Eleven Biotherapeutics

Equity Research

Company Quick Take

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Price: $11.16 (10/3/2014)
Price Target: $35.00

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: EBIO
Market Cap (MM)	$181.6

AC Phase II Hits With CAPT Model; Future Plans To Be Unveiled In Early 2015

The Cowen Insight

The reported EBI-005 Phase II results last Thursday were positive in the CAPT model, which now informs Eleven of the appropriate pathway forward and the correct model for measuring the late-phase allergic response. We will learn more of the specifics of the regulatory process early next year and we continue to believe that very little-to-no valuation is being ascribed to this AC indication.

The Industry Standard CAPT Model Now Identified As Appropriate For Measuring The Late-Phase Allergic Response

Eleven reported results from EBI-005's (topical IL-1 inhibitor) Phase II program in allergic conjunctivitis. The Phase II program consisted of two studies, employing two distinct models with 6 allergen challenges over 2.5 weeks, in moderate to severe allergic conjunctivitis patients: (1) a modified conjunctival allergen provocation test (CAPT); and (2) a modified environmental exposure chamber (EEC) model. The main endpoint, the mean change from baseline in patient-reported ocular itching compared to vehicle control, was statistically significant in the CAPT model, but not in the EEC model. While these results initially appear mixed, Eleven was exceedingly clear going into the data that both models were being evaluated to identify an appropriate model/pathway for late-phase ocular allergy response to take forward to Phase III and that significant optionality exists as we previously wrote here. Therefore, while the EEC study was not successful, the successful CAPT study results will be used to forge a pathway forward – and we will likely learn of that pathway in early 2015 after the company meets with the FDA. Furthermore, we are comforted by the fact that the CAPT model – which was employed in the successful study and will most likely be used going forward – is the model that the majority of approved ocular therapeutic agents have used for registration studies. Ultimately, this data suggests that EBI-005 could be a potentially useful treatment option for later-stage moderate to severe patients who currently have a lack of effective treatment options available. Many of these patients have to resort to steroid treatment, which is commonly associated with significant side effects. The bottom line is that we continue to believe that very little-to-no valuation is being ascribed to the allergic conjunctivitis indication, which we believe is overly conservative when this program has potential to advance into Phase III within the next year. Recall, much of the focus is on the company's EBI-005 Phase III dry eye disease program (discussed below) that will have pivotal data in early 2015.

Specifics Of The EBI-005 Phase II Allergic Conjunctivitis Results

As noted above, while the study employing the EEC model (~100 patients; 50 per arm, treatment and placebo) did not achieve statistical significance on its endpoints, the study using the CAPT model (~50 patients; 25 per arm, treatment and placebo) did. A 5mg/mL EBI-005 dose was used and the most important endpoint of ocular itching achieved statistical significance at the second to last (p=0.033) and the final – (p=0.045) assessment time points. The final assessment time point was pre-

specified. We would note that achieving statistical significance in such a small study is impressive. Looking ahead, potential registration studies could be 200 patients or more, which would further increased the powering and probability of a statistically significant outcome.

Other exploratory endpoints in the CAPT study of ocular tearing (second to last, p=0.027; final, p=0.044) and associated nasal symptoms (second to last, p=0.004; final, p=0.011) were also statistically significant. These were not met in the EEC study. Overall, 27% of subjects reported a mild adverse event and the safety and tolerability of EBI-005 compared to vehicle control was balanced, with no treatment-related serious adverse events and no immunogenicity. The final results will be submitted at an upcoming ophthalmology conference.

EBI-005 Pivotal Dry Eye Data Readout On Track For Early 2015 – Shire Filing Disclosure Indicates That The Dry Eye Regulatory Environment Is Improving

Additionally, the pivotal Phase III EBI-005 clinical trial in dry eye, which is ongoing, continues to enroll patients on schedule and topline data is expected in early 2015. A 12-month dry eye safety study should be initiated in the second half of this year as well, which is also on plan. Importantly, physicians continue to assert that the scientific rationale behind EBI-005 and Eleven's other programs remain sound and that the new ocular pain symptoms endpoint for the dry eye trials is very relevant (commercially/clinically) to the disease. In our EBIO initiation in early March, we discussed at length the historically difficult dry eye disease regulatory environment, which is centered around the requirement of meeting two potentially non-correlated co-primary endpoints (signs and symptoms). However, we also noted how that environment has been easing/improving in recent years with what appears to be a more amenable FDA. Examples of this have been the emergence of the "totality of the data" thesis and the FDA's willingness to allow Shire to explore a novel, more simplistic and straightforward, patient-reported eye dryness symptoms endpoint (as opposed to the more complicated tradition OSDI measurement). Additionally, it appears the Agency may be amenable to allowing positive Phase III results for the signs and symptoms endpoints in separate Phase III studies (which is discussed in our note here). The bottom line is that it appears that the Agency is considering a more pragmatic pathway and the regulatory environment is improving. Ultimately, we believe this bodes well for Eleven Biotherapeutics' Phase III EBI-005 dry eye program.

