# Calvine Partners

CALVINE

## Basilea Pharmaceutica

15 March 2023

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|---|---|
| **Share Price (CHF)** | **50.5** |
| **CP Fair Value (CHF)** | **91** |
| Market Cap (CHFm) | 662 |
| Net Cash (CHFm) | 109 |
| EV (CHFm) | 722 |
| Country | Switzerland |
| Code | BSLN |
| Index | SIX |


Source: Calvine Partners Research

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## The anti-infectives future

The earlier than expected delivery of profitability for Basilea is a laudable achievement. The current anti-infectives franchise is highly profitable. In addition, the curtailment of investment in oncology has resulted in a significantly lowered commitment to R&D. The resulting cash generation has allowed Basilea to pay down debt while still investing to maintain a strong anti-infectives franchise.

### Cresemba still dominant

Revenues at Basilea are dominated by Cresemba, and this looks set to continue in the near term. We have previously highlighted that this is due in no small part to the capabilities of its partners – particularly Astellas in the US and, increasingly, Pfizer in other key territories. While Cresemba may be maturing in some markets, we anticipate near-term growth to remain, with key markets of China and Japan being prominent additions. More recently, we have been impressed by apparent success in identifying and developing novel anti-fungals believing that this portends well for Basilea, adding to its in-house efforts through in-licensing. We have updated our views on increasing competition to Cresemba, highlighting the near-term FDA action date for olorofim (June 17th). We expect Basilea to renew its efforts to in-license novel anti-fungals to ensure the longevity of the franchise and believe that its in-house expertise should be a strong attraction for potential licensors.

### Increasing importance of ceftobiprole

Given the high quality of data generated by ceftobiprole in its Phase 3 development, we expect 2023 to feature a US regulatory approval and for Basilea to deliver an appropriate commercial partner. Ceftobiprole promises to be a meaningful new addition to empiric treatment for patients with bacteraemia, given its coverage of Gram-positive and Gram-negative infections and the lack of treatment options (particularly where resistance is suspected). Our forecasts suggest that peak sales in the US alone could approach $400m. Basilea is in a strong financial position. With that in mind, we expect a commercial agreement to maximise the long-term value of the ceftobiprole franchise, focusing on delivering a lucrative royalty rate.

### Sustainable profitability ahead

Our forecasts suggest that a combination of the anti-infectives franchise's continued near-term growth and materially reduced R&D spending should enable continued profitability. We suspect that the current focus is to deliver new product candidates into the pipeline, with the company focusing on opportunities in the late preclinical up to Phase 2 stage. We are confident that the company can deliver, and our forecasts for R&D spending continuing at current levels reflect this.

## New strategy is executing

2022 a year of solid execution

FY'22 has witnessed a year of significant transformation at Basilea. The decision to exit oncology has been realised with programmes offloaded, and the winding down of the considerable oncology R&D spend now apparent. Lead oncology candidate derazantinib was returned to Merck & Co. (formerly Arqule). At the same time, three preclinical programmes targeting PARG, TTK/PLK1 and CLK kinases have been partnered with Nodus Oncology, SillaJen and Redona (formerly Twentyeight-Seven Therapeutics). The requisite oncology expertise in these companies is important, given that Basilea has retained an ongoing financial interest. Additionally, Basilea received one-off payments during 2022 of CHF 15m from this source, helping to offset some of the costs incurred in their development. Also, Basilea has secured its long-term financial future, effectively extending the maturity of its convertible debt while paying down the rest.

### Looking to the future

Anti-infectives activity apparent

Basilea has successfully executed its strategic decision to focus on the anti-infectives franchise and deliver sustainable profitability. With this objective now achieved, we look forward to the next stage in broadening the anti-infectives franchise. The key here is the 5$^{th}$ generation cephalosporin antibiotic ceftobiprole, branded as Zevtera outside the US. Despite the protracted length of time that ceftobiprole has been seeking a presence in the US, there are several initiatives which have helped secure its long-term future.

Renewed ceftobiprole importance

The availability and subsequent granting of Qualified Infectious Disease (QIDP) status have provided 10 (5+5) years of exclusivity in the US as well as Priority Review. Additionally, prior to the TARGET and ERADICATE studies, earlier completed Phase 3 trials provided substantial evidence of efficacy and safety. This included not just the severe skin infection indication but also bacteraemia, given that there were patients in those trials who also had bacteraemia. As a result, we believe that TARGET and ERADICATE were effectively de-risked before they started.

The attraction of BARDA provided approximately 70% of the development costs with non-dilutive funding of up to $136.4m. The agreement was signed in April 2016 with the intention of developing ceftobiprole in the US for *Staph aureus* bacteraemia (SAB), acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial

pneumonia (CABP) – although the latter indication was not a subject of the agreed Special Protocol Assessment (SPA).

Every precaution taken

Basilea also sought to reduce the regulatory risk associated with Phase 3 development by agreeing a Special Protocol Assessment with FDA. SPAs are a useful approach to agree on the trial endpoints and hopefully smooth the approval process should those endpoints be achieved. The key uncertainty for us was the requirement of a positive outcome for both trials for a regulatory submission.

