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U.S. Generics: FDA Policy Changes, Growing Use of 505b2, and Supply Shortages; Topics from a Roundtable Discussion

Ticker	Rating	CUR	14 Mar 2014 Closing Price	Target Price	TTM Rel. Perf.	EPS 2013A	EPS 2014E	EPS 2015E	P/E 2013A	P/E 2014E	P/E 2015E	Yield
HSP	M	USD	42.10	37.00	14.9%	2.01	2.09	2.17	20.9	20.1	19.4	NA
MYL	O	USD	52.63	61.00	51.9%	2.89	3.47	4.06	18.2	15.2	13.0	NA
TEVA	O	USD	48.88	50.00	1.3%	5.00	4.28	3.64	9.8	11.4	13.4	2.8%
ACT	O	USD	214.52	225.00	117.8%	6.00	9.37	12.80	35.8	22.9	16.8	NA
SPX			1841.13			108.65	117.83	130.73	16.9	15.6	14.1	2.0%

O – Outperform, M – Market-Perform, U – Underperform, N – Not Rated

Highlights

On March 11, 2014 we hosted a round table symposium with management from several generic companies as well as industry experts. This note summarizes our takeaways from the event.

- **FDA approval process.** The agency has two big overlapping efforts underway: implementing GDUFA and increasing product quality. The changes are driving some industry dynamics:
  - From July 2014 forwards, ANDA applicants will need to show batch stability on three batches for six months as opposed to one batch for three months. As a result, R&D teams are working round the clock to submit before July. Participants predicted a 2Q14 bolus of filing ("full year worth") and noted that going forwards upfront cost may keep the marginal participant off market (in small products, for late entrants who expect lower share and profit it may be too costly to make three batches and wait several years for approval).
  - As part of GDUFA, FDA promised to respond to 60% of ANDA filings made after October 1st 2014 within 15 months (currently files are reviewed in ~36 months on average). An alternative strategy to filing before July is to wait and file in October to be included in the fast review pool. As FDA is likely to pick and choose easy applications, this is a good strategy for re-filing modifications to existing products which are included in statistics.
  - The two tier ANDA review model is now in effect. Product in short supply, first filers and complex products are reviewed faster. In some cases (e.g. shortage injectables) this has become a strategy – focus on complex product to get faster facility inspections and approvals. Products not being reviewed under accelerated process take 36 months to 40 months before FDA issues approval or response letters. This later pool will take some time to get better. The agency made lots of new hires who will take time to come up to speed. There is increasing reliance on non-OGD reviewers, which are also reviewing NDA filings which are inherently more interesting and generate more fees. Thus ANDA files may be reviewed slower.
  - The FDA is increasingly issuing many more refuse to receive (RTR) letters and quick to issue complete response letters (CRLs). If an application gets rejected twice, it is 'out of the queue' – FDA does not include it in its metrics (and thus it moves to the back of the line). There is thus real effort to make sure every submission is pristine. Fewer applications are/will be made, but with higher quality. This will lead to approvals on new products becoming more staggered, not as many simultaneous

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launches. We note that since the start of the fiscal year (Oct. '13) to Feb. '14, FDA approved/tentatively approved 196 applications, issued 582 CRLs and 56 RTRs.

