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Equity Research
Biotechnology

Aurinia Pharmaceuticals Inc. (NASDAQ:AUPH, US$6.30; TSX:AUP, C$8.44)

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Bloom Burton Securities Inc.

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Rating:	BUY
Risk:	Speculative
12 month Price Target:	US$16.00

Price	$6.30
Implied Return	154.0%
Fiscal Year End	31-Dec
52 Week Range	$5.06-$7.85
Shares Outstanding (MM)	85.3
Market Cap. (MM)	$537.6
Float (MM Shares)	66.8
Avg. Daily Volume (MM)	0.60

	2017A	2018A	2019E	2020E
EPS	($0.92)	($0.76)	($0.72)	($0.32)
cash and STI (MM, end period)	$165.6	$125.9	$65.2	$39.9

This report is priced as of last trading day close. All values in US$ unless otherwise noted.

Filtering the Noise. Nearing a High Probability Phase 3 Readout.

Aurinia management and board are currently distracted by a dissident shareholder who proposes adding three new directors to the board at the company's upcoming AGM on June 26. The 14% shareholder cites, among other things, share performance, independence and share ownership of the board, and governance.

Our Take on AUPH Shareholder Activism

In our opinion, Aurinia's strategic plan has been generally well-executed. Admittedly, we have low visibility into the extent to which the board is responsible, and the company did just name a new CEO, Peter Greenleaf, following the retirement of Aurinia founder, Richard Glickman. That said, Mr. Greenleaf appears to be well-suited for the role of CEO of Aurinia at this time, having previously served as CEO at a number of biotech and commercial pharma companies (link). Additionally, the current directors appear to bring more big market biotech experience to Aurinia's board than the dissident-proposed nominees (link).

Since Aurinia's founding, management has accomplished the following: 1) established lupus nephritis (LN) as the lead indication for voclosporin (VCS) – in contrast to the transplant and psoriasis indications previously pursued by Isotechnika, which led to that company's demise; 2) designed and executed a successful, large, randomized phase 2b LN trial which we believe is highly predictive of success in the ongoing AURORA phase 3 (primary results expected in 4Q-2019); 3) expanded opportunities for VCS by initiating phase 2 trials in focal segmental glomerulosclerosis (FSGS – interim data expected later this year) and dry eye syndrome (DES – mixed, but, in our opinion, encouraging results reported in January: link); 4) added 10 years of potential patent protection to VCS (link); and 5) continues work to clearly differentiate VCS in LN (discussed below).

There *has* been a lull in AUPH stock following the reporting of phase 2 AURA results in August 2016 (AUPH up ~70% from prices prior to the AURA read-out, but up only 10% over the past year). However, the next big, binary event is fast approaching, and we believe the event has a relatively high probability of success (in large part due to management's execution leading up to the event). If AURORA is positive (or negative), the range-bound share price will become a thing of the past, and no replacements on the board will change that.

Potential to Meaningfully Differentiate VCS (in More Ways Than One)

In addition to the primary readout for AURORA expected in 4Q, Aurinia is pursuing several other lines of investigation which could help physicians and investors position VCS along the spectrum of "good drug for LN" (Bloom Burton's base case: US$8.00 per AUPH share) to "great drug for LN" (Bloom Burton bull case: >US$40.00 per share).

The key variable influencing our base and bull case valuations is long term nephrotoxicity which we believe in turn will drive differentiation/pricing of VCS, how the drug is used (episodic treatment of flares or chronic treatment) and peak market penetration.

With this update, we are maintaining our rating of BUY TOP IDEA (Speculative Risk) and target price of US$16.00*. We are currently assigning a 25% probability to the "great drug" (no nephrotoxicity) scenario; 55% for "good drug", and 20% for failure.

We note that there have been several indications going as far back as 2001 which suggest that VCS could emerge as a materially differentiated therapy ("great drug") for treating LN (discussed below), and further support could come from multiple sources later this year. We believe investors should BUY AUPH with key milestones visible; risk of phase 3 failure relatively low; our base case supporting a 25% potential 1-year upside, and our bull case supporting a potential 7x return.