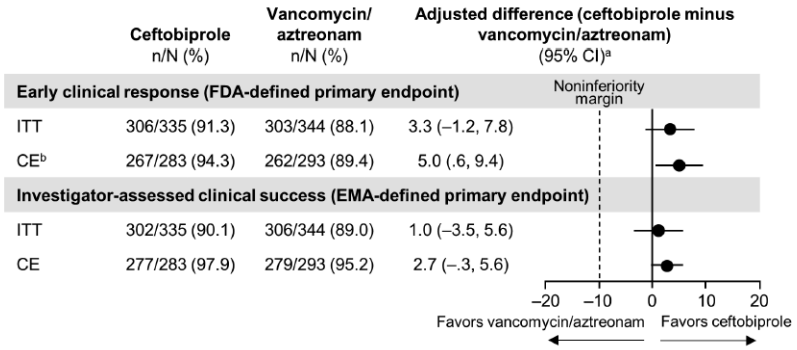
Peer-reviewed

Fortunately, both TARGET and ERADICATE have delivered positive results, with ceftobiprole meeting all primary and secondary endpoints. The results of TARGET were published in the peer-reviewed journal *Clin Infect Diss*. 2021 Oct 5;73(7):e1507–e1517.

Impressive data in ABSSSI

Although severe skin infections are generally well-served, current empiric treatments often target Gram-positive bacteria. Gram-negative infections can be more problematic, and ceftobiprole does offer coverage of important Gram-negative bacteria. The results of TARGET were positive, meeting the criteria for the FDA (early clinical response) and EMA (clinical response at the test of cure visit) with ceftobiprole demonstrated to be non-inferior to vancomycin plus aztreonam in the intention to treat (ITT) population. It is also worth noting that in the TARGET study, ceftobiprole was superior to vanco + aztreonam in the clinically evaluable (CE) patient population (secondary endpoint).

The TARGET study




Source: Overcash et al., Clinical Infectious Diseases

Additionally, time to microbiological eradication was significantly shorter with ceftobiprole, and the results were similar irrespective of MSSA or MRSA.

Given the unmet need and the lack of treatment options for patients suffering from resistant infections, we believe the

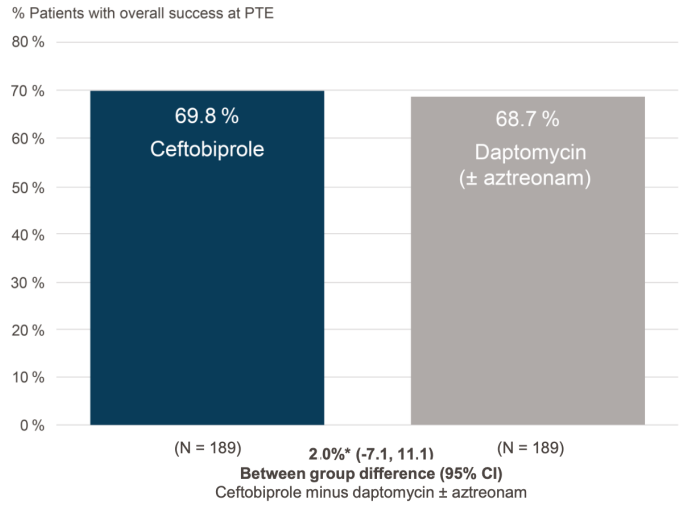
SAB indication presents a significantly more lucrative opportunity.

ERADICATE results were presented at ID week and subsequently published in *Open Forum Infectious Diseases*, Volume 9, Issue Supplement 2, December 2022

SAB data is equally impressive

The primary endpoint of ERADICATE evaluated overall success at post-treatment evaluation (day 70 post-randomisation +/-5 days). Ceftobiprole was associated with an overall success rate of 69.8% in the mITT population at 70 days, which compared favourably to daptomycin (68.7%). With a NI delta of +2% (-7.1%-11.1%), the result of ERADICATE was well within the predefined 15% NI margin for the primary endpoint.

The ERADICATE study



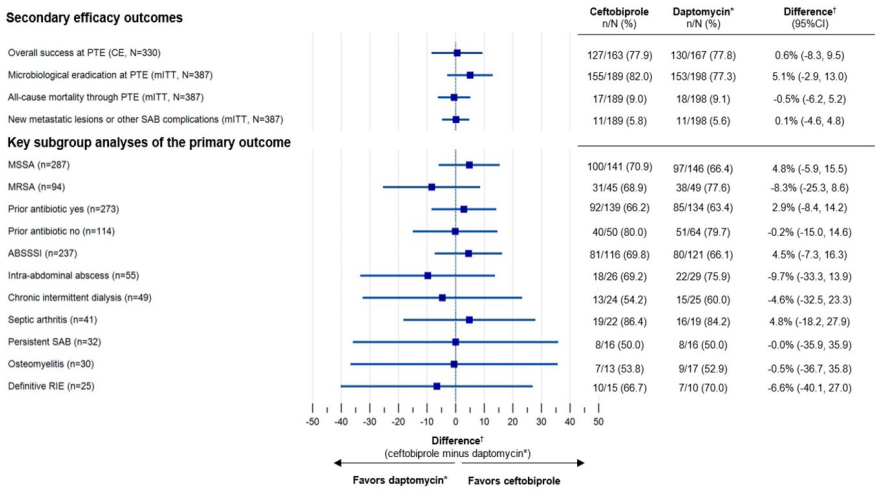

Source: Company Reports

Notably, the primary endpoint results were similar between the treatment groups irrespective of whether patients were infected with MSSA or MRSA bloodstream infections at baseline. This result was also reflected when contributing underlying conditions were evaluated and included skin and skin structure infections, abdominal abscesses, chronic dialysis, septic arthritis, osteomyelitis, definite right-sided IE, and in patients with persistent SAB.

