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IDEAS

COVERAGE LIST UPDATE

XENE | EPIX | ACST

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Over the past 3-months we have initiated coverage on three companies; Xenon Pharmaceuticals (Nasdaq: XENE), ESSA Pharma (Nasdaq: EPIX), and Acasti Pharma (Nasdaq: ACST). After we issue our initiation reports, we generally will not issue follow-on reports, rather we will send around email updates when appropriate. This is the first such update, for two of the three names we cover, have had material changes to their business since our initiation report. For our most timely commentary, we recommend you follow us on Twitter (@encodeIp), where we discuss not only names under coverage but also other names of interest in the life sciences.

Xenon Pharmaceuticals

We published our research on Xenon in October while it was trading in the $8s. The stock has performed very well since then, driven predominantly by the licensing agreement Xenon entered into with Neurocrine (NBIX) on December 2nd. Under this agreement, Xenon has licensed the exclusive rights to their Nav1.6 and Nav 1.6 / Nav 1.2 compounds, including their clinical stage asset XEN901, to Neurocrine in exchange for $50mm upfront and up to $1.7b in clinical, regulatory and commercial milestones. We will not get into all the details of the deal, but would highlight a few aspects; (1) the upfront payment consisted of $30mm cash and $20mm purchase of Xenon equity at $14.196 (2) there is a near-term $25mm milestone payment, 45% payable in cash and 55% payable in Xenon equity purchase, expected once XEN901 IND has been accepted by FDA, currently guided for mid-20.

We like this deal for Xenon. In our report, we had discussed the likelihood that Xenon would need to partner one of more of their clinical stage compounds, but had assumed that XEN1101 would be the asset they chose to partner. By partnering XEN901, the company is signalling that it intends to focus heavily on its later stage potassium channel (Kv7) products, XEN1101 and XEN496. The deal also takes pressure off the company's balance sheet, which was going to be stretched in 2020 with four drugs entering / in the clinic. Subsequent to the Neurocrine deal, Xenon raised an additional $50mm of its ATM. After the Neurocrine deal and raise off their ATM, we estimate Xenon's pro-forma cash to be $175-180mm, and S/O of ~32mm. The company should have a 3-year cash runway, comfortably seeing it through key clinical readouts for XEN1101 and XEN496.

We believe 2020 is the year where Xenon closes the valuation gap with its later-stage CNS peers, Sage (SAGE), Axsome (AXSM), and Zogenix (ZGNX). In 2020 the company will be enrolling a pivotal Ph3 study in children with KCNQ2-DEE with XEN496, and reporting data on XEN1101 from a large Ph2b study in adults with focal epilepsy. We also should see pipeline expansion in 2020, as Xenon management noted on their last conference call, "...we also continue to explore other possible neurological indications for XEN1101……..you can expect to hear more from us in the very near future about the broad development opportunities and our expanded plans for XEN1101." In previous calls Xenon management has mentioned ALS, tinnitus, and major depressive disorder as indications of interest for XEN1101. The company is well financed to pursue a Ph2 program in any of these indications.

ESSA Pharma

There is nothing new to report on ESSA. The company issued its YE press release (Sept 30 is their fiscal YE) reiterating its guidance that it will file an IND for EPI-7386 in 1Q20 and start their Ph1 in men with mCRPC 1H20. As of Sept 30th the company reported a cash balance of $53.3.

In our November 11th initiation report, we highlighted Arnivas (Nasdaq: ARVN) as the most relevant therapeutic peer for ESSA. Since then Arnivas has more than doubled. Arnivas, a Ph1 oncology company, now carries a >$1.5B cap, but we think ESSA should be able to close the valuation gap in 2020. We recognize that Arnivas is valued more as a platform play, and has two drugs in Ph1, only one of which is focused on mCRPC. Nonetheless, we believe investor enthusiasm towards Arnivas, is reflective of investor interest in novel mechanisms for late-stage prostate cancer, and something ESSA can tap into once it enters the clinic later this year.

Acasti Pharma

We initiated on Acasti November 25th, recommending caution to investors as we headed towards the first Trilogy study readout. We were concerned with the opaqueness of the earlier Ph2 data with CaPre, and felt we didn't have enough historical clinical evidence to comfort us in the probability of Ph3 success. Although our recommendation that investors remain on the sidelines for the first Trilogy readout contemplated the possibility of a miss on the primary endpoint, our call was more predicated on the possibility of an underwhelming hit on the primary (20-25% TG-lowering). Nonetheless, we made the right call, as the data from Trilogy 1 were undoubtedly negative, albeit with some questions left to be answered.

