Flexion Therapeutics

(FLXN-NASDAQ)

Stock Rating: **Outperform**
Industry Rating: **Outperform**

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Our Answers on Flexion vs. Competition

Event

We have received some questions lately about potential competition to Flexion's FX006 for OA knee pain. In this note we outline some of what we think are the advantages of Flexion's strategy and product.

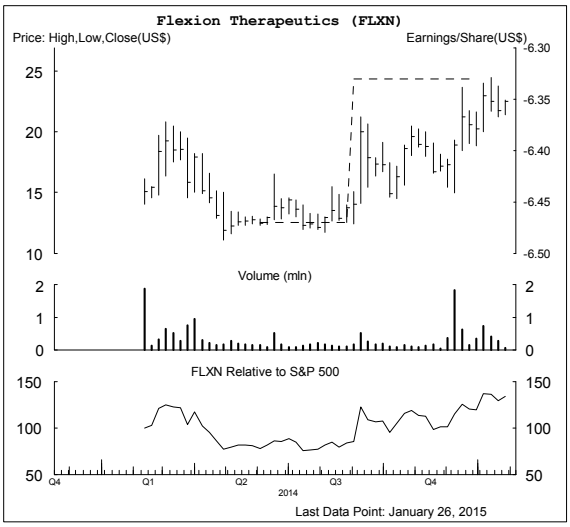
Impact & Analysis

Several investors have asked about potential competition to Flexion's FX006 program in recent weeks given the recent S-1 filing by Carbylan. We believe that Flexion's program, based on the widely used steroid at the clinically used dose, is being developed in a sound manner. Flexion's FX006 has data that reached statistical significance, Flexion has already successfully navigated the IND process, is conducting studies in the U.S. (and has data from the U.S.), has dose-ranging data, has data that shows residence time in the joint (synovial PK data in humans), and has clinically meaningful endpoints. We believe the competitor's S-1 and other information indicate: 1) the most recent and most advanced clinical trial completed is a Phase II study from 2011 that did not meet statistical significance on its primary endpoint; 2) Carbylan has not submitted an IND; 3) it has conducted clinical studies only outside of the U.S.; 4) Carbylan uses 10mg of TCA in its formulation, although standard of care is 40mg; and 5) the product is hyaluronic based. While we do not dismiss any competition and will continue to watch Carbylan, we believe these are very different programs, and we believe Flexion has an attractive risk-reward profile.

Valuation & Recommendation

We maintain our $36 price target.

Price (26-Jan)	$22.53	**52-Week High**	$24.48
Target Price	$36.00	**52-Week Low**	$11.06



(FY-Dec.)	2013A	2014E	2015E	2016E
EPS	na	- $2.18	- $3.08	- $2.70
P/E		na	na	na
CFPS	na	- $2.23	- $3.14	na
P/CFPS		na	na	na
Rev. ($mm)	na	$0	$0	na
EV	$267	$865	$865	na
EBITDA ($mm)	na	-$29	-$52	na
EV/EBITDA	na	na	na	na

Quarterly EPS	**Q1**	**Q2**	**Q3**	**Q4**
2013A	na	na	na	na
2014E	-$0.85a	-$0.38a	-$0.45a	-$0.66
2015E	-$0.75	-$0.75	-$0.82	-$0.75

Dividend	$0.00	**Yield**	0.0%
Book Value	-$4.15	**Price/Book**	-5.4x
Shares O/S (mm)	14.7	**Mkt. Cap (mm)**	$331
Float O/S (mm)	14.4	**Float Cap (mm)**	$324
Wkly Vol (000s)	324	**Wkly $ Vol (mm)**	$5.5
Net Debt ($mm)	-$5	**Next Rep. Date**	na

Notes: All values in US$
First Call Mean Estimates: FLEXION THERAPEUTICS INC (US$) 2014E: -$1.97; 2015E: -$2.54; 2016E: -$2.60

Details & Analysis

We believe that Flexion is on the right track with its development program for OA knee pain.