Data in resistant infections reassuring

Secondary endpoints included all-cause mortality and microbiological eradication. Data on these endpoints were also presented at IDWeek. Overall success rate in the clinically evaluable patient population was 77.9% (vs 77.8% with daptomycin. Microbiological eradication was 82% (vs 77.3% with daptomycin), while all-cause mortality was 9% (vs 9.1% with daptomycin). Finally, the emergence of new SAB complications was 5.8% (vs 5.6% with daptomycin).

ERADICATE secondary endpoints




* Daptomycin with or without aztreonam.
† Between-group difference of ceftobiprole minus daptomycin ± aztreonam, adjusted for actual stratum (dialysis status and prior antibacterial treatment use) using Cochran-Mantel-Haenszel weights method.

Source: Holland et al., Open Forum Infectious Diseases

Ceftobiprole relevant broadly

Changing clinical practise will take time, we suspect. There are some challenges ahead, given that the available US guidelines for both SAB and ABSSSI are significantly outdated. The IDSA guidelines for ABSSSI were last issued in 2013. As a result, they do not incorporate more recent approvals, including dalbavancin (a second-generation lipopeptide). Ceftobiprole offers important Gram-negative coverage, and data from TARGET effectively show that it is relevant to a broad selection of patients with ABSSSI. Each of the three types of ABSSSI was well represented (cellulitis/erysipelas, infected wounds and cutaneous abscess). In addition, 93% of patients had Gram-positive infections and 13% Gram-negative infections, clearly supporting ceftobiprole as a monotherapy for empiric treatment of patients with ABSSSI.

Suitable for empiric therapy

New guidelines for SAB are due

The IDSA SAB guidelines date from 2011, and while there has been a paucity of new antibiotics approved for complicated SAB, an update is overdue. We note that new guidelines are currently in development. Hopefully, given the quality of the data delivered by ERADICATE, ceftobiprole will be included despite not yet being approved.

Treatment with a beta-lactam antibiotic remains first line for patients with susceptible infections (MSSA). SAB treatment can last up to six weeks if the disease has become metastatic, compared to two weeks if the bacteraemia remains uncomplicated. Antibiotics typically used for MSSA include anti-Staphylococcal penicillins such as flucloxacillin and first-generation cephalosporins such as cefazolin.

MRSA, on the other hand, leads to poorer outcomes, with 15%-50% mortality rates in patients with MRSA bacteraemia.

The glycopeptides vancomycin and daptomycin are first-line treatments in MRSA bacteraemia, requiring 4-6 weeks of intravenous therapy. Metastatic infections often require surgical intervention and can result in extended hospitalisation.

Resistance issues are looming

Worryingly, although still relatively rare, there is a growing risk of resistance to both agents. The lipoglycopeptide dalbavancin may be used (currently off-label) as an alternative to vancomycin-resistant infections and has the added benefit of offering a lower level of renal injury and a long half-life, resulting in a much-reduced dosing schedule. Dalbavancin provides the potential for a shorter and less invasive treatment regimen, lowering risks associated with prolonged central venous access.

To formally prove the potential of dalbavancin in complicated SAB, the DOTS (dalbavancin as an option for treatment of SAB) trial has been designed as a prospective Phase 2b study. DOTS enrolled 200 SAB patients who had already experienced bacteraemia clearance before randomisation with two doses of dalbavancin or 4-8 weeks of standard intravenous antibiotic therapy. According to clinicaltrials.gov, the primary completion date is June 2023. However, we believe that more comprehensive data will be required to lead to changes to the dalbavancin label.

Limitations of current treatments well known

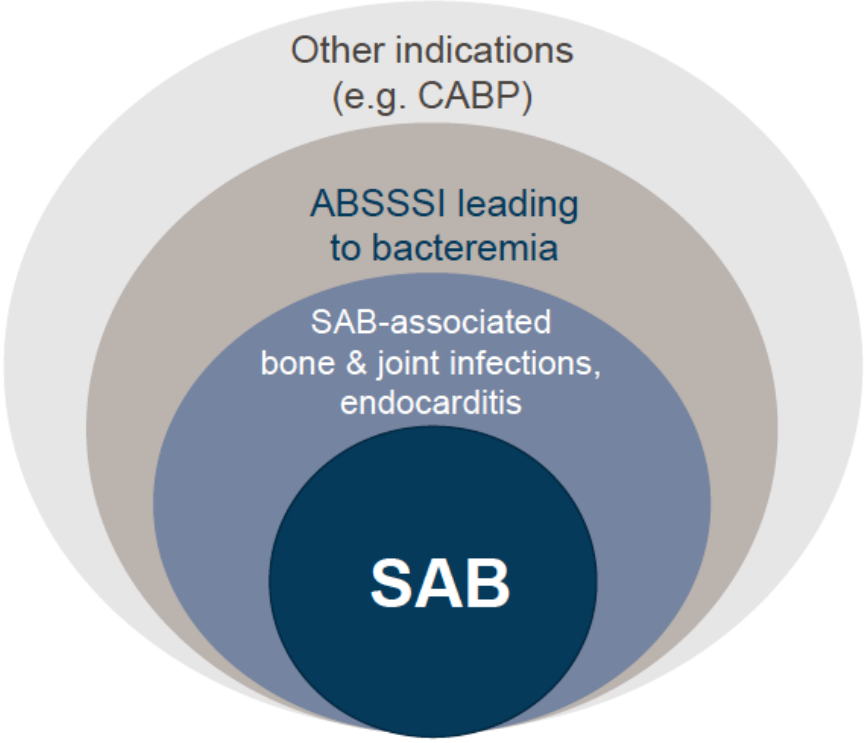
We have previously highlighted the limitations of currently approved antibiotics for the treatment of complicated SAB. Both daptomycin and vancomycin have concerns over emerging resistance (and the potential for cross-resistance), as well as vancomycin's poor tissue distribution and risk of renal toxicity. Additionally, daptomycin is inactivated in the lung, rendering it useless for the treatment of respiratory infections. Ultimately, there is a clear need for additional antibiotics in SAB with a notable shortage of high-quality controlled studies. Salvage therapy using a non-approved (off-label) antibiotic (such as dalbavancin and ceftaroline) has proven to be a last resort approach in those with a persistent infection.

