2018 is an Ideal Entry Point for Aurinia Pharmaceuticals

- Aurinia Pharmaceuticals is a single-asset clinical-stage biopharmaceutical company developing voclosporin, a potentially best-in-class calcineurin inhibitor
- Voclosporin is in Phase III trials for treatment of lupus nephritis (LN) and has a high probability of FDA approval based on Phase IIb data
- Voclosporin is also well-positioned for expansion into dry eye syndrome, a relatively segmented market, and FSGS, another renal indication
- Aurinia's current valuation makes for an ideal entry point for long-term investment

Company Information

Aurinia Pharmaceuticals (AUPH) is a Canadian-based clinical-stage biopharmaceutical company currently developing voclosporin for the treatment of lupus nephritis ((LN)), an inflammation of the kidney caused by systemic lupus erythematosus (SLE). The company boasts a highly seasoned management team. Most of the leadership, including the current CEO, were previously at Asperva Pharmaceuticals that was acquired by Galencia for C$ 915 million in 2008. This management team executed one of the largest and most significant LN studies ever conducted called the Aspreva Lupus Management Study ("ALMS"), which resulted in the emergence of mycophenolate mofetil (MMF) as a new standard of care for patients suffering from this devastating and potentially fatal disease. This bodes well for Aurinia, as in addition to a tremendous amount of experience in LN, it now holds certain rights to this large ALMS database and the license for voclosporin in LN.

Financials

The company has a market cap of ~$500 million and an enterprise value of $322 million. In 2017, Aurinia raised $162.3 million through a public offering and received another $12.8 million from the exercise of warrants and options. As of 2018, the company still has cash and cash equivalents of $131.4 million. Additionally, the company has a very low burn rate of $14.38 million per quarter, indicating a 2-3 year runway, which Aurinia claims is sufficient to carry voclosporin through all its planned clinical trial endpoints

and NDA submission. This financial security de-risks investments made in anticipation of any ongoing studies.

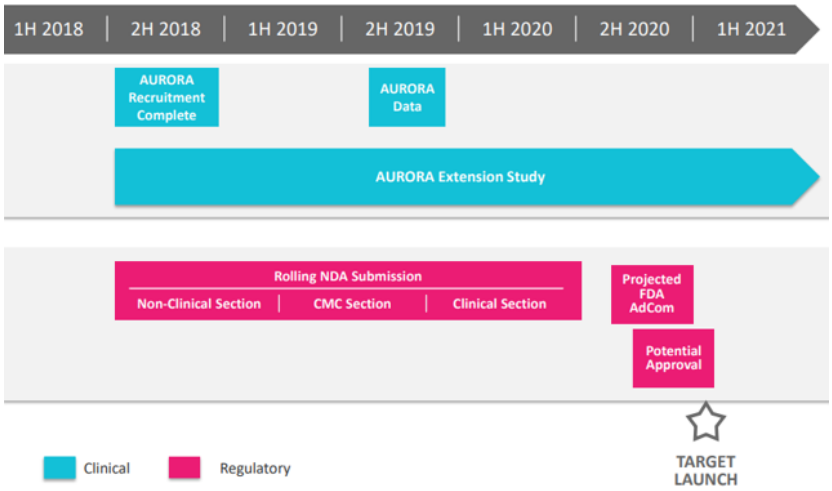
Thesis Technology

Aurinia's investigational drug, voclosporin, is a potentially best-in-class calcineurin inhibitor ((CNI)) with promising clinical data across its explored indications. Voclosporin acts as an immunosuppressant with a dual mechanism of action. By inhibiting calcineurin, voclosporin blocks IL-2 expression and T-cell mediated immune responses. In kidney podocytes, it exhibits an additional cytoskeleton-stabilizing effect by preventing dephosphorylation of synaptopodin. While legacy CNIs such as cyclosporin and tacrolimus are effective at remitting renal disease, they are not currently prescribed as a first-line therapy due to unpredictable drug metabolism. Legacy CNIs require careful drug level monitoring and often elicit side effects such as new-onset hypertension and hyperglycemia. In contrast, voclosporin has been developed with a predictable PK/PD relationship, enabling flat dosing for all patients regardless of subject-related factors. Additionally, treatment with legacy CNIs commonly alters blood pressure and induces electrolyte disorders; in contrast, patients treated with voclosporin exhibit stable blood pressure and blood magnesium and potassium concentrations on similar time-scales. As a next-generation CNI, voclosporin also exhibits increased potency and improved glucose and lipid profiles compared to legacy CNIs. An oral formulation of 23.7 mg to be taken twice daily is being developed for the treatment of two chronic renal diseases: lupus nephritis and focal segmental glomerulosclerosis (FSGS). Currently, no drug is approved for LN or FSGS in the United States or Europe, and the level of unmet need in this area is high. Therefore, the drug will follow a fast-tracked regulatory review process, meaning potentially quicker investment returns. Additionally, the company has developed voclosporin ophthalmic solution (VOS) containing 0.2% voclosporin for the treatment of dry eye syndrome ((DES)).