In the past week, we have received some questions regarding Flexion and a potential competitor, Carbylan, which also is developing a product for the treatment of pain associated with the knee.

We thought it might be helpful to investors to explain what we think are some of Flexion's advantages and how they differ from the Carbylan program as described in its S-1 filing.

Flexion's Drug Is a Longer-Acting TCA

Flexion's FX006 is triamcinolone acetonide in a drug delivery formulation that helps it last longer. The components of the product are both known entities to the FDA, a steroid and the microspheres that suspend and encapsulate the steroid.

Carbylan is working on its own unique hyaluronic acid (HA) and combining it with a low dose of triamcinolone acetonide (which Flexion abbreviates as TCA and Carbylan calls TA).

The basic concept of Hydros-TA is to combine hyaluronic acid with a steroid to get the early benefit of steroids along with the later benefits of hyaluronic acid. Physicians have long been using HA and TCA as treatment for osteoarthritis and have gained comfort and familiarity with these drugs. Flexion's FX006 contains the widely used TCA in a drug delivery platform to make it last longer, while Carbylan is introducing a new and unique HA.

From a commercial standpoint, it is not clear that physicians would be willing to switch from their favorite HA, something they've been using for typically years, to a new HA with which they have no experience. In addition, if physicians want the benefit of steroids, there is nothing to stop them from mixing their preferred steroid at its standard dose with their preferred HA as many of them do now.

Flexion's Drug Fits the Current Treatment Paradigm and Addresses a Need

Each year there are about three million TCA injections into knees in the U.S. Flexion's drug will, if approved, replace regular TCA injections, which can be injected only every 12 weeks despite providing only a couple of weeks of pain relief, with Flexion's extended release formulation, which Flexion has shown could provide pain relief for up to 12 weeks. Simple – docs doing one injection continue with the same injection. The medical need is longer pain relief, not immediate pain relief. We believe FX006 addresses the longer pain relief the market needs.

Today, the standard of care is to inject 40mg of TCA, and if approved, Flexion's drug would provide the same 40mg TCA dose.

- **Flexion's FX006 comprises TCA and has been used widely for the treatment of knee OA. Carbylan's HA is, from what we can tell, a new HA.**
- **Based on the S-1 filing, it seems that Carbylan's Hydros-TA contains only 10mg of TCA, which is less than the current standard of care 40mg.**

The American Academy of Orthopedic Surgeons guidelines from May 2013 state, "we cannot recommend using HA," because of "lack of efficacy."

> "We cannot recommend using hyaluronic acid (HA) for patients with symptomatic OA of the knee…based on supporting evidence from three high-quality and 11 moderate-quality research studies that met the inclusion criteria." American Academy of Orthopedic Surgeons, *Clinical Practice Guidelines*, May 2013.

Flexion's Phase II Met Statistical Significance

Flexion has completed a Phase IIb dose-ranging clinical trial where FX006 demonstrated clinically meaningful and significantly better pain relief compared with the current injectable standard of care, TCA. In both Phase IIa synovial fluid PK studies, a single intra-articular injection of FX006 demonstrated therapeutic concentrations of drug in joint fluid for at least 12 weeks.

Carbylan's study (COR1.0 Phase IIb) did not meet statistical significance, according to its S-1. It does not appear that any p-values are provided in the S-1 for the COR1.0 study at 26 weeks, the primary endpoint of the study. We assume that Carbylan must have the p-values for its primary endpoint for this study at the different time points, including at 26 weeks. To assess the data, we would like to know the p-values.

In the S-1 it states, "While there was not a statistically significant difference between Hydros-TA and Hydros over 26 weeks, there was a statistically significant 12.4 mm improvement in pain scores at the two-week time point for Hydros-TA versus Hydros (p=0.04)."