Commercial partner is the key

We look forward to Basilea securing a relevant commercial partner to ensure an effective US launch. At the recent FY'22 results call, Basilea highlighted the broad relevance of ceftobiprole following approval in SAB, ABSSSI and CABP. The CABP (apparently late) addition has long been planned, and we note that there are sufficient Phase 3 data available to aid with this approval despite not formally being part of the SPA agreed with FDA. The company described a likely commercial scenario starting with SAB and subsequently

involving other complications such as SAB-associated bone and joint infections, bacteraemia caused by ABSSSI and other indications.

Ceftobiprole's commercial oppoprtunity




Source: Company Reports

Much will depend on the partner with respect to the final commercial strategy, although targeting the most acute unmet need would appear to be a sensible approach.

$250m peak sales in SAB alone

We forecast ceftobiprole to achieve a 15% peak penetration of the US bacteraemia market, resulting in an un-risked peak sales opportunity of $250m. Patients with SAB usually receive antibiotics for between 2-6 weeks. In our financial model, we have assumed that patients receive treatment for 5 weeks at circa $7500 per treatment.

Additionally, the ABSSSI indication remains an important element of the regulatory filing process in the US, with both studies required for FDA approval. Ultimately, this is a large market, and our analysis suggests that even a small market share should generate meaningful revenues for ceftobiprole. We have assumed that ceftobiprole is able to secure a 3-4% share of the large ABSSSI market at peak, recognising that much will depend on the capabilities of the partner selected. Nevertheless, such is the size of the ABSSSI indication in the US, even this modest market penetration suggests an un-risked peak sales market potential of $130m. Overall,

Peak sales approaching $400m

therefore, we forecast that ceftobiprole could deliver peak in-market sales of $380m.

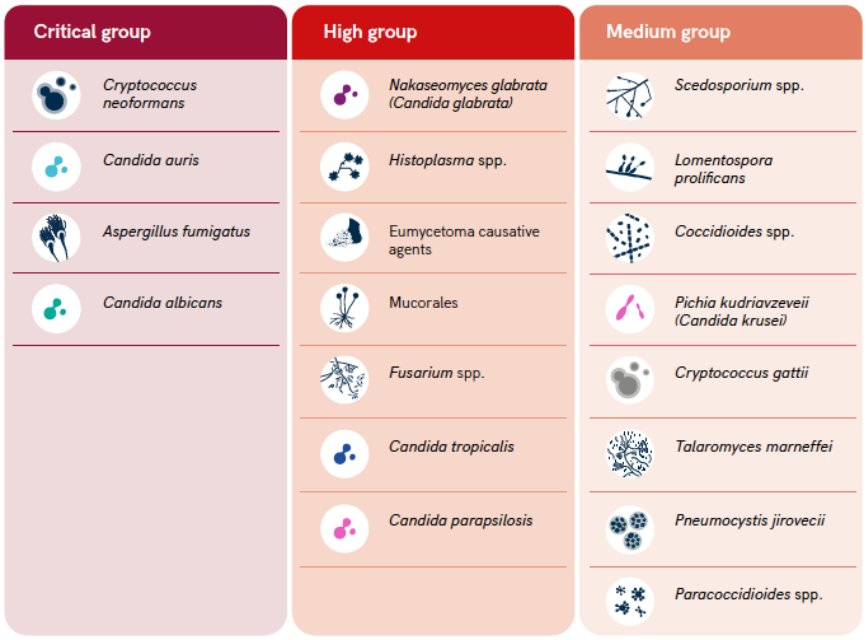
## Cresemba powering ahead

The antifungal Cresemba (isavuconazole) has long dominated Basilea's anti-infectives franchise and now represents the largest antifungal by sales value in the critical US market.

Early signs of novel therapies

After many years of apparent inactivity in the field of anti-fungals, there have been notable advances with fosmanogepix now under the stewardship of Pfizer. Additionally, olorofim has been filed for regulatory approval in the US (for treating invasive fungal infections in patients with limited or no treatment options) and partnered with Shionogi elsewhere. In tandem with these advances, it is important to note that the threat from fungal disease has recently been reflected in the WHO releasing (October 2022) its first-ever list of health-threatening fungi.

WHO's categorisation of fungal infections




Source: World Health Organization

The report categorises fungal infections into those which are critical threats and comprise *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Candida auris* and *Candida albicans*. The high-priority group includes Mucorales, *Fusarium* spp, *Histoplasma* spp, *Candida tropicalis*, *Candida parapsilosis* and *Candida glabrata*. The medium priority group comprise a further eight fungal infections.