Voclosporin Clinical Trials

The global Phase IIb trial of voclosporin in LN (AURA-LV) tested the performance of voclosporin as an add-on treatment to the current LN standard of care, which is treatment with an off-label immunosuppressant MMF in combination with tapered oral corticosteroids. The primary endpoint of the Phase IIb trial was the percentage of patients who achieve complete renal remission at 24 weeks. The trial results were promising, with

significantly higher, 32.6% of patients on low-dose voclosporin experiencing complete renal remission compared to 19.3% in the control subjects that were treated with the standard of care alone. Moreover, patients treated with voclosporin achieved remission faster than control subjects, and the remission was durable: all the patients in complete remission at 24 weeks remained in complete remission at 48 weeks. Overall, the treatment was very well-tolerated, with no significant differences in the incidence of drug-induced adverse events between the voclosporin and the placebo groups. The most common adverse events reported were diarrhea, vomiting, and upper respiratory tract infection. The Phase III clinical trial to evaluate voclosporin in LN (AURORA) is highly similar in design to AURA-LV, with the exception that its primary endpoint is later, at 52 weeks. AURORA is on track to complete enrollment in 2018, with an estimated primary completion date in December 2019. The similarity between the two trials is encouraging that the Phase III data will be just as positive as the Phase II data. If this thesis holds true, the likelihood of voclosporin approval for LN is high.



Meanwhile, Aurinia's other programs are also making progress. A Phase II proof-of-concept study of voclosporin in FSGS was initiated in June 2018. In addition, a Phase IIa head-to-head tolerability study of VOS versus Restasis® (cyclosporine 0.05%) for the treatment of DES began in July 2018. The latter will be a four-week study of approximately 90 patients, with data expected to be available by the end of 2018. Assuming the trial data are promising, investing ahead of these potential catalysts could provide a worthwhile upside. For investors considering a long position, Aurinia anticipates that if approved, patent protection for voclosporin for the treatment of LN and FSGS will extend until at least October 2027, and VOS has IP protection until 2031.

Market Potential for Voclosporin

Aurinia's lead indication for voclosporin is lupus nephritis, which is inflammation of the kidneys in patients with systemic lupus erythematosus that can lead to kidney damage and failure. In the US, the estimated prevalence of SLE is as high as 78.5 cases per 100,000 or approximately 260,000 patients. However, the NIH reports that up to 50% of adults with SLE will develop LN. Thus, the US market size for this indication is approximately 130,000 patients. LN is a major risk factor for morbidity and mortality in SLE patients and can lead to chronic kidney disease with up to 30% of patients progressing to end-stage renal disease (ESRD) requiring costly interventions such as dialysis and kidney transplantation despite standard-of-care treatment. The annual medical costs of an LN patient are estimated to be nearly $60,000. Given that there are no FDA or EMA-approved therapies for LN, voclosporin could address a major unmet need. Aurinia also plans to expand its renal franchise by developing voclosporin for the treatment of focal segmental glomerulosclerosis, a cause of nephrotic syndrome. The incidence of FSGS is difficult to estimate but has been reported as 7 cases per 1 million or approximately 2,300 cases per year in the US. Although FSGS is a relatively rare disease, there is a clear unmet need for treatment as there are also no FDA or EMA-approved therapies. Current treatment consists of off-label use of glucocorticoids or other immunosuppressive drugs. Aurinia hopes to develop voclosporin as a first-line treatment for FSGS with recent initiation of a Phase II open-label trial for this indication.

In addition to its renal program, Aurinia is also developing a voclosporin ophthalmic solution for the treatment of dry eye syndrome. DES is a common problem with approximately 16.4 million adults in the US affected. Current treatments include artificial tears, topical cyclosporine (Restasis), and topical lifitegrast (Xiidra). A short, four-week, Phase II trial comparing the ocular tolerability of voclosporin ophthalmic solution and Restasis, which can have a high rate of side effects, was just initiated in July 2018 with results expected in the second half of 2018. Pursuing this additional indication is a relatively low-risk move for Aurinia that, if successful, could result in a nice boost to voclosporin's market potential.