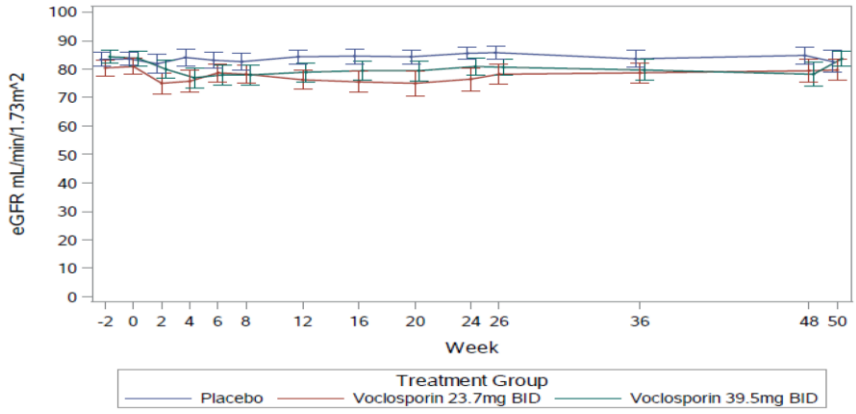
(continued next page)

*BB target based on sum-of-the-parts (LN: US$15.30; DES: US$0.75), probability-adjusted analysis (Exhibits 4, 5 and 6).

A mosaic of data points suggests that VCS may be materially differentiated from Prograf (tacrolimus) and Neoral (cyclosporine), a drug which differs from VCS by a single double bond carbon extension. The mosaic includes:

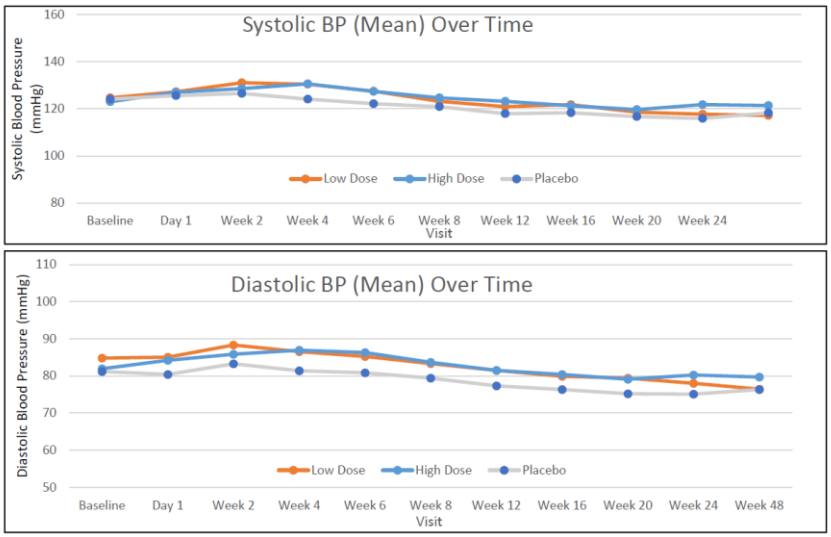
- In 2001, Isotechnika scientists published work showing that kidneys of rabbits treated with VCS exhibited no signs of interstitial fibrosis or tubular changes which are commonly associated with long term cyclosporine and tacrolimus exposure (link, link, link)
- In humans, acute effects of cyclosporine and tacrolimus exposure include arteriole vasoconstriction which leads to reductions in glomerular filtration rate (GFR) – in clinical trials, GFR typically drops 15% to 20% on average with the two older calcineurin inhibitors; link, link). With VCS, the early GFR impact appears a little less pronounced (~10% decline), and the effect is transient with GFR generally returning to normal in VCS-treated patients (Exhibit 1)
- There have been no reported cases of hyperkalemia with VCS which suggests that Aurinia's drug, is impacting the sodium potassium-ATPase pump differently from either cyclosporine or tacrolimus (which cause hyperkalemia in 5%-40% of patients; link), while maintaining robust immunosuppression, proteinuria reduction and podocyte stabilization (all beneficial in LN). Hypomagnesemia has also not been observed with VCS, unlike tacrolimus which frequently causes hypomagnesemia, leading to possible neurological side effects including tremors and seizures (link)
- Indications of lower risk of diabetes, dyslipidemia and hypertension, also potentially important differentiators in LN (link; link; link; link), further suggest that VCS is affecting cellular pathways differently from cyclosporine and tacrolimus, while still achieving potent immunosuppression. Cyclosporine, and to a greater extent, tacrolimus, cause new onset diabetes mellitus (NODAT) in up to 40% in transplant patients (link; link; link), likely due, at least in part, to enhancement of expression and activity of the sodium glucose co-transporter (SGLT) which increases intestinal glucose absorption (link; link). In the phase 2b PROMISE study, comparing VCS head-to-head against tacrolimus in renal transplant recipients, a voclosporin dose of 0.4 mg/kg bid (similar to the flat 23.7 mg bid dose being used in the phase 3 AURORA LN trial – see below), led to 1 patient of 62 (1.6%) developing NODAT, whereas tacrolimus (dosed per package insert) caused NODAT in 11 of 67 (16.4%) patients (link). Cyclosporine has been linked to hyperlipidemia in about 60% of transplant patients (link; link) – in the AURA-LV VCS phase 2b study in LN, dyslipidemia occurred in 6.7% of patients vs 6.8% in the placebo arm (*source*: Tumlin et al. 2017 ER-EDTA presentation). Cyclosporine and tacrolimus are also known to induce hypertension (link; link), possibly due to alterations in phosphorylation of endothelial NO synthase (eNOS) (link). Again, from AURA-LV, there was no significant difference in blood pressure over the 48-week treatment period with either low dose (23.7 mg bid) or high dose (39.5 mg bid) VCS (Exhibit 2).
- Due to VC's unique side chain, VCS-cyclophilin complexes induce conformational changes in calcineurin which are different from cyclosporine-cyclophilin complexes, resulting in ~3-fold greater potency of VCS (link) and potentially serving as the basis for other differential effects, several of which Aurinia is investigating in mechanistic studies, discussed below.

