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U.S. Pharmaceutical/Biotech Industry Update

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〈Summary〉

○ Macro trends of the U.S. pharmaceutical industry remain challenging. In 2012, U.S. pharma sales decreased by 1% to reach $325.8bn. Healthcare utilization in terms of office and non-emergency hospital visits continued to decline. There was also increasing headwind from greater use of generics, lower levels of price increases and reduced spending on new medicine. U.S. pharmaceutical spending is expected to be flat to slightly up for 2013. Sales of specialty drugs continue to grow robustly (close to 20%), while primary care drugs languish in decline. By 2019-2020, half of pharma sales will be from specialty drugs.

○ On the other hand, there have been some favorable developments for the industry, including a more accommodative FDA, industry having past the 2012 patent cliff, and a generally improving R&D pipeline.

○ On the M&A front, many deals in the recent past have boosted big pharma's pipelines. With the recent run-up in biotech stock price, valuation has become more challenging for pharma to consider M&A. In lieu of licensing or acquisition of biotech companies, large pharma are increasingly pursuing peer alliances, which have created value in the industry.

○ Biotech has enjoyed buoyed stock price, and IPO window has opened wider for high-quality companies. Biotech companies have taken advantage of the favorable financing condition by raising a large amount of funding from public investors. Oncology and orphan drug biotech companies have performed especially well, which highlights the attraction of specialty medicine.

○ With the peak of LOEs behind them, generic players are putting their emphasis on high-barrier generics as well as the specialty pharma side of their business. Biosimilar represents a huge opportunity. Companies need to make significant investments in developing biosimilars. Therefore many alliances have formed.

EXECUTIVE SUMMARY

- **Macro trend of the pharmaceutical industry remains challenging.** In 2012, U.S. pharma sales decreased by 1% to reach $325.8bn. Patent cliff in 2012 was a big contributor. There were also lower levels of price increases and reduced spending on new medicine Healthcare utilization in terms of office and non-emergency hospital visits continued to decline. In 2013, we will likely see flat to modest growth in the 0-1% range, as low single-digit volume growth is offset by price erosion due to genericization. In 2014, due to the implementation of ACA, we will see a bump-up in growth rate. However, the one-time boost is unlikely to alter the fundamental weakness in drivers behind pharmaceutical market. Within pharma market, continuing the pattern from recent years, growth in specialty drugs will continue to significantly outpace primary care medicines. Express Scripts forecast for its commercial business, specialty drugs will grow at close 20% per annum while traditional drugs will decline by 1-2% per annum. As a result, specialty drugs will represent 50% of drug expenditure by 2019-2020.

- **The friendly regulatory environment is a positive for the industry. Since the fall of 2011, we have observed the U.S. FDA has become more accommodative to the industry.** Initially this was reflected in the changed regulatory stance for obesity drugs. The record number of NME approvals in 2012 and 2013 also attest to this trend. In the reauthorization of PDUFA V, biotech industry has secured an approval pathway through the greater use of accelerated approval based on surrogate endpoints, which could lead to faster drug approvals. There is also a new "breakthrough" designation to expedite high-priority drug development.

- **Post 2012 patent cliff, large pharma is looking forward with an improving R&D pipeline.** Large pharma have passed the peak of LOEs in 2012. Although most large pharma are looking at 2012 patent cliff in the rear view mirror, in 2013 pharma are still annualizing the LOEs occurred in 2012. Therefore a number of large pharma are expecting declining annual sales. On the R&D front, late-stage pipeline attrition has continued unabated. However, several pharma companies appear to be flush for their R&D portfolios. One showcase of large pharma's R&D prowess is in the oncology area. Large pharma are leading the industry in cancer immunotherapy (i.e., targeting PD1, PD L1and other immune checkpoints). GSK has developed two novel therapies for melanoma in house that will become the standard of care. In contrast, biotech companies that have traditionally been innovative in cancer seem to be busy acquiring compounds cast off by big pharma. While the center of gravity in cancer research seems to have shifted from biotech to pharma, the orphan drug field is still dominated by many innovative biotech companies. Many biotech companies in orphan disease field have seen their market capitalizations grow substantially over the last year. Big pharma are taking notice and have been buying into the space through acquisitions, partnership, or venture funding.

