What is Next for Endocyte (ECYT)?

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Overview of Recent Events

Endocyte (ECYT) has made a dramatic move higher in recent weeks based off renewed clarity on the clinical and regulatory path forward. ECYT will be allowed to re-import its European Doxil supply to restart it phase III PROCEED trial in platinum resistant ovarian cancer (PROC). In addition, the company has confirmed with EU regulators that the phase II data is strong enough to submit EC-145 for conditional approval in 3Q2012 (keeping in mind that submission is very different than approval). The European regulators have also confirmed that progression free survival (PFS) is the endpoint required for both conditional and final approval. Finally, the FDA has confirmed that PFS would be an appropriate endpoint for accelerated approval based off of the PROCEED trial and that final approval would require an overall survival (OS) endpoint. These are all very positive developments and the stock price reacted as one would expect. The question is where will the price move next and what should investors focus upon?

Where is ECYT Moving?

Even after the significant move higher after the earnings and conference call, ECYT still on sports a market cap of $175M (price of $5) with about $128M in cash at the end of 2011. So the big move has basically just put the market cap above cash levels. Of course, small cap biotech companies do not trade on cash, they trade on catalysts. So what are the next series of catalysts and what effect will they have on the price?

Before looking at these catalysts and their potential effect on the price, it is important to think about underlying assumptions about the activity of EC-125. Rather than take a single view, I want to compare two sets of assumptions. The bear case assumes that EC-145 is basically inert and will have no effect on either PFS or OS. Keep in mind, however, that there is very little data to support the bear case. While the OS data was statistically insignificant, there was consistently a PFS benefit shown for EC-145 in the FR++ group. That being said, I want to see how the upcoming catalysts would affect the price if the bears are correct. The second case is the base case, which is consistent with the data to date, i.e. that EC-145 has a PFS benefit in the FR++ group but no OS benefit. Of course, there is a third "bull case" in which there is a PFS and OS benefit (which I think is possible) but I am more concerned with downside risk. If the bullish case is accurate, then it is fairly clear how the price will react to upcoming catalysts.

Table 1 provides a list of the known upcoming catalysts through the OS data from the PROCEED trial in 2016. In addition, the table notes whether the catalyst would be negative, neutral, or positive and does so for both the bear case and base case. The first point to note is that even with the bear case a negative catalyst before late 2013 is unlikely. This seems pretty bullish so how could this be true for the bear case? Simply answered, it is in the nature of the upcoming catalysts. We already know that the AACR presentation will show an improvement in OS hazard ratio. In addition, the starting of clinical trials are usually positive and at worst neutral catalysts. In addition, submission for regulatory approval is generally viewed as positive (and at worse neutral). So the first real chance for the bear case to manifest itself is in the EU regulatory decision in late 2013.

So even if one assumes the worst about EC-145, it is unlikely that you would see confirmation of the negative bias for at least 18 months if not 24 months

Table 1		Expected Effect	
Catalyst	Expected Timing	Bear case	Base case
Present updated PRECEDENT OS data at AACR	March 31- April 4 2012	Neutral to Positive	Neutral to Positive
Renew enrollment in Phase 3 PROCEED trial in early Q2 2012	Early 2Q2012	Positive	Positive
Start Phase 2b/3 non-small cell lung cancer trial in early Q2 2012	Early 2Q2012	Neutral to Positive	Neutral to Positive
Submit EU marketing applications for conditional authorization of EC145 and EC20 for treatment of FR(++) PROC	3Q2012	Positive	Positive
Submit IND for folate tubulysin drug	1Q2013	Neutral to Positive	Neutral to Positive
EU decision on marketing applications	2H2013	Negative	Positive
PFS data from PROCEED Phase 3 trial	1H2014	Negative	Positive
OS data from PROCEED Phase 3 trial	1H2016	Negative	Negative

Of course, even with the bear case that EU decision might still be a positive catalyst as the EU has seen the phase II data and even with the OS hazard ratio around 1.4, they encouraged the company to submit for approval. We also now know that the OS hazard ratio is actually better (currently close to 1.0), which would only increase the odds of approval. So, while it is possible that the bear case would get its negative catalyst in late 2013, it is more likely they would have to wait until PROCEED PFS data in the first half of 2014. So even if one assumes the worst about EC-145, it is unlikely that you would see confirmation of the negative bias for at least 18 months if not 24 months. Of course, taking the base case then the EU regulatory is likely to be positive as will the PROCEED PFS data, which means you have until 2016 for a truly negative catalyst.