Exhibit 1. eGFR returns to baseline in VCS-treated LN patients



Source: Tumlin et al. 2017 ER-EDTA presentation

Exhibit 2. No significant difference in blood pressure



Source: Tumlin et al. 2017 ER-EDTA presentation

Additional support for differentiation of VCS with respect to long-term nephrotoxicity, neurotoxicity, diabetes risk and cardiovascular risk may be provided in advance of, and in parallel with the primary efficacy endpoint readout for AURORA.

AURORA

AURORA is an ongoing 358-patient, placebo-controlled phase 3 trial (randomized 1:1) evaluating whether VCS (23.7 mg bid) in combination with background standard of care of MMF/CellCept + low dose steroids, is able to increase the overall remission rates over a treatment period of 52 weeks. Enrolment of patients into AURORA completed in September 2018. The phase 3 study, for the most part, mimics the design of Aurinia's Phase 2b clinical trial, AURA-LV, but is focused on the most effective dose from AURA-LV, with more patients per arm (179 patients in each arm of AURORA vs 88 in AURA-LV).

In the three-arm AURA-LV study (23.7 mg bid VCS, 39.5 mg bid VCS, placebo), treatment of patients with 23.7 mg VCS led to a complete remission rate of 49% at 48 weeks vs 24% among placebo-treated patients (p<0.001), and 40% among VCS 39.5 mg bid-treated patients (p=0.026 vs placebo). Partial remission, a secondary endpoint, was also significantly increased with VCS (Exhibit 3).

Exhibit 3. Complete and Partial Remission results from phase 2b AURA-LV clinical trial (n=265) at 24 and 48 weeks.