- **Quality and pricing.** In general, all speakers agreed pricing will be stable, if not increasing.
  - First, prices will increase because of the higher spend on quality manufacturing and quality by design development costs (30%-50% higher). This is true for both API and finished good. Manufacturers are now ready to exit unprofitable products and thus prices adjust to reasonable levels.
  - FDA is looking to increase inspections internationally to parity with the US. The question is whether this will lead to shortages as additional companies face import bans (Depakote ER was a recent shortage example caused by import ban on Wockhardt). Some speakers noted most large Indian companies have been inspected regularly already, others suggested it is likely someone will find itself in trouble if only as a matter of statistics (you can always find a fault).
  - The delays and uncertainties in approvals are also causing prices to rise. Companies with products that are approved are in a better negotiating position as buyers are less certain when other supplies will be approved. Further, staggered entry of products usually translates to more pricing discipline (see the case of Cymbalta).
  - Are buyers not pushing for lower prices, especially now that they are consolidating? Well, there is pressure on the low end commodity products where supply is abundant. However, these large companies need a lot of product and are concerned about quality and reliable supply ('we had a lot more factory tours and some tours of our API suppliers'). Prices have to be competitive, but if roughly at the same range 'buyers are not looking right now at the last penny'.
  - Specifically on injectables, prices are up 20% YoY in the injectable segment as result of shortages (SCB analysis). In this segment, industry folks are still seeing sporadic shortages and companies are able to take advantage of them to raise prices. Some companies are planning inventory and manufacturing schedule with some slack to be able to take advantage of potential future shortages. There was a divergence of opinions about the five-year view of the generic segment, with some projecting over-capacity and cyclical price decline while others being more optimistic.
- **Concerns on labeling.** As a reminder, because current FDA regulations require generic labels to be identical to innovators, patients can't sue the generic companies for failure to warn about risks of the products they sell (SCOTUS Mensing decision). There is now a proposed FDA rule to allow generics to change their label, opening them to lawsuits. All speakers were adamant this is a very bad idea and (i) believed the initiative was politically motivated coming from the trial lawyers lobby, not FDA; (ii) suggested the industry will sue FDA if the rule is finalized; (iii) argued they will have to raise prices to cover additional insurance costs and (iv) to be safe, they will add warning to their label each time they get a customer complaint and "you will end up with two pages of warnings". (v) Those with more faith in the government believed the law will not pass, others were more skeptical.
- **505b2 is becoming a big focus.** One of the meetings focused exclusively on 505b2 but it came up with all companies. We learned that 505b2 is a broad umbrella – allowing an applicant to rely on any data outside its own submission for approval (not just an NDA by another company) and the agency has been liberal in allowing filings with data coming from various sources (OUS experience, papers) – sometimes with very limited need for new clinical data. The companies noted that (i) 505b2 guarantees rapid review (no 36 month backlog) and can result in substitutable product; (ii) they are now convinced they can market products with modest sales forces in some specialties (under 100 reps). Also (iii) this is far from being a generic industry-only approach. Big pharma is pushing into the 505b2 in a big way – see Androgel. Two examples discussed were: (i) the GLP-1 – "why would you want to make a generic Victoza when you can improve on it?" as an applicable strategy for large company; (ii) Opana ER as

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example of capturing share with 505b2. The 505b2 product (Oxymorphone XR) was able to reach 20% market share without a sales force, by electronic marketing to physicians.

- **Product insights.** We apologize in advance for masking the source of the comments, as speakers preferred not to be identified.
  - **Victoza and GLP-1 generics**. Byetta generics were filed. A couple of speakers predicted 'two to three submissions' were made on Victoza on the 4-year anniversary of the product (Jan 25th 2014), while others noted this is a challenging product and argued there are submissions, but they are primarily 505b2.
  - **Mesalamines**. There were several companies predicting 2015 approvals for several of the oral products (Asacol, Lialda, Pentasa) and near term filing on Delzicol.
  - **Restasis**. We asked in every meeting about interest in Allergan's ophthalmic emulsion. None of the speakers were aware of filings, all noting this is a difficult product. Perrigo specifically stated they are not developing Restasis, which came to us as a surprise.
  - **Neupogen** is being submitted to FDA in 2Q14 by one company without efficacy trials (PK/PD only). The same product will be submitted in the EU this year. The same company expects to submit Neulasta in time for US market openings.
  - **Copaxone**. At least one additional company filed recently. Another comment (from a person not currently affiliated with any company involved with Copaxone) was for high confidence in Sandoz product approvability near term, while predicting delay of Mylan's product. The rationale for Mylan's product delay is that the tests done by Teva on overseas material suggest Natco/Mylan's product has an incomplete deprotection step (part of the synthesis) which would require process redesign and re-submission of the application. We note Mylan's recent statements that it successfully fixed the original product marketed OUS.
  - **GHB**. Generics for the Jazz products are being held back by REMS program, but are otherwise approvable. The generics are working through the process of convincing FDA to let them do separate REMS than the innovator (a repeat of the Suboxone saga). They are predicting 2015 approval.
  - **Additional filings** also for Lovenox, Lidoderm, Duragesic, Amphetamines.

Investment Conclusion

The discussion made us a bit more confident about the near term future of the generic industry. The stronger prices we have seen in injectable segments are creeping into oral generics and we may be in 1-2 years of price stability or even net price increases. This is a positive for all our generic coverage names and in particular Mylan, which is most exposed to this segment. That said, there is a wave of new entries into the differentiated product segment which suggests that in 3-5 years we may see broader pressure (especially if the FDA sticks to its approval timelines and more products come to market, faster).

We have also become a convert for the value of 505b2 products. Starting early in the year we became aware that essentially all generics are heading in that direction. The discussions at DCAT provided us with a logical foundation for the trend. We now understand much better why Teva believes 'industrializing NTE' is a viable approach and can see the strategy working in specific specialties (pain, respiratory, ophthalmics, dermatology). This will be an execution story for the generics entering new specialties and we also see nice opportunities for incumbent branded companies like Allergan and Valeant in dermatology to fill their pipelines quickly via partnerships with some of these companies.