Aside from the catalysts noted in table 1, there are some others that might occur. First, the NSCLC trial will read out data at some point but it is not clear when that would be. The 2H2013 timeframe seems like a reasonable estimate, which could move up the potential of a negative catalyst for the bear case but it is not quite clear if one should read into that trial from the PROC results. Second, there is always the risk of a secondary but the company is relatively cash flush at this point and would likely not need to raise until 2014. Third, since EC-145 is wholly owned, there is always the possibility of a partnership. The company has noted the possibility of a European partnership (or a broader one if appropriate) but is not giving any guidance as one would expect. Clearly a partnership would be a positive catalyst but one cannot estimate when (or if) it will occur.

In sum, knowing that small cap biotechs are driven by catalysts, one does not have to assume my bullish case to see the price move higher with comparatively low downside risk (especially with a company still trading near cash levels). Without some negative news out of nowhere, all of the expected catalysts in 2012 and well into 2013 will likely to be positive or, at worse, neutral. As such, the risk/reward even after its recent run seems biased toward reward over the next 18 months (or longer if one takes the base or bullish case).

Drug Conjugation Technology Allows Us to Generate Multiple SMDCs for Multiple Diseases

Endocyte Platform

Program	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
ONCOLOGY - Folate Receptor					
EC145	Platinum Resistant Ovarian Cancer				
	Non-small Cell Lung Cancer				
EC0489	Solid Tumors				
EC0225	Solid Tumors				
EC17	Solid Tumors				
EC0531	Solid Tumors				
EC20	Folate Receptor				
ONCOLOGY - PSMA					
EC1069	Prostate Cancer				
EC0652	PSMA				
INFLAMMATION - Folate Receptor					
EC0746	Inflammation				
EC0565	Inflammation				

The Bottom Line

ECYT will be a volatile stock moving forward, especially after its recent run. Despite this move, it is still not a stock that appears grossly over-valued or even fairly valued ($175 million market capitalization company with $128 million in cash). It has a wholly owned phase III asset that will be submitted for its first regulatory approval later this year as it expands the program into another indication (NSCLC). In addition, given the obsession that biotech investors place on catalysts, the next 18 to 24 months stack up fairly well for ECYT with a series of events that should be viewed as positive. Finally, it is a platform company that has a number of potential extensions into new molecules.

Despite my bullish views, there is certainly a bearish attitude among some that seems to rest on the OS results. The only way to definitively counter that argument would be positive PROCEED OS data but that is years away. So there will be an ebb and flow of sentiment around ECYT, where the import and meaning of the PRECEDENT OS data will likely be debated and divide individuals. That being said, ECYT remains cheap both compared to its potential and compared to other companies with Phase III assets being submitted for regulatory approval.

Why the Obsession with OS?

While I certainly understand the obsession with overall survival as an important endpoint and indicator of activity, a couple of points need to be made. First, OS is not needed for conditional approval in the EU and it is not even needed for final approval in the EU. So if you are interested in ECYT for its approval prospects in the EU, OS data is not going to have any major impact on that outcome. Second, OS is not even needed for accelerated approval in the US. So if OS is not going to be a deciding factor for EU approval and for accelerated US approval, why are some people so obsessed with it?

In general, OS is the gold standard for outcomes in that we both want drugs to extend lives and it is unquestionably an objective standard. I think that is completely reasonable and agree with it. A blanket obsession with OS, however, can be misleading and is certainly the case for ECYT. Not only is it not needed for the upcoming regulatory catalysts but the trial was never designed to provide a clear OS signal. While some would like to paint this second point as an excuse, poor science, or predictive of future results, that is simply not true. Focusing on OS may make a good story and follow the negative narrative that has enveloped ECYT but investing on stories and narratives without digging into the results is problematic.

Of course, what this negative narrative misses is the data that will be presented at AACR. The company has already noted that with further maturation, the OS data has become better (hazard ratio decreased to 1 from 1.4). This clearly does not mean that EC-145 now shows an OS benefit but it reinforces the view that the first OS analysis was an inaccurate representation of the true effect (for my full analysis of that data see). If the bears are correct, then why is the hazard ratio improving as we get more information? Of course, the debate over OS is actually a moot point to a certain extent as we do not need to assume an OS effect to see ECYT moving higher in the near term but it is certainly something to follow in the years to come.

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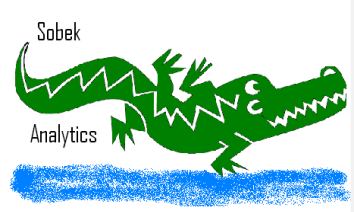

Disclaimer

I am not a certified financial analyst. All the information provided in this report is my interpretation and may contain errors. Please, do not invest based solely on my opinions as it is critical for all investors to conduct their own due diligence and invest in ways that best fit their own needs. All errors (if any) in this report are mine and due to my misinterpretations. In addition, I am long shares of ECYT. In addition, my entire position is hedged through the selling of April $7.50 covered calls.