We will briefly discuss the Trilogy 1 data, and upcoming milestones and cadence of data, but first would like to comment on a troubling trend we saw with Acasti and how investors can learn from this failure. The troubling trend we are referring to is a lack of data transparency. When a company is entering Ph3 studies, but can't provide investors with peer-reviewed Ph2 evidence to support their move into Ph3, be concerned. Acasti's Ph2 COLT study was never published in a peer-reviewed journal. The data were presented at a few low-science conferences, but never subject to peer review or criticism. Then there's the Ph2 Trifecta study, where the only information available comes from Acasti press releases. If you ask the company for the Trifecta data, they will not provide it to you, and will simply point you to their press releases. However, in their corporate slides, they happily cherry-pick aspects of Trifecta, combine them with COLT, and make their argument as to why CaPre should work. We highlight the risks associated with lack of data transparency not only to forewarn investors when they encounter a similar situation, but also to foreshadow what we may see from Acasti in the coming weeks as they release more data from the Trilogy studies.

So that leads us to Trilogy 1, and the data release this week. Acasti announced that CaPre reduced TG's by 30.5% vs baseline at week 12, but placebo (corn starch) also had a profound TG reduction of 27.5% at week 12. The company did not formally present the primary endpoint data, the difference in TG reduction difference between CaPre and placebo at week 12, other than stating the obvious, that the study did not meet statistical significance. Acasti did not provide the actual percentage difference in TG reduction between treatment and placebo at week 12, nor did they provide any p-values, or baseline information. The company highlighted that 5 clinical sites (of the 54) had unusually high TG reductions in the placebo arm, and it is investigating this anomaly. While we agree that the TG lowering percentage in the placebo arm appears abnormally high, it seems unlikely that 5 sites are the root of this problem. It wouldn't surprise us if there were eventually a better explanation for the large placebo effect, but it will not change the overall outcome of a failed trial.

Acasti did provide a few other endpoints in their Trilogy 1 press release, specifically 26 week TG reduction data and 12 week TG reduction in patients on background statin therapy. Again, no p-values or baseline values, or in the case of the statin data the actual number of patients in this group, were provided. We find the disclosure of these two endpoints curious given that Acasti had previously stated in their Q3 press release, "According to the SAP, the primary endpoint must first be positive with statistical significance prior to analyzing the secondary and exploratory endpoints. These endpoints will then be analyzed in the following order: 1) additional TG secondary endpoints, including TG reduction at Week 26, which is intended to show CaPre's persistence of effect, TG reduction in various subgroups to show consistency of effect..." Then when the company announced the delay in reporting Trilogy 1 in late December they had changed their disclosure around Trilogy 1 data to, "Other important secondary endpoints such as non-HDL (high-density lipoprotein) cholesterol, HDL cholesterol and VLDL (very low-density lipoprotein) may

now also be reported with the top-line results." In the end, we didn't get any of the secondaries they said could be disclosed with the top-line, and instead got different secondary data.

As we have emphasized, Acasti has a history of poor data disclosure and transparency, and we are now witnessing it play out with Trilogy 1. This study was a failure, no amount of data mining, data cherry picking, etc., will change that they missed their primary endpoint badly. Even if a post-hoc analysis was performed that removed the patients from the 5 "abnormal sites" in question (we are likely talking about a maximum of 10 patients), CaPre would still not show the 20% difference vs placebo necessary to achieve the primary endpoint. We see no scenario where Trilogy 1 can be viewed as positive, however, we assume Acasti will try to convince investors otherwise.

In the meantime, we await the results of Trilogy 2, now guided for mid-Feb. Although unlikely to be successful, it is possible that CaPre could squeak over the 20% TG-lowering threshold vs placebo and achieve the primary endpoint. In the unlikely scenario that Trilogy 2 hits, we feel the company still has a tough path forward, both in their communication with FDA and the capital markets. After Trilogy 2 top-line, Acasti said they would complete their audit of abnormal sites from Trilogy 1 and report on their findings by the end of Feb. Lastly we should see data from all the secondary and exploratory endpoints from both studies by the end of Q1.

We still recommend caution, and pessimism, when looking at Acasti as an investment.

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