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We currently have outperform ratings on Teva, Actavis and Mylan with price targets of $50, $225 and $61. Hospira is rated market-perform with PT $37.

Details

See above.

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Valuation Methodology

U.S. Pharmaceuticals/Specialty

We value generic companies on next year EPS multiples. Companies with diverse revenue sources and better strategic positions are given a higher multiple.

Teva Pharmaceutical Industries Ltd

Based on our Teva 2015 EPS of $3.64, we arrive at a target price of $50 (~13.5x).

Mylan Laboratories Inc

Mylan is a core generic name. Based our 2015 EPS of $4.06, we arrive at a target price of $61 (~15x).

Hospira Inc

Hospira is in a long term transition. We arrive at a price target of $37 is based on ~10x our 2017 EPS of $3.42.

Actavis Pharmaceuticals Inc

Based on our Actavis 2015 EPS of $12.80, we arrive at a target price of $225 (~17x).

Risks

U.S. Pharmaceuticals/Specialty

Actavis Pharmaceuticals Inc

The key downside risks to our Actavis thesis and to our target price are:

i) More than expected pricing pressure in the differentiated generics business.

ii) More than expected competition in the international businesses Actavis participates in.

Hospira Inc

The key risks to our Hospira thesis and to our target price are:

Downside

i) Failure to remediate injectable generic and/or infusion pump manufacturing

ii) Company inability to execute its OUS growth initiative

iii) Growing competition in the injectable generic space

Upside

i) Quicker time to remediate SIP and pumps than expected

ii) Success in the biosimilar market

Mylan Laboratories Inc

The downside risks to our Mylan thesis and target price are:

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i) No differentiated opportunities from the company's undisclosed generic pipeline.

ii) Competition in the commodity segment is more severe than we anticipated.

iii) Manufacturing issues appear in one of the company's main sites.

iv) Delay in approval of generic Lidoderm, Advair, Insulins or Copaxone.

Teva Pharmaceutical Industries Ltd

The downside risks to Teva achieving our price target are:

i) Deterioration of Copaxone revenue due to rapid entry and adoption of oral MS agents (Gilenya, BG12).

ii) Inability to monetize its Paragraph IV portfolio or adverse rulings and substantial fines on at-risk launches.

iii) Intensifying global competition in commodity generics beyond our current estimates.

iv) Failure of late stage branded/specialty/biosimilars programs.

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  Outperform: Stock will outpace the market index by more than 15 pp in the year ahead.

  Market-Perform: Stock will perform in line with the market index to within +/-15 pp in the year ahead.

  Underperform: Stock will trail the performance of the market index by more than 15 pp in the year ahead.

  Not Rated: The stock Rating, Target Price and estimates (if any) have been suspended temporarily.
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12-Month Rating History as of 03/16/2014

Ticker	Rating Changes		
ACT	O (RC) 06/22/12		
HSP	M (RC) 12/19/11		
MYL	O (RC) 09/10/13	M (RC) 03/25/13	O (RC) 08/09/10
TEVA	O (RC) 05/09/11		

Rating Guide: O - Outperform, M - Market-Perform, U - Underperform, N - Not Rated
Rating Actions: IC - Initiated Coverage, DC - Dropped Coverage, RC - Rating Change

HSP / Hospira Inc

Date	Rating	Target(USD)
02/03/11	O	57.00
03/21/11	O	60.00
04/27/11	O	63.00
09/15/11	O	49.00
10/19/11	O	40.00
11/30/11	O	36.00
12/19/11	M	32.00
06/28/13	M	37.00

MYL / Mylan Inc

Date	Rating	Target(USD)
01/31/11	O	26.00
04/25/11	O	28.00
01/02/13	O	31.00
02/27/13	O	33.00
03/25/13	M	33.00
07/29/13	M	35.00
09/10/13	O	44.00
01/02/14	O	48.00

TEVA / Teva Pharmaceutical Industries Ltd

Date	Rating	Target(USD)
01/31/11	M	58.00
04/22/11	M	53.00
05/09/11	O	55.00
12/12/12	O	50.00
05/10/13	O	47.00
10/30/13	O	43.00
01/23/14	O	50.00

ACT / Actavis plc

Date	Rating	Target(USD)
01/24/11	M	56.00
04/28/11	M	64.00
06/30/11	M	68.00
07/26/11	M	68.00
01/21/12	M	64.00
04/26/12	M	80.00
06/22/12	O	82.00
07/20/12	O	86.00
08/22/12	O	89.00
10/22/12	O	99.00
04/11/13	O	105.00
05/03/13	O	118.00
05/28/13	O	135.00
06/28/13	O	140.00
10/10/13	O	161.00
01/02/14	O	180.00

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