Strong underlying growth

Several factors have driven the underlying growth in demand for antifungal treatment. In particular, the use of aggressive chemotherapy regimens, as they relate to haematological

cancers, have been a significant driver of invasive fungal infections. Furthermore, it is notable that the number of stem cell transplantations has effectively more than doubled in the past 20 years. The COVID-19 pandemic also highlighted the risk in patients with this respiratory pathogen, and an increase in the incidence of co-morbid fungal infections with aspergillosis, mucormycosis, and candidaemia reported. Additionally, new patient groups at risk from fungal infections have been suggested, including those with COPD and other respiratory tract infections.

Limited treatment choice

Unfortunately, the development of new antifungals has not kept pace with the emergence of resistance. As a result, available antifungals are still limited to only three classes (polyenes, the azoles and the echinocandins). Increasing resistance is a real concern seen with the azoles and Aspergillus, as well as Candida and the increased use of echinocandins.

As a result, the outlook for patients with invasive fungal infections remains bleak. Mould infections are particularly concerning in the immunocompromised patient population and represent a significant source of morbidity and mortality. For aspergillosis, the mortality rate varies from 30%-60% and can be higher in high-risk patient populations such as chemotherapy-induced neutropaenia.

Many have drawbacks

Moreover, antifungal classes have limitations that can restrict their use in clinical practice. The echinocandins suffer from poor bioavailability and require injection. The echinocandins are used for salvage therapy and in combination, particularly for mould infections. The polyenes (such as amphotericin B) suffer from limited efficacy and substantial toxicities (acute renal failure) in high-risk patients leading to the successful introduction of lipid formulations.

Still significant sales potential

The azoles, on the other hand, represent the most widely used class of antifungals. Their widespread use, however, has resulted in increased resistance in several geographies, with its emergence developing by various mechanisms. Major advantages of the second-generation triazoles, posaconazole and voriconazole, include their extended antifungal spectrum and availability in both oral and intravenous formulations (voriconazole). As the leading branded antifungal VFEND (voriconazole) generated peak sales of about $900m.

However, the use of these agents is often limited by their variable bioavailability, severe adverse events, significant drug-drug interactions, and the emergence of resistance. Cresemba, on the other hand, has an extended spectrum with

Cresemba's profile very attractive

activity against yeasts, moulds, and dimorphic fungi. It also possesses an excellent safety profile which, combined with good pharmacokinetic properties, has led to its success in the treatment of various severe and potentially life-threatening fungal infections. Also important to its commercial success is the good volume of distribution, and oral bioavailability, combined with highly predictable pharmacokinetics with little interpatient variability.

IA is the main target for Cresemba

Cresemba is approved in the US for the treatment of invasive aspergillosis (IA) as well as for the treatment of mucormycosis. Undoubtedly, IA represents the major commercial opportunity for Cresemba. Mucormycosis is much rarer, although its prevalence is increasing. Mucormycosis results in high morbidity and mortality (40-80% in neutropenic patients and disseminated infections) and results in a burden to the US healthcare system of circa $100,000 per patient.

Central to Cresemba's commercial success in the US have been the capabilities of partner Astellas. Outside of the US, Cresemba is sold by Pfizer, firstly in Europe (in June 2017) and then in Asia Pacific (in December 2017). For Pfizer, the originator of voriconazole (branded as Vfend), adding Cresemba provided an antifungal that can be positioned as an alternative to voriconazole per the current guidelines and which also offers a more benign tolerability profile.

Cresemba is well suited to empiric treatment

Fortunately, invasive aspergillosis is relatively uncommon and mucormycosis even less so. Both are, however, challenging to diagnose, which is reflected in the underreporting of these conditions. In its favour, isavuconazole's broad spectrum (including Mucorales) has positioned it well in the empiric setting, compared to alternative agents (such as voriconazole), where infection is suspected but not confirmed. Mucorales are inherently resistant to the echinocandins as well as voriconazole.

## Cresemba is maturing and competition looms

Cresemba has been a highly rewarding success story for Basilea, its licensees and distributors. We forecast continued growth in major markets despite its maturity, mainly due to an increasing number of at-risk immunosuppressed patients. Cresemba has also enjoyed a protracted rollout as Basilea has identified new distributors and licensing partners. Currently, Cresemba is now available in over 70 countries and marketed in 60 of those. In the near term, we look forward to growth receiving a boost from availability in China and Japan. China, in particular, is a particularly exciting prospect, representing approximately 20% of the global market.

Maximising Cresemba's potential

Given the unmet need, efforts are underway to identify and develop new antifungal classes. However, this is not an easy task and certainly compared to other anti-infectives, given the similarity between fungal and human processes. Nevertheless, there has been significant progress, and we have previously highlighted new molecules in development, such as olorofim (F2G/Shionogi), fosmanogepix (Amplyx/ Pfizer) and ibrexafungerp (Scynexis). Fortunately for the Cresemba franchise, these do not appear to present a near-term competitive threat.

Novel therapies approaching

Limited number of new molecules

Olorofim (F2G) is a member of the ortomide antifungal class targeting fungal dihydroorotate dehydrogenase (DHODH), which is involved in pyrimidine synthesis. Although not a broad-spectrum antifungal, it has broad microbiologic activity against several important invasive moulds. Available orally, olorofim is distinct from its peers, having achieved FDA Breakthrough Therapy Designation. In a strong endorsement of its commercial potential, F2G was able to attract the attention of Shionogi in a licensing agreement which provided both funding for development as well as commercial rights in Europe and Asia. Signed in May 2022, F2G received $100m in upfront payments and could receive up to $380m in regulatory and commercial milestones and double-digit sales royalties. Olorofim has an FDA action date of 17 June 2023 with a proposed label for the treatment of invasive fungal infections in patients who have limited or no treatment options.

