basilea to look at additional cancers, perhaps using a basket study type approach given the paucity of available patients.

Anti-infectives franchise still important

Need for novel antifungals keener than ever

For those familiar with the inception of Basilea, it is perhaps unsurprising that the antifungal Cresemba (isavuconazole) continues to dominate the company's financial performance. While the commercial allure of new antibiotics may have been blunted by antibiotic stewardship and last resort status, the need for antifungals remains a critical unmet need driven by an increase in the severely immunocompromised patient population (primarily as a result of aggressive chemotherapy). The development of new antifungals has been slow, and we would highlight the importance of novel therapies reflected by the recent acquisition of Amplyx by Pfizer to access fosmanogepix (currently in Phase 2). The narrative announcing the acquisition reminded us that no antifungal from a novel class has been approved by FDA for 20 years.

Cresemba's progress is well deserved

A combination of Cresemba's differentiated profile (extended-spectrum and safety) and partners with excellent existing franchises (Astellas and Pfizer) have continued to deliver growth in key markets like the US and Europe. Basilea has also enlisted a group of highly effective distributors, and Cresemba should be launched in 60 countries by year-end, with a target of 70 by the end of 2022. Further growth from new geographies, as well as increased penetration, suggests continued good growth from Cresemba.

Still much to go for

We have previously highlighted the importance of guidelines such as ECIL-6, which positions isavuconazole favourably versus market leader voriconazole in invasive aspergillosis. With Cresemba selling annually approximately CHF266m in end product sales (to end March 2021), there is still some way to go to match the $900m attained by voriconazole at its peak. However, as clinical experience with Cresemba increases over time, we anticipate that the willingness of physicians to use this differentiated antifungal in the treatment of invasive moulds should increase, particularly should the relevant guidelines evolve and provide a greater emphasis on its use in earlier lines of therapy.

SAB is the key for ceftobiprole

In its current guise, market expectations for Zevtera (ceftobiprole) are modest, with sales outside the key US market in the limited HAP (non-VAP) indication. The key for ceftobiprole is US approval which requires a positive Phase 3 outcome in the challenging *Staph aureus* bacteraemia indication. We have previously highlighted supportive data from this patient population in previous (cSSSI, HAP/VAP) studies and support for demand from the off-label use of ceftaroline in SAB patients. The market need is clear, particularly given that daptomycin represents the only recently approved SAB antibiotic.

Need for empiric therapy

Should the results of ERADICATE prove positive, then Basilea should be well placed to find a suitable commercial partner. Despite our qualms about big pharma's appetite for antibiotics, ceftobiprole offers broad potential as empiric therapy, particularly where MRSA is suspected. While many of the ABSSSI infections that result in hospitalisations are caused by Gram-positive bacteria, there remains a significant proportion that involves, at least in part, Gram-negative organisms. In addition to Gram-positive coverage, ceftobiprole offers Gram-negative coverage.

Cost defrayed by BARDA

It is important also to remember from Basilea's perspective it has received approximately 70% of the cost of Phase 3 development through non-dilutive funding from BARDA. Our analysis of the market opportunity suggests that in total (both SAB & ABSSSI), ceftobiprole could deliver peak sales approaching $450m.

Moreover, we expect that the addition of the SAB indication should raise ceftobiprole's profile amongst clinicians as a differentiated 5th generation cephalosporin antibiotic. A better profile could have an impact on its use in other infections where MRSA is suspected.

Partnering the next challenge

Basilea has made it very clear that it will seek to partner ceftobiprole. Without knowing the partner or details of the financial terms, our forecasts credit the company with end sales but also burden the company with the total costs. We look forward to positive Phase 3 ERADICATE data and the attraction of a suitable 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 to treat CAP and HAP (excluding VAP), we see the more significant market opportunity in the *Staph aureus* bacteraemia indication. While data from those patients in the four completed Phase 3 trials, who suffered from bacteraemia, support this approach, there is uncertainty associated with this difficult to treat patient population. This uncertainty is reflected in the probability adjustment we have employed. 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 further 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 launch for ceftobiprole, our projections do not incorporate the expected upfront payment that the company would receive from a commercial partnership. Consequently, we are forecasting a negative cash position but recognise many puts and takes to our forecasts. Additionally, we have effectively taxed the company on its first year of profits despite the observation that significant tax losses will materially reduce the tax burden in the near term.

Financial Model and Summary

Strong partners capitalising on Cresemba's potential

The current financial performance at Basilea now more accurately reflects the underlying demand for Cresemba and Zevtera. Cresemba continues to deliver robust in-market sales thanks to its extended-spectrum and benign safety profile. Undoubtedly, the strong existing antifungal franchises at Astellas and Pfizer have helped drive Cresemba growth in key markets.