The 24 and 48-week top-line efficacy results are summarized below:

Endpoint	Treatment	24 weeks	Odds ratio	P-value*	48 weeks	Odds Ratio	P-value*
Complete Remission	23.7mg VCS BID	33%	2.03	p=.045	49%	3.21	**p<.001**
	39.5mg VCS BID	27%	1.59	p=.204	40%	2.10	**p=.026**
	Control Arm	19%	*NA*	*NA*	24%	*NA*	*NA*
Partial Remission	23.7mg VCS BID	70%	2.33	p=.007	68%	2.34	**p=.007**
	39.5mg VCS BID	66%	2.03	p=.024	72%	2.68	**p=.002**
	Control Arm	49%	*NA*	*NA*	48%	*NA*	*NA*

**All p-values are vs control*

Source: Aurinia

The lack of a dose response in AURA-LV did raise a small red flag, but was not completely unexpected. Immune attack is a complex process, and for drugs that modulate immune response, sometimes lower doses can be equally or more effective (eg., Benlysta phase 2; link). We believe that the immunosuppressive benefits of voclosporin demonstrated in earlier transplant (link) and psoriasis trials (link), and the approval of tacrolimus for treatment of LN in Japan, largely mitigates the risk associated with the lack of dose response in AURA-LV.

Another red flag in AURA-LV: a mortality imbalance at 24 weeks (13 deaths were reported across the trial - 10 in the low-dose voclosporin arm, 2 in the high dose arm and 1 in placebo), has been attributed to sicker patients in the low dose arm,

and also a higher proportion of Asian patients for whom the standard of care prior to the AURA-LV trial would have been lower (all deaths occurred in Bangladesh (7), Philippines (2), Sri Lanka (2) and Russia (2)).

That the imbalance was caused by confounding factors is further supported by the fact that voclosporin has been tested in hundreds of patients in phase 2 and 3 trials in psoriasis, and a phase 2/3 trial in kidney transplant (in combination with MMF and steroid similar to AURA-LV), and a mortality signal did not arise in those trials; that deaths in the AURA-LV high dose arm were not higher (in fact were lower) than in the low dose arm, and that there were no further deaths in the VCS arms between weeks 24 and 48.

AURORA 2

At the same time that primary efficacy results will be reported for AURORA, we estimate that 50-80 patients will have been on study for 2+ years (AURORA patients are given the option of rolling into the AURORA 2 continuation study, which remains randomized). For these patients, GFR at 2 years will provide good insight into health of patients' kidneys after 24 months exposure to VCS.

Additionally, some patients in AURORA 2 may opt for "post-biopsies" which are occurring at a few of the 187 study locations. Unlike pre-biopsies which were required to confirm active nephritis per AURORA's inclusion criteria, post-biopsies are optional and not a formal endpoint in the phase 3 trial. Nonetheless, pre- and post-biopsy comparisons may provide additional insight into the long term kidney effects of VCS.

Mechanistic Studies

As well as clinical data, Aurinia is also investigating, in preclinical models, whether VCS differentially affects relevant molecules and pathways in glomerular cells (eg., calcineurin A-alpha and A-beta – both inhibited by cyclosporine and tacrolimus with A-alpha specifically linked to normal kidney development and function (link), and TGF-beta which is a key mediator of fibrosis (link)). While results from these studies will not serve as conclusive evidence for humans, the preclinical findings may help us better understand no fibrotic or tubular damage was observed in VCS-treated rabbits (referenced above), and could bolster any potential indications from AURORA and AURORA 2 that VCS is generally benign in humans.

If VCS does emerge as a markedly less nephrotoxic drug with lower propensity for metabolic disturbances, we forecast that it could become a $2 billion per year drug in LN alone (60% peak penetration; $40,000 annual treatment cost). In diseases such as diabetic nephropathy where calcineurin inhibitors are not generally used because of their toxicities, VCS could become a realistic option, although our forecasts and valuation model currently include only LN and DES.

Exhibit 4. U.S. and ROW lupus nephritis peak sales estimates based on "Great Drug" (effective with no long-term nephrotoxicity) and "Good Drug" (effective but with moderate long-term nephrotoxicity) voclosporin profiles.