Late-stage trials suggest promise

Fosmanogepix appears to have a broad spectrum of activity against various Aspergillus and Candida, including those that are resistant to the echinocandins. However, it appears to have a lack of activity against some Mucorales. The importance and relevance of the activity of fosmanogepix have been reflected in the awarding of fast-track status by FDA for various invasive fungal infections, including invasive aspergillosis, candidiasis and mucormycosis.

But competitive threat to Cresemba is distant for now

Ibrexafungerp (SCY-078) may also share the same target as the echinocandins but targets a different binding site. Ibrexafungerp displays fungistatic activity against Aspergillus and fungicidal activity against Candida. Given a general lack of cross-resistance with the echinocandins and their availability in oral form, there is the potential for ibrexafungerp to be used as an oral step-down therapy to injectable echinocandins in the short term. Brexafemme (branded oral ibrexafungerp) was approved for treating recurrent vulvovaginal candidiasis and represented the first approval of a new antifungal class for 20 years. More relevant for Basilea, we note that there is a small ibrexafungerp Phase 2 study ongoing in IA, with a primary completion date of April 2023. It is worth highlighting that the study evaluates Ibrexafungerp in

Co-administration with a mould-active azole in IA

combination with a mould active azole (voriconazole), comparing the combination to voriconazole alone. Notably, an intravenous formulation of ibrexafungerp is in development and, according to Scynexis, should be available by 2025.

Replenishment of antifungal pipeline a near-term priority

Given the maturity of Cresemba in major markets, and the US in particular, replenishment of the antifungal pipeline should be a near-term priority. Although novel antifungals appear to be highly sought-after assets, we believe that a combination of Basilea's anti-infectives expertise and strong financial position should make the company a partner of choice for prospective licensors. Undoubtedly, Basilea is determined to ensure the longevity of the antifungal franchise as part of its anti-infective ambitions. As a result, we believe that Basilea would be a fully committed partner, providing speedy development and significant resources.

## Risks

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

While the antibiotic Zevtera (ceftobiprole) 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 (SAB) indication, particularly where MRSA is suspected. There is partnering risk until a partner is secured and commercial risk depending on the existing franchise of the partner. Basilea has historically proven to be adept at securing relevant commercial partners.

With the focus returning to anti-infectives, Basilea needs to re-populate its development pipeline. Cresemba is maturing, with loss of exclusivity expected from 2027 in the US and Europe. To ensure the longevity of the franchise, we would like to see clinical stage addition(s) in the antifungal field. Basilea should be an attractive partner, although novel assets here could be expensive.

Our financial forecasts suggest sustainable profitability. However, the current low level of R&D spending may need to rise should Basilea successfully progress multiple anti-infective programmes into late-stage trials.

## Financial Model and Summary

Cresemba is maturing in the US

The outstanding FY'22 financial performance once again reflected the importance of Cresemba, with revenues significantly outpacing the company's initial FY'22 guidance. As Cresemba matures, Basilea and its partners must maximise the remaining sales potential. Although exclusivity in the US wanes from 2027 and as early as 2025 in Europe, success in the paediatric population could extend Europe into 2027. In the near term, we have highlighted the FDA action date for olorofim in the US. Still, we note that the originator F2G does not have a US commercial partner. At least initially, approval would likely be for treating invasive fungal infections in patients with limited or no treatment options, suggesting a limited competitive threat to Cresemba.

Longer-term growth elsewhere

New territories will be critical to the longer-term growth of Cresemba, with launches in China and Japan likely representing substantial opportunities. Both oral and IV preparations of Cresemba are now available in China, which, according to the company, represents 20% of global sales for newer antifungals. Cresemba has been approved for invasive aspergillosis and invasive mucormycosis. Numbers for China are difficult to find, but data presented at ECCMID in 2013 suggested 162,000 cases of IA and 2,726 cases of mucormycosis. With other growth drivers, including a marked increase in organ transplantation (particularly lung) in China over the past few years, these numbers are clearly conservative. Recent studies have shown that IA is responsible for most invasive mould infections, with many patients treated historically with amphotericin B outside of China and Singapore.

The need for new antifungals is evident

Basilea has a strong cash position with CHF108.6m in cash and investments at the end of FY'22. The near-term focus for the company should be to deploy this cash to strengthen the long-term proposition of the anti-infectives franchise. Here, we would highlight the importance of adding a clinical-stage antifungal programme, given Cresemba's waning exclusivity in the US and Europe and the recent failure of the programme in-licensed from Fox Chase Chemical Diversity Center. Although we also highlighted potential pressures from new research advances in antifungals elsewhere, it is encouraging to see that expertise and demand clearly exist here. Given Basilea's history and strong cash position, we believe the company should be able to deliver new candidates and remove any uncertainty associated with prospects for its antifungal franchise.

Ceftobiprole finally approaching approval

As Cresemba matures, ceftobiprole's US approval takes on greater significance. Although there is both a recognition of the need for new antibiotics and no shortage of apparent initiatives to pay for them, there appears to be a lack of willingness from the pharma majors to invest significantly in their development. On the plus side, we note that several alternative sources of funding are available with the Novo REPAIR fund, CARB-X (part funding the DXR inhibitor programme), as well as financing through the PASTEUR Act (when/if approved) in the US and the AMR Action Fund.