Market Competition in LN

There is no drug specifically approved for the treatment of LN in the United States or Europe. However, Aurinia faces several key competitors with active

clinical trials in this field. AstraZeneca (AZN) is pursuing a Phase 2 clinical trial of Anifrolumab, a Type I IFN receptor monoclonal antibody, which will evaluate the safety and efficacy of two intravenous treatment regimens in adult subjects with active proliferative LN. This trial's data is expected in the second half of 2018. GlaxoSmithKline (GSK) has two clinical trials evaluating Belimumab in patients with LN. Belimumab, a B lymphocyte stimulator (BLyS) inhibitor, is already approved for treatment of patients with active SLE but has not been rigorously tested for treatment of LN. In one study, Belimumab was administered following treatment with rituximab and cyclophosphamide ((CTX)) in LN patients. This study's Phase 2 trial data was recently released, and an interim analysis showed the treatment did not significantly improve clinical outcome at 24 weeks, but the trial is ongoing. The other study, a Phase 3 trial, will determine the efficacy of Belimumab alone in patients with active LN, with data expected in July 2019. Boehringer Ingelheim has ongoing a Phase 2 clinical trial to investigate AbbVie's (ABBV) drug BI-655064, an anti-CD-40 antibody, as an add-on therapy to standard of care treatment for active LN with data expected in December 2019. Finally, Roche (RHHBY) and Genentech have a Phase 2 clinical trial of Obinutuzumab, a humanized anti-CD20 monoclonal antibody, to evaluate the efficacy and safety of Obinutuzumab as an add-on treatment to MMF in participants with proliferative LN. This trial data is expected in December 2019.

Compared to its competitors, Aurinia's voclosporin is a front-runner since it is already in Phase III and will have a first-to-market advantage if approved. Considering it is a small molecule that can be dosed orally once daily, it has a marked advantage over monoclonal antibodies that typically require invasive administration and are costly to generate. Payers may be reluctant to cover the cost of a monoclonal antibody if its efficacy is not dramatically better than its small molecule competitor. Therefore, despite these other drugs developments, the investment case is still strong for Aurinia.

Market Competition in DES

Two FDA-approved medications are available for the treatment of DES that would pose commercial competition, both of which target the immune component of the condition. These include Restasis (cyclosporine 0.05%) by Allergan Inc. (AGN) and Xiidra (lifitegrast 5%) by Shire PLC (SHPG). Restasis generates roughly $1.6 billion in annual sales and Xiidra is estimated at around $200 million. Over-the-counter drugs for DES such as lubricants and artificial tears generate around $540 million in annual sales. If VOS can

capture even 10% of the total market, it will return over $200 million a year in revenue.

Similar to Aurinia, several companies have calcineurin inhibitors (i.e. cyclosporine derivatives) in their pipelines for DES, attempting various formulations of the compound in attempts to improve its efficacy and tolerability. One major competitor in this space is Sun Pharmaceutical Industries (SMPQY), which has recently completed a phase 3 trial of Seciera (cyclosporine 0.09%). The Phase 3 data for Seciera were positive, showing significant improvement of clinical symptoms, faster onset of action, and superior tolerability compared to Restasis. Seciera is currently under review for FDA approval, and a favorable review would result in product launch by end of 2018. Another big competitor is Cyclokat (cyclosporine 0.1%) by Santen Pharmaceutical Co. (SNPHY). This product has already launched in Germany in 2015 and in Thailand in 2017 and is currently in phase 2 development for the US market.

Since cyclosporine-based formulations are being developed by other companies in the DES field, VOS will face head-to-head competition on several fronts. Additionally, Xiidra (an antagonist of LFA-1 binding to ICAM-1) improves symptoms in as early as two weeks compared to 3 to 6 months by Restasis treatment. The challenge for voclosporin is to capture market share from Restasis and other cyclosporine-based formulations for DES by improving the speed, efficacy, and/or tolerability of treatment. Since Aurinia claims voclosporin is a more potent, tolerable, and predictable form of cyclosporine in other contexts, we are optimistic that it will be able to compete with other formulations in this class and capture sufficient market share to provide return on investment.

Company Risks

As a small, single-asset company, Aurinia faces unsystematic risk. For the foreseeable future, success of the company hinges entirely on the success of voclosporin. Aurinia has not disclosed plans to diversify their product portfolio, so any new competitor in the space, a regulatory change, a shift in management, or a product recall could threaten the investment outlook. Additionally, the company faces market risk in developing VOS due to high competition and recent advances in the DES therapy space. Lastly, the margin of improvement of voclosporin compared to the standard of care is significant but small, meaning that there is a narrow range to account for potential variability in the next trial.

Summary

The price per share of Aurinia Pharmaceuticals has been flat for the past few years, but the catalysts in the upcoming year make it an ideal time to invest. A strong management team, healthy financial position, and promising phase 2 data for voclosporin in LN, and strong IP protection until 2031 indicate a high probability of long-term success.

This article was written by Christopher Cheung, Kuan-Hung Lin, Shrenik Mehta, and Marcela Preininger under the guidance of the EVEXIA Bio Fund leadership team as part of the fifth cycle of the Analyst Training Program (ATP).