Flexion believes that it is important to show a benefit over standard of care over an extended period of time, and Carbylan's two-week benefit, let alone benefit over its own HA and not standard of care, is not how Flexion chose to design its own trials. Flexion believes that one must be able to show that the formulation with TA is better than TA alone.

Flexion Has Already Navigated the IND Process

Flexion already went through the IND process several years ago. It should be noted that according to Flexion, following very good pre-IND meetings, Flexion filed its IND, the agency had questions that needed to be addressed, and it delayed its development plan by months. An IND review often includes a review of critical pre-clinical data (including toxicology) and the clinical data in detail. It is at that stage the FDA can ask for a lot of additional study or a new direction in the clinical program, and this can add significant time to the clinical development.

Flexion's Data Is from U.S. Sites

Flexion's clinical data is being generated globally, with a representation in the critical U.S. market. We believe having U.S. physician exposure prior to approval can help the commercial success (and clinical success) of a drug in development.

All of Carbylan's Phase IIb (COR1.0) previous clinical study sites (Phase II), and all of its current ongoing Phase III study sites (COR1.1) are outside the U.S. (only Australia, Canada, New Zealand, Europe, and the Caribbean). Carbylan hopes to start another Phase III (COR1.2) study in mid-2015 and include U.S. sites.

It is interesting that in the July 2011 press release it states, "The COR1.0 clinical trial was conducted at eight clinical sites in Canada, Belgium, and the Netherlands." However, in the S-1 it states that the COR1.0 trial "was conducted in eight clinical centers in Canada, Europe, and the Caribbean." Somewhere along the line, the Caribbean was added, yet the number of study sites (8) and the number of patients (98) remained the same.

Flexion's Timeline Is Clear

Flexion expects to have top-line data in hand in 2H15 from its Phase IIb trial and Flexion's Phase III should begin, as expected, in early 2015 and deliver results in 1H16. Overall, the clinical program is moving ahead well.

In July 2011, Carbylan stated that it "plans to begin evaluating Hydros-TA in a large, multi-center trial in the U.S. in 2012." Most recently in the S-1, the timeline has stated that it will begin in 2015.

Flexion's Endpoints Are Clear

Flexion's Phase III trial, a 12-week study like the Phase IIb, is an international, multi-center, randomized, blinded, single-dose study in 462 patients with OA of the knee. There will be three arms that include a 40mg dose of FX006, placebo, and a 40mg dose of immediate-release TCA. The primary objective of the trial will be to provide the second pivotal efficacy dataset against placebo at 12 weeks for an NDA submission. In addition, the trial will provide a key comparative dataset against the current standard of care, 40mg immediate-release TCA. Because TCA is not believed to last for 26 weeks, Flexion chose a shorter duration for its studies.

Flexion has stated that it believes it is critical to test its product and that any product seeking approval will have to test against the 40mg standard of care.

Carbylan is comparing in a clinical trial Hydros-TA (which is its own HA coupled with 10mg of triamcinolone acetonide) versus Hydros alone versus TA (10mg alone). Hydros is an unapproved new molecular entity (according to the S-1). The 10mg. dose of TCA is below the most commonly used standard of care dosage.

Dose Range

Flexion's FX006 demonstrated clinically meaningful and significantly better pain relief compared with the current injectable standard of care in a completed Phase IIb dose-ranging clinical trial. Flexion had originally planned on doing a planned repeat-dose safety clinical trial in 2H14 with a one-year follow-up; however, the FDA announced in September 2014 that it will no longer require data from a repeat-dose safety trial of FX006 for approval. The FDA indicated to Flexion that the company's ongoing Phase IIb confirmatory trial of FX006 (the data readout of the

ongoing study will be in the 2H15), along with data from the Phase III trial, will suffice for registration as a single-dose administration. Flexion believes that it is important to show the FDA the rationale for the doses selected and to be able to answer how higher or lower doses might perform in terms of pain relief, which Flexion has done in a previous study.

We are not certain there has been any dose-ranging studies conducted to date with Carbylan's Hydros TA.