Ceftobiprole offers an attractive licensing proposition

From Basilea's perspective, the availability of circa 70% of R&D funding for ceftobiprole from BARDA has represented an important source of non-dilutive financing. Furthermore, ceftobiprole's award of QIDP status (as part of the GAIN Act) has provided 5 years of additional exclusivity, providing 10 years of total exclusivity. With our peak sales forecast approaching $400m along with the clear unmet need in the SAB indication along with ABSSSI and CABP, we believe that ceftobiprole should be an attractive proposition and remain sanguine regarding the ability of Basilea to deliver a commercial partner before the US approval. We have also suggested that with a clear 10-year time horizon and a strong cash position, Basilea should seek to maximise the royalty rate, which we anticipate could be north of 20%. Historically, our forecasts have incorporated both the sales and associated costs of self-marketing, which we have retained until details of any collaboration are disclosed.

Basilea has a strong track record

Further de-risking in 2023

Our forecasts include new guidance for 2023F, reflecting higher revenue and significantly reduced operational spending. As a result, our forecasts continue to reflect a period of positive cash flow and sustainable profitability. Given the scale of operating losses carried forward, we do not anticipate tax payments for the next several years. With ongoing uncertainty associated with the value of antibiotic assets, all eyes are now on the company's ability to secure a relevant partner for ceftobiprole in the US. Successful completion should materially de-risk the commercialisation of ceftobiprole and remove a key overhang from the Basilea investment case.

## Basilea Income Statement (CHF' 000)

| Year to December | 2021A | 2022A | 2023E | 2024E | 2025E | 2026E |
|---|---|---|---|---|---|---|
| **Total revenue** | **148122** | **147765** | **156232** | **149231** | **143218** | **179927** |
| COGS | (24,072) | (24,603) | (28,669) | (29,846) | (28,644) | (32,387) |
| **Gross profit** | **124,050** | **123,162** | **127,563** | **119,385** | **114,575** | **147,541** |
| Gross margin | 83.7% | 83.3% | 81.7% | 80.0% | 80.0% | 82.0% |
| R&D | (93,157) | (73,804) | (49,994) | (53,723) | (54,423) | (53,978) |
| SG&A | (29,721) | (30,815) | (31,246) | (32,831) | (35,805) | (39,584) |
| Total cost and operating expenses | (146,950) | (129,222) | (109,909) | (116,400) | (118,871) | (125,949) |
| Non-underlying items | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| **Operating profit US GAAP** | **1,187** | **18,543** | **46,323** | **32,831** | **24,347** | **53,978** |
| Finance income | 66 | 326 | 4,182 | 3,809 | 2,438 | 3,063 |
| Finance expense | (8,151) | (9,848) | (8,088) | (8,105) | (3,122) | (3,140) |
| Other financial income | 1,676 | 2,015 | 0 | 0 | 0 | 0 |
| Other financial expense | (1,573) | 1,066 | 0 | 0 | 0 | 0 |
| Underlying PBT | (6,810) | 12,102 | 42,417 | 28,535 | 23,663 | 53,902 |
| PBT IFRS | (6,795) | 12,102 | 42,417 | 28,535 | 23,663 | 53,902 |
| Loss before tax | (6,810) | 12,102 | 42,417 | 28,535 | 23,663 | 53,902 |
| Tax | (37) | 45 | 0 | 0 | 0 | (7,654) |
| **Underlying net income** | **(6,847)** | **12,147** | **42,417** | **28,535** | **23,663** | **46,248** |
| **Net income US GAAP** | **(6,832)** | **12,147** | **42,417** | **28,535** | **23,663** | **46,248** |
| EPS Basic (CHF) | (0.66) | 1.02 | 3.58 | 2.41 | 2.00 | 3.90 |
| **EPS Diluted (CHF)** | **(0.61)** | **1.02** | **3.55** | **2.39** | **1.98** | **3.87** |