- **Many flavors of deals have boosted big pharma's pipeline.** On the M&A front, large biopharma are reaping the rewards of good acquisitions they made in the past. In hindsight, biopharma struck a number of good deals in the 2011-2012 timeframe. With the recent big run-up in biotech stock price, valuation has become almost prohibitive for acquisitions in hot areas such as oncology and orphan drugs. In lieu to licensing from or acquiring biotech companies, large pharma are increasingly pursuing peer alliances. This trend has often led to win-win scenarios for participants.

- **Biotech has enjoyed buoyed stock price, and IPO window has opened wider for high-quality companies.** After a prolonged period of depressed valuation, big biotech companies have enjoyed a significant rerating in their valuation. All major biotech companies have enjoyed a jump in their share price, which is supported by their solid and improving businesses. Small biotech companies also experienced appreciating share prices, which helped them raise a record amount of follow-on offerings. Strong post-market performance of recent IPOs has opened the IPO window for a broader array of biotech companies.

- **With the peak of LOEs behind them, generic players are actively looking outside for new areas for growth.** Given some headwinds within the generic industry (i.e., lack of new blockbusters, price competition for commodity generics, negative developments on the legal front), generic players are increasing looking outside of the core small molecule generics market for growth. Within generic space, they are investing in high-barrier generics, including biosimilars, respiratory drugs, patch, injectable drugs, etc. They are also diversifying outside of the generic industry to specialty pharma. A major opportunity lies in biosimilars. $70-80bn worth of biologic drugs will lose exclusivity by the end of this decade. Recent approval of biosmilar Remicade in Europe highlights the progresses biosimilars have made. We expect more deals to come.

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A. Long-term Healthcare Spending Forecast by CMS

In their annual forecast of U.S. Healthcare spending (see Table 1), CMS researchers estimate National Health Expenditure (NHE) increased at the same pace as GDP (3.9%) in 2011. Health spending is projected to grow modestly at 4.2% and 3.8% respectively in 2012 and 2013. Then in 2014, with the implementation of ACA, national health spending is projected to rise by 7.4% or 2.1% faster than the case in the absence of reform. From 2015-2021, NHE is projected to grow at 6.2% annually, faster than the 5% CAGR forecasted for the GDP growth.

Prescription drug spending is estimated to grow by 3.9% in 2011 to reach $269.2bn. Growth in drug spending is expected to moderate to 2.9% in 2012 and 2.4% in 2013 respectively because of patent expiries. In 2014, due to the implementation of ACA, prescription drug spending is expected to increase by 8.8% (4.7% faster than in the absence of ACA). In 2015-2021, the diminished impact of patent expirations and increased use of specialty drugs are expected to drive drug spending growth to an average of 6.6% per year.

Table 1 Projected Health Spending in the U.S.