Derazantinib development has been measured

Basilea has invested heavily in pursuing its goal of delivering an oncology franchise, diversifying its historical reliance on anti-infectives. The lead programme is the FGFR inhibitor derazantinib. With three other FGFR inhibitors now approved, this is a highly competitive field. Given also that these are highly targeted therapies, the market potential in approved indications is more limited. So new entrants have to offer a highly differentiated proposition if they are to provide a sensible economic return.

Keen to maximise the commercial potential

We have viewed the initial bile duct cancer indication for derazantinib (and the broader class) as proof-of-principle providing modest sales potential and validating the class. On the other hand, the urothelial cancer indication can support several participants, and gastric cancer remains wide open. For its part, Basilea is awaiting the results of the ongoing clinical trials, which should provide details of the potential differentiation of derazantinib over its peers.

Combination the key we suspect

Derazantinib's applicability for patients with other FGFR aberrations, in addition to gene fusions, would likely aid the commercial potential in bile duct cancer. However, we believe that it is the potential to boost the activity of the checkpoint inhibitor (PD-1/PD-L1) class that will provide differentiation and lead to regulatory filings in bladder and gastric cancer. Additionally, a more benign safety profile should boost the overall perception of derazantinib with physicians and key opinion leaders.

Competitive landscape a moving feast

The dose intensification strategy for derazantinib in bladder and gastric cancer at such a late stage was largely unexpected. We suspect that Basilea was reacting to the developing competitive landscape, particularly in bladder cancer, where erdafitinib and enfortumab have raised the commercial barrier. In any event, the data (on maximum tolerated dose) is supportive of pushing the dose in monotherapy, while combination with the CKI atezolizumab suggests a safety profile in line with the individual agents.

Partnering derazantinib should help maximise clinical and commercial potential

Nevertheless, we look forward with keen anticipation to data from FIDES-02 and FIDES-03 during 2022 and beyond to provide greater clarity. A positive outcome should lead to regulatory filings and provide sufficient confidence to attract a pharmaceutical partner. In an increasingly competitive field, the future expeditious development and commercial progress of derazantinib are better exploited by a partner with an existing oncology franchise and, in all likelihood, one with a PD-1/PDL-1 programme (approved or in development).

Lisavanbulin is very promising – still outside forecasts

Lisavanbulin is beginning to provide an insight into its potential. If successful, this could be a transformational treatment for patients with glioblastoma. Results so far in those patients that have benefited have been profound and impressively durable. If EB1 proves to be a relevant and reliable biomarker, we expect to see development move into other cancers, with Basilea identifying several difficult to treat cancers as potentially tractable to this approach. As a small molecule microtubule targeting agent, we have high hopes for the targeted approach that Basilea is following.

Positive SAB data could rekindle interest in ceftobiprole

The anti-infectives franchise has delivered steady growth thanks to the continued rollout of Cresemba. Growth seems assured with patent life to 2027 in the US and Europe and a target of 70 countries by the end of 2022. The potential for Zevtera ex-US) remains limited with a HAP (excluding VAP) label. However, the US opportunity should provide a significant boost to sales potential ($250m peak sales in SAB) should a positive SAB result (ERADICATE) in 2022, join the positive ABSSSI readout, and fulfil the requirements of the Special Protocol Assessment (SPA). Hopefully, the addition of the SAB indication, the overall good MRSA activity and the benign safety profile associated with the cephalosporin class should lead to the attraction of a suitable commercial partner.

Derazantinib is the key to long term success

We have tweaked our forecasts for 2021 to reflect the better than expected H1 performance. Our total revenue forecast of CHF137m compares to the updated guidance of CHF134m-144m. With respect to future revenue development, much depends on the outlook for derazantinib in particular. Lisavanbulin is earlier stage and is not currently included in our financial model or valuation. A positive outcome in glioblastoma should result in inclusion and significant upside to our forecasts and valuation.

We remain encouraged by the cost control efforts at Basilea, which have resulted in the company maintaining its commitment to fund its late-stage oncology portfolio. While we have assumed that spend continues at approximately current levels, data for derazantinib in 2022 should result in

the attraction of a commercial partner resulting in a lower R&D spend on its clinical progress. Similarly, although lisavanbulin could take up some of the slack, this depends entirely on the outcome of the ongoing Phase 2 glioblastoma study and the relevance of EB1 as a predictive biomarker.

The pipeline outside of the programmes mentioned above is progressing, and we note the announcement regarding the ongoing development of a novel kinase inhibitor. All going well, this novel cancer candidate could enter clinical development in H1 2022.

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)

Year to December	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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