We would reiterate that our consultants continue to indicate that Restasis is a fairly poor treatment given its efficacy and tolerability profile, nonetheless, is the market leader and the only approved dry eye drug with roughly $1B in sales. Our consultants stress that a "better" therapeutic option could expand dry eye prescription utilization by 3-4x the current Restasis use, making the prescription target market likely actually closer to $3-4B. Most importantly, given the profile, they indicate that EBI-005 would be an exceedingly welcome addition to the treatment paradigm. Our model has "peak" sales of roughly $500MM, but we believe this is clearly a conservative number if the initial clinical profile holds up in Phase III. Stated another way, there is no reason why EBI-005 couldn't be a $1B+ drug, in our view.

The Valuation Is Attractive Here

Assuming clinical and commercial success for EBI-005 (while excluding any potential other pipeline assets, including the AC indication for EBI-005) we arrive at a base valuation of $35 per share. This assumes that Eleven takes the product to market via their own sales force in 2017, and that by year 5 of the launch EBI-005 has reached $500MM+ in sales. Alternatively, a potential acquirer with its own commercial infrastructure — which would significantly lower our spending assumptions in the DCF — would argue for a valuation of the EBI-005 opportunity alone of $50-55. Given

the approaching data readouts and our belief in the likelihood of clinical success, and the potential commercial outcomes, we would be adding at these levels.

Figure 1 EBI-005 Dry Eye Market Build

ESTIMATED U.S. DRY EYE TREATMENT MARKET											
	2012	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	CGR	Comments
Restasis U.S. Penetration Of Est Dry Eye Market (AGN)	80%	80%	80%	78%	74%	67%	62%	56%	51%		- Leading treatment - market creator
Estimated Patients ('000)	1,825	2,070	2,180	2,185	2,190	2,120	2,080	2,010	1,975		- Generics may not come upon market expiry; poor compliance
Average Price Per Year Due To Low Utilization	$685	$720	$765	$805	$845	$885	$930	$975	$1,025		- ~5% annual price increases
Annual Prescriptions ('000)	2,820	2,955	$3,112	$3,119	$3,126	$3,026	$2,969	$2,869	$2,819		
Estimated Sales U.S. ($MM)	$750	$895	$1,000	$1,055	$1,110	$1,125	$1,160	$1,175	$1,215	+6%	- US sales dominate
Lifitegrast U.S. Penetration Of Est Dry Eye Market (SHPG)				4%	8%	13%	16%	20%	22%		- First treatment to address symptoms of dry eye
Patients ('000)				39	89	159	205	266	323		- Compliance should be better than Restasis due to efficacy
Average Price Per Year				$1,610	$1,690	$1,770	$1,860	$1,950	$2,050		- Priced at a premium to Restasis; and higher utlization
Annual Prescriptions ('000)				46	106	189	244	316	384		
Estimated Sales U.S. ($MM)				$50	$120	$225	$305	$415	$530		- Expected to rapidly gain market share
EBI-005 U.S. Penetration Of Est Dry Eye Market							4%	8%	10%		- Second player to reach market that treats symptoms effectively
Patients ('000)							81	144	186		- Potential 2018 U.S. market launch
Average Price Per Year							$1,860	$1,950	$2,050		- Pricing in-line with Lifitegrast
Annual Prescriptions ('000)							96	172	221		
Estimated Sales U.S. ($MM)						**$50**	**$120**	**$225**	**$305**		- Strong launch anticipated in exceedingly large market
Steroids/Tears/Others U.S. Estimated Penetration Of Dry Eye Market	21%	20%	20%	19%	18%	17%	15%	14%	13%		- Use declines with the entrance of new, more effective products
Patients ('000)	1,510	1,630	1,740	1,735	1,765	1,730	1,695	1,665	1,640		- Compliance low and similar to Restasis; short duration of treatment
Average Price Per Year	$215	$225	$235	$245	$255	$270	$285	$300	$315		- Mainly generic or low priced products
Estimated Sales U.S. ($MM)	$195	$220	$245	$255	$270	$280	$290	$300	$310	+6%	- Use remains steady
Total U.S. Dry Eye Market Sales (MM)	**$945**	**$1,115**	**$1,245**	**$1,360**	**$1,500**	**$1,680**	**$1,875**	**$2,115**	**$2,360**	**+12%**	- Larger % of market penetrated due to multiple treatment options
% Growth	**+15%**	**+18%**	**+12%**	**+9%**	**+10%**	**+12%**	**+12%**	**+13%**	**+12%**		- Growth should be rapid given new, more effective drugs