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2015-2021 CAGR
NHE ($trillion)	$2.6	$2.7	$2.8	$2.9	$3.1	$3.3	$3.5	$3.7	$3.9	$4.2	$4.5	$4.8	
% growth	*3.9%*	*3.9%*	*4.2%*	*3.8%*	*7.4%*	*5.7%*	*6.3%*	*5.9%*	*3.5%*	*9.2%*	*6.7%*	*6.5%*	*6.2%*
GDP ($trillion)	$14.5	$15.1	$15.7	$16.4	$17.2	$18.2	$19.2	$20.2	$21.3	$22.3	$23.0	$24.4	
% growth	*4.2%*	*3.9%*	*4.0%*	*4.4%*	*5.1%*	*5.7%*	*5.6%*	*5.3%*	*5.2%*	*4.8%*	*3.2%*	*5.9%*	
NHE % GDP	17.9%	17.9%	17.9%	17.8%	18.2%	18.2%	18.3%	18.4%	18.1%	18.9%	19.5%	19.6%	5.0%
Hospital Care ($bn)	$814.0	$848.9	$884.7	$920.7	$982.7	$1,038.3	$1,106.6	$1,170.7	$1,240.0	$1,317.7	$1,404.1	$1,495.7	
% growth	*4.9%*	*4.3%*	*4.2%*	*4.1%*	*6.7%*	*5.7%*	*6.6%*	*5.8%*	*5.9%*	*6.3%*	*6.6%*	*6.5%*	
Home Health Care ($bn)	70.2	72.9	77.5	81.9	88.3	94.5	101.2	108.4	117.1	126.6	137	148.3	
% growth	*6.2%*	*3.9%*	*6.4%*	*5.7%*	*7.8%*	*6.9%*	*7.1%*	*7.1%*	*8.1%*	*8.1%*	*8.2%*	*8.3%*	
Nursing Care Facilities and Continuing Care Home Health Care	143.1	151.3	155.2	163.2	172	181.1	191	201.7	213.6	226.2	239.9	255	
% growth	*3.2%*	*5.8%*	*2.6%*	*5.1%*	*5.4%*	*5.3%*	*5.5%*	*5.6%*	*5.9%*	*5.9%*	*6.0%*	*6.3%*	
Prescription drugs ($bn)	259.1	269.2	277.1	283.7	308.7	327.3	347.8	371.1	394.9	420.9	450.7	483.2	
% growth	*1.2%*	*3.9%*	*2.9%*	*2.4%*	*8.8%*	*6.0%*	*6.2%*	*6.7%*	*6.4%*	*6.6%*	*7.1%*	*7.2%*	*6.6%*

Source: Compiled by MHBK/IRD based on data from CMS National Health Expenditure Projections 2011-2021

Recent research by healthcare economist David Cutler has suggested there may be a permanent downward shift in the growth of the healthcare spending beyond the impact of the recession. Several structural changes may be occurring to bend the cost curve downward. These include the slowing of technology innovation; high cost sharing for patients (e.g., people under consumer-directed health plan /CDHP increased from 8% of insured population in 2008 to 19% insured population in 2012); greater provider efficiency. This emerging trend may not have been adequately incorporated into CMS's official forecast as shown above. CMS forecasts mostly subdued spending growth to 2018 but a tick-up after 2018. If the slow growth trend from 2009-2012 continues, CMS forecast may overshoot by as much as $770bn over the ten year period from 2012-2021 and by $401bn or 14% in 2021 (David M. Cutler and Nikhil R. Sahni, *Health Affairs*, May 2013).

One critical driver of U.S. healthcare spending is ACA. In February, Congressional Budge Office (CBO) released updated estimate of ACA (see Table 2). In an 11-year forecast span, ACA is expected to inject on average $120bn a year into the U.S. healthcare system. Many constituencies in healthcare including pharmaceuticals will benefit.

Table 2 CBO's February 2013 Estimate of the Budgetary Effects of ACA

Effects on The Federal Deficit ($bn)	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2013-2023 Total
Medicaid and CHIP Outlays	2	17	37	54	62	68	72	75	79	84	89	638
Exchange Subsidies and Related Spending	4	28	55	96	122	137	143	147	154	161	169	1,216
Small-Employer Tax Credits	2	3	4	3	1	2	2	2	2	2	2	26
Gross Cost of Coverage Provision	7	47	96	153	186	206	217	224	236	247	260	1,879
Penalty Payments by Uninsured Individuals	0	0	-3	-5	-6	-6	-6	-6	-7	-7	-7	-52
Penalty Payments by Employers	0	-5	-10	-12	-14	-16	-17	-18	-19	-20	-56	-150
Excise Tax on High-Premium Insurance Plans	0	0	0	0	0	-10	-17	-21	-25	-30	-33	-137
Other Effects on Tax Revenues and Outlays	-1	-1	-2	-9	-18	-24	-28	-31	-32	-32	-33	-211
Net Cost of Coverage Provision	6	41	81	127	148	151	149	149	154	159	164	1,329

Source: Compiled by MHBK/IRD based on data from Congressional Budget Office.
Note: Estimates above do not include effects on the deficit of other provisions of the ACA that are not related to coverage, which in the aggregate reduce deficits.