Source: Calvine Partners Research

## Basilea Cash Flow Statement (CHF' 000)

| Year to December | 2021A | 2022A | 2023E | 2024E | 2025E |
|---|---|---|---|---|---|
| Net profit/(loss) | (6,831) | 12,147 | 42,417 | 28,535 | 23,663 |
| Depreciation and amortization | 754 | 1,097 | 760 | 803 | 850 |
| Gain on disposal of assets, net | (71) | 0 | 0 | 0 | 0 |
| Stock-based compensation | 4,322 | 3,598 | 0 | 0 | 0 |
| Interest and accretion of debt issuance cost | 1,593 | 497 | 534 | 534 | 534 |
| Accounts receivable | (16,251) | (8,242) | (1,260) | (220) | 331 |
| Other receivables | (15,813) | 10,829 | 0 | 0 | 0 |
| Inventories | (1,591) | (1,461) | 48 | (666) | 1,002 |
| Accounts payable | (2,538) | (10,427) | 3,349 | 221 | (23) |
| Deferred revenue | (2,556) | (1,233) | (1,233) | 0 | 0 |
| Accruals and other current liabilities | 5,440 | (846) | 0 | 0 | 0 |
| Other operating cash flow items | 1,522 | 1,098 | 0 | 0 | 0 |
| **Net cash provided by/used in operating activities** | **(32,020)** | **7,057** | **44,615** | **29,206** | **26,357** |
| | | | | | |
| Cash flow from investing activities | | | | | |
| Payments for short-term investments | (35,000) | 0 | 0 | 0 | 0 |
| Maturities of short-term investments | 41,023 | 94,951 | 0 | 0 | 0 |
| Payments for long-term investments | 0 | 0 | 0 | 0 | 0 |
| Proceeds from sale of assets | (1,588) | 0 | 0 | 0 | 0 |
| Investments in tangible assets | (581) | (3,138) | (855) | (941) | (1,035) |
| Investment in intangible assets | (279) | (165) | (332) | (332) | (332) |
| **Net cash used in/provided by investing activities** | **3,575** | **91,648** | **(1,188)** | **(1,273)** | **(1,367)** |
| | | | | | |
| Cash flow financing activities | | | | | |
| Net proceeds from exercise of stock options | 1,866 | 3,520 | 0 | 0 | 0 |
| Repayment of Convertible loan | (23,212) | (123,547) | (44,000) | (38,400) | 0 |
| Issuance of Convertible bonds | 0 | | | | |
| Senior secured loan | | 73,875 | | | |
| Purchase of treasury shares | (4,254) | 656 | | | |
| Issuance of new shares | 42,240 | 250 | | | |
| **Net cash provided by financing activities** | **16,640** | **(45,246)** | **(44,000)** | **(38,400)** | **0** |
| | | | | | |
| Effect of exchange rate changes on cash and cash equivalents | 501 | 155 | 0 | 0 | 0 |
| | | | | | |
| Net change in cash and cash equivalents | (11,304) | 53,614 | (573) | (10,467) | 24,989 |
| Cash and cash equivalents at beginning of period | 66,256 | 54,952 | 108,566 | 107,993 | 97,526 |
| **Cash and cash equivalents at end of period** | **54,952** | **108,566** | **107,993** | **97,526** | **122,515** |

Source: Calvine Partners Research

## Basilea Balance Sheet (CHF' 000)

| Year to December | 2021A | 2022A | 2023E | 2024E | 2025E |
|---|---|---|---|---|---|
| Non-current assets | | | | | |
| Tangible assets, net | 2,018 | 4,277 | 4,705 | 5,175 | 5,693 |
| Intangible assets, net | 632 | 578 | 578 | 578 | 578 |
| Long-term investments | 2,390 | 1,266 | 1,266 | 1,266 | 1,266 |
| Other non-current assets | 1,161 | 39,363 | 39,363 | 39,363 | 39,363 |
| Total non-current assets | 6,201 | 45,484 | 45,912 | 46,382 | 46,900 |
| | | | | | |
| Current Assets | | | | | |
| Cash and cash equivalents | 53,700 | 84,659 | 107,993 | 97,526 | 122,515 |
| Short-term investments | 96,253 | 0 | 0 | 0 | 0 |
| Accounts receivable | 24,947 | 33,152 | 7,988 | 8,208 | 7,877 |
| Other receivables | 39,500 | 28,552 | 28,552 | 28,552 | 28,552 |
| Inventories | 22,783 | 24,244 | 24,196 | 24,862 | 23,860 |
| Other current assets | 3,883 | 4,756 | 4,756 | 4,756 | 4,756 |
| Total current assets | 241,066 | 175,363 | 173,485 | 163,904 | 187,560 |
| **Total assets** | **247,267** | **220,847** | **219,396** | **210,286** | **234,460** |
| | | | | | |
| Current liabilities | | | | | |
| Convertible senior unsecured bonds | 123,505 | | | | |
| Senior secured debt | | 37,467 | 36,360 | | |
| Accounts payable | 10,617 | 191 | 3,540 | 3,761 | 3,738 |
| Deferred revenue | 1,233 | 1,233 | 1,233 | 1,233 | 1,233 |
| Accruals and other current liabilities | 39,053 | 35,959 | 35,959 | 35,959 | 35,959 |
| Total current liabilities | 174,408 | 74,850 | 77,092 | 40,953 | 40,930 |
| | | | | | |
| Non-current liabilities | | | | | |
| Convertible senior unsecured bonds | 94,544 | 95,000 | 95,534 | 96,068 | 96,602 |
| Deferred revenue, less of current portion | 11,926 | 10,693 | 0 | 0 | 0 |
| Senior secured debt | | 36,360 | | | |
| Other non-current liabilities | 24,996 | 24,661 | 24,661 | 24,661 | 24,661 |
| Total non-current liabilities | 131,466 | 166,714 | 120,195 | 120,729 | 121,263 |
| **Total liabilities** | **305,874** | **241,564** | **197,287** | **161,682** | **162,193** |
| | | | | | |
| Shareholders equity (deficit) | | | | | |
| Share capital | 12,992 | 13,093 | 13,093 | 13,093 | 13,093 |
| Additional paid-in capital | 1,029,796 | 1,037,120 | 1,037,120 | 1,037,120 | 1,037,120 |
| Accumulated other comprehensive loss | (21,617) | (3,784) | (3,784) | (3,784) | (3,784) |
| Treasury shares held by a subsidiary | (56,559) | (56,071) | (56,071) | (56,071) | (56,071) |
| Loss carried forward | (1,016,388) | (1,023,220) | (1,011,073) | (968,656) | (940,121) |
| Net loss for the year | (6,832) | 12,147 | 42,417 | 28,535 | 23,663 |
| Total shareholders' equity (deficit) | (58,608) | (20,715) | 21,702 | 50,237 | 73,900 |
| **Total liabilities and equity (deficit)** | **247,266** | **220,849** | **218,989** | **211,918** | **236,093** |

Source: Calvine Partners Research

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