Source: Cowen and Company; PriceRx

Valuation Methodology And Risks

Valuation Methodology

Pharmaceuticals/Specialty

For our valuation methodology, we arrive at fair value utilizing a discounted cash flow (DCF) approach to derive our 12-month price target.

Investment Risks

Pharmaceuticals/Specialty

Risks include: (1) growing competitive dynamics in the specialty pharmaceuticals space; (2) the ability of management to execute on external growth by successfully acquiring new strategic, accretive products; (3) the ability to grow organically and keep the product pipeline robust; (4) potential regulatory delays, rejections, or failures of pipeline products; (5) economic sensitivity of any self-pay products or weakening consumer demand; (6) domestic or international pricing pressures for marketed products; and (7) failure to execute on new product launches.

Risks To The Price Target

Eleven is a development-stage specialty pharmaceutical company and with that carries risk. Failure to successfully develop EBI-005 could result in a significant decrease to our valuation.

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
EBIO	Eleven Biotherapeutics

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Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

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Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period

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Buy – The fundamentals/valuations of the subject company are improving and the investment return is expected to be 5 to 15 percentage points higher than the general market return

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Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	440	59.95%	105	23.86%
Hold (b)	278	37.87%	10	3.60%
Sell (c)	16	2.18%	0	0.00%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

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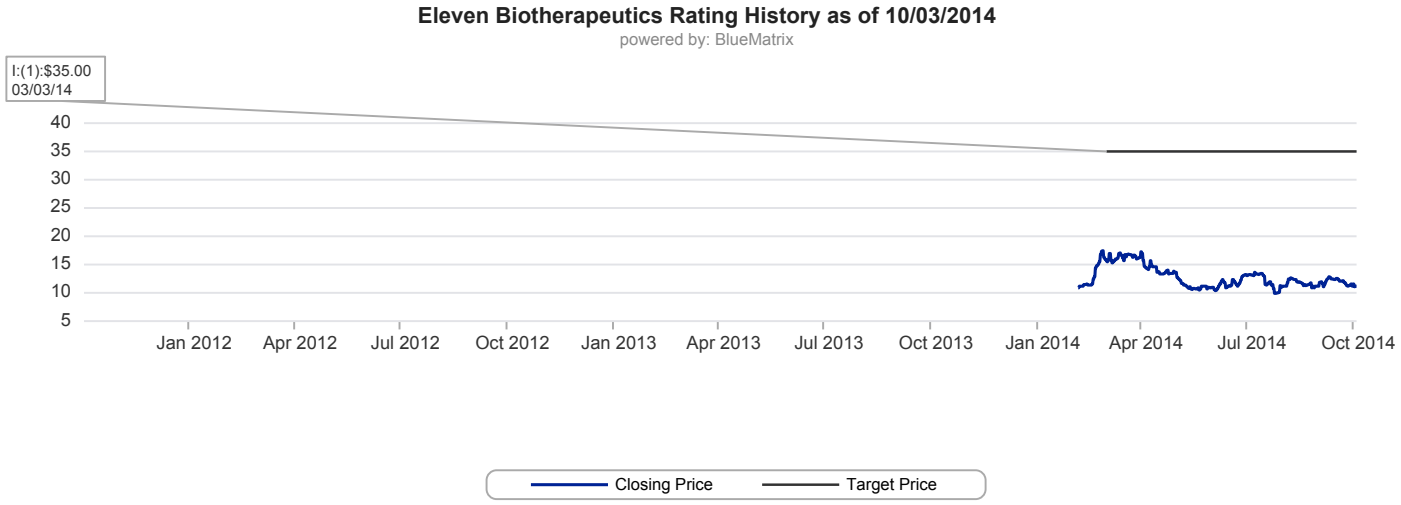

Legend for Price Chart:

I = Initiation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | $xx = Price Target | NA = Not Available | S=Suspended

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