Flexion Has Recent Data to Back Up Claims of Duration in Joint

Flexion released data on the synovial fluid study that showed that FX006 may provide pain relief for three months or more. This data, we believe, was very important (second only to Phase III data) as it shows the likelihood of the drug's meeting the clinical need – lasting longer than the current therapy. Flexion believes that it is important for the FDA to have data that shows how long a compound stays within the joint. We believe Flexion's synovial PK study was critical in establishing this duration.

Flexion believes that data in a Carbylan patent entitled "modified hyaluronic acid polymer compositions and related methods" (more specifically described and depicted in the patent as Figures 4 and Example 16) seems to indicate that the steroid TA is released fully by approximately day 14 (datapoint 12).

Summary

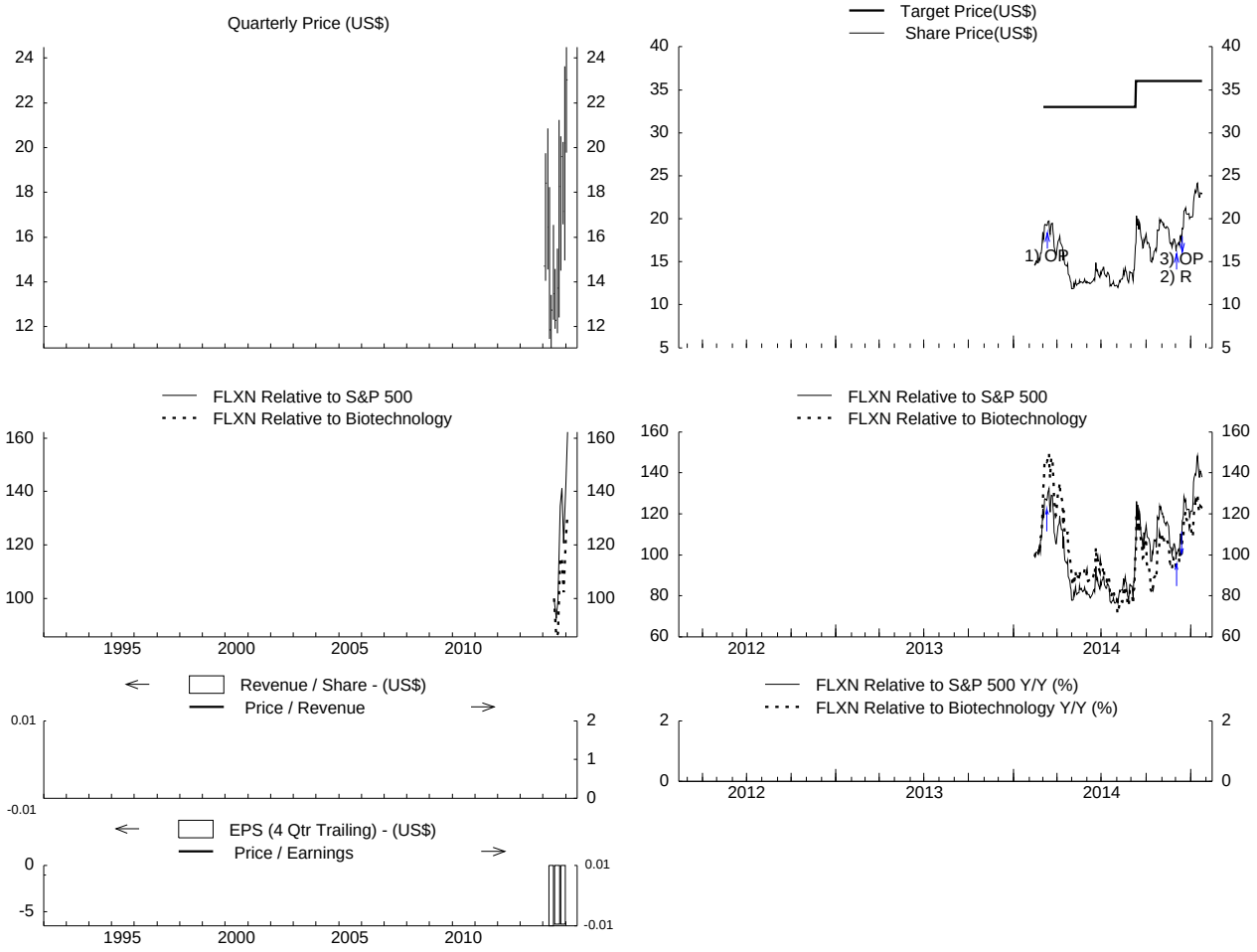
In summary, we never dismiss potential competition, but based on our review, we believe Flexion's approach differs significantly from the competition mentioned. We believe that Flexion is doing the right things to move its program ahead in a sound manner. We think that Flexion's potential benefit in duration addresses a medical need. This is not to say that Flexion and its development program do not have risks – we have outlined those in previous notes and reports. A product is not approved until it is approved, and until it is, there is risk of non-approval and its potential consequences should be considered carefully by investors. That said, to minimize clinical and commercial risks, the clinical program should be sound and driven by a clear understanding of the FDA requirements (including an IND process) and current medical need and clinical practice. Ideally, the clinical program is run by opinion leaders in key markets, who will help shape and drive the key insights needed to shape the development program. We believe Flexion has taken those steps.