	United States		ROW	
Patients with Systemic lupus erythematosus (SLE)	1,500,000		3,500,000	
Diagnosed population (33.3% U.S.; 10% ROW)	500,000		350,000	
Diagnosed SLE patients with lupus nephritis (40%)	200,000		140,000	
LN patients treated with MMF (forecast 70% U.S.; 50% ROW)	140,000		70,000	
Achieving complete remission (MMF + steroids: 25%*)	35,000		17,500	
Fail to achieve remission (75%)	105,000		52,500	
Scenario	No LT Neprhotox	LT Nephrotox	No LT Nephrotox	LT Nephrotox
Peak Voclosporin penetration	60%	35%	50%	25%
Average Tx cycles (24 weeks)/year	1.5	0.5	1.5	0.5
24 week Tx cycles	94,500	18,375	39,375	6,563
Cost (per 24 week cycle)	$20,000	$15,000	$10,000	$7,500
Peak Sales ($MM)	$1,890.0	$275.6	$393.8	$49.2

*23.9% of control patients achieved complete remission in AURA

Source: Lupus Foundation of America; company reports; Bloom Burton estimates

Exhibit 5. Voclosporin (oral) valuation (lupus nephritis indication)

	Patent Protected to 10/2027		Patent Protected to 12/2037		
	No LT Nephrotox	LT Nephrotox	No LT Nephrotox	LT Nephrotox	Phase 3 Fails
Peak sales (2025)	$2,283.7	$324.8	$2,283.7	$324.8	
Multiple of peak sales	3.0	3.0	6.0	6.0	
Value at peak	$6,851.2	$974.5	$13,702.5	$1,949.1	
Discount 5 years (12%)	$3,181.7	$452.6	$6,363.5	$905.2	$0.0
Cash YE 2020	$39.9	$39.9	$39.9	$39.9	$39.9
Cash from warrants and options	$108.5	$108.5	$108.5	$108.5	$0.0
EV	$3,330.2	$601.0	$6,511.9	$1,053.6	$39.9
Shares (fd)	103.3	103.3	103.3	103.3	85.3
AUPH value per share	$32.22	$5.82	$63.01	$10.20	$0.47
Weighting	15.0%	35.0%	10.0%	20.0%	20.0%
Weighted value	$4.83	$2.04	$6.30	$2.04	$0.09
AUPH PWV per share					$15.30

Source: Bloom Burton estimates

Exhibit 6. Peak sales estimates and risk adjusted valuation of VOS (ophthalmic solution) in DES.

VOS for Dry Eye Syndrome			
U.S. patients with dry eye syndrome (MM)	26.0		
Moderate to severe (MM)	7.0		
Patients treated currently (MM)*	1.0		
% moderate to severe patients currently treated	14%		
2028 forecast moderate to severe patients treated (%)	20%		
Estimated patients treated 2028 (assume 3% annual growth; MM)	1.8		
Estimated 2028 VOS penetration	5%	10%	20%
Estimated 2028 VOS U.S. patients treated (MM)	0.09	0.18	0.35
Annual patient cost ($575 per month, retail)	$6,900	$6,900	$6,900
Estimated average compliance	30%	30%	30%
Estimated 2028 annual U.S. VOS sales (retail - US$MM)	$183.6	$367.1	$734.2
Estimated 2028 AUPH U.S. net VOS sales (50%, US$MM)	$91.8	$183.6	$367.1
Estimated 2028 AUPH ROW net VOS revenues (US$MM)	$45.9	$91.8	$183.6
Estimated 2028 AUPH global net VOS revenues (US$MM)	$137.7	$275.3	$550.7
Multiple of peak sales	3.5	3.5	3.5
Value (US$MM)	$481.8	$963.7	$1,927.3
Discount 8 years (12%)	$173.3	$346.6	$693.1
Probability-weighted value (40%)	$69.3	$138.6	$277.3
Estimated cost of phase 2b and phase 3 (US$MM)	$75.0	$75.0	$75.0
NPV (US$MM)	-$5.7	$63.6	$202.3
NPV per share	-$0.07	$0.75	$2.37

*Source: Bloom Burton estimates; *Ocular Surgery News*

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HOLD	3	18%
SELL	0	0%
Total	17	100%