We maintain our $36 price target and Outperform rating.

Companies mentioned (priced as of the close on March XX, 2015):

Company Name (TKR, $X.XX, Rating/Not Rated)
Company Name (TKR, $X.XX, Rating/Not Rated)
Company Name (TKR, $X.XX, Rating/Not Rated)

Flexion Therapeutics (FLXN)



FYE (Dec.)	EPS US$	P/E Hi - Lo	DPS US$	Yield% Hi - Lo	Payout %	BV US$	P/B Hi - Lo	ROE %
Range*:		na na		NC			>15 >15	
Current*	-6.33	na	0.00	0.0	0	-4.2	-4.9	

FLXN - Rating as of 11-Feb-14 = NR

	Date	Rating Change	Share Price
1	11-Mar-14	NR to OP	$19.29
2	2-Dec-14	OP to R	$16.85
3	12-Dec-14	R to OP	$18.91

* Current EPS is the 4 Quarter Trailing to Q3/2014.
* Valuation metrics are based on high and low for the fiscal year.
* Range indicates the valuation range for the period presented above.

Last Price (January 22, 2015): $23.02
Sources: IHS Global Insight, Thomson Reuters, BMO Capital Markets.

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Methodology: We arrive at our target price using a discounted cash flow analysis, as well as a sector multiple applied to discounted earnings.
Risks: In addition to the normal risks inherent in pharmaceutical companies, such as regulatory, reimbursement, and competitive risks, our valuation of FLXN carries several other risks. Among the risks to our valuation is FLXN's dependence on approval of their lead product and anticipated sales and profitability to drive the value of FLXN.
Unseen side effects, safety issues, and competitive threats have not been taken into account in our valuation and if any of these were to emerge, it is likely FLXN shares would be significantly and negatively impacted. FLXN is currently running at a substantial loss, and with this fact comes several other risks, including the potential need for financing. One cannot be certain that FLXN would be able to secure additional financing and at what cost. Our valuation includes a value for the current pipeline of additional products FLXN is investigating. We have estimated a public market value for these assets based on what a similar company might be valued in a public market. Less is known about these programs relative to FLXN's lead program and given their early naure, they carry substantial development risk.
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Buy	Outperform	43.4%	16.2%	60.6%	42.6%	51.7%	55.6%
Hold	Market Perform	52.6%	8.1%	36.6%	53.0%	45.8%	39.5%
Sell	Underperform	3.9%	8.3%	2.8%	4.5%	2.5%	4.9%

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