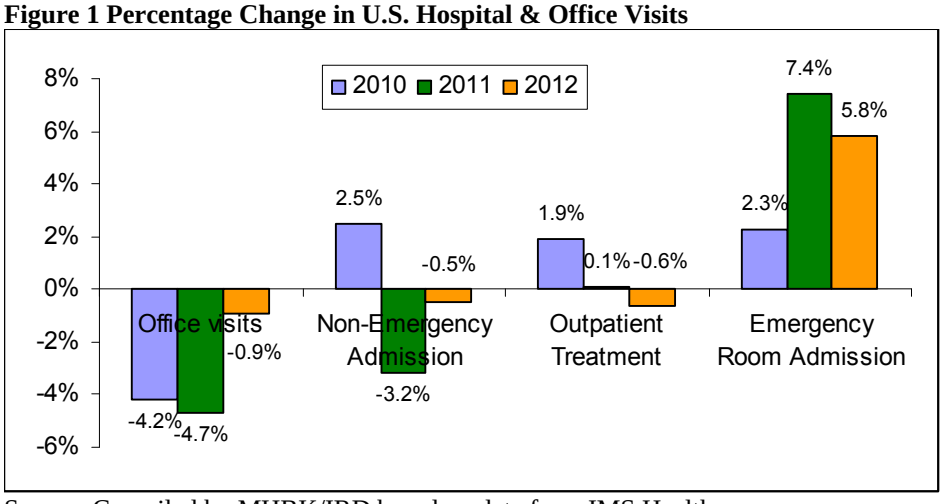
B. U.S. Pharmaceutical Industry Growth Trend

According to IMS Health, U.S. pharmaceutical market declined by 1% to $325.8bn in 2012. We note the big difference between the statistics of CMS (above in session A) and IMS is due to different methodologies. In general, industry participants have relied on IMS data as they are collected from bottom-up. We use CMS data to primarily look at trend of growth in a big picture. Patent cliff in 2012 was a major contributor to the sales decline. Utilization of healthcare continued to be subdued in the U.S. (see Figure 1). Patient office visits declined by 0.9% in 2012, which was a moderation from the prior two years. Non-emergency admission visits was down 0.5%. To make up for the less care delivered through these two channels, emergency room admissions grew by 5.8%.

Another headwind for healthcare utilization is caused by employers' continued cost shift to consumers. Consumer-driver health plans (CDHP), typically with high deductibles and 20% or more co-insurance after reaching a deductible, now count for 19% of insured population, which is up from 8% in 2008. For total medical expenses, patient out-of-pocket costs have risen more than three times from an average of $326 in 2008 to $1,146 last year.

On a real per capita basis, spending on medicines declined by 3.5% in 2012, which is a result of declining use of branded drugs, greater availability of generics, lower levels of price increases and reduced spending on new medicines. Helped by the record amount of LOEs (loss of exclusivities) in 2012, generic penetration continued its march upward, reaching 84%, a 4% increase from 80% in 2010. Generics now make up 28% of total spending. IMS Health forecasts generic usage will reach 87% by 2017.

Figure 1 Percentage Change in U.S. Hospital & Office Visits



Source: Compiled by MHBK/IRD based on data from IMS Health

Continuing the recent trend, growth of specialty medicine has outstripped primary care medicine (see Table 3). The trend began 5-10 years ago and has picked up pace recently given the widening gap between the two classes medicines. The main factors contributing to the gap include:

- Patent expiries have substantially eroded value of primary care medicine. Meanwhile specialty drugs are often biologics and so far have escaped from significant generic erosion.
- Innovation in primary care medicine is often hard as existing drugs set a high bar. Examples include the dyslipidemia market and gastric ulcer market. Many late-stage projects for primary care market have failed. Meanwhile, there exist high unmet medical needs in specialty diseases and innovation is easy to clear low hurdle.
- Because of the different value proposition, specialty medicine has enjoyed good pricing power. Manufacturers in areas such as multiple sclerosis, inflammatory disease, orphan drugs and oncology often adopt aggressive pricing at launch and follow with substantial annual price increases. Meanwhile, the multiple alternatives in primary care medicine means payers can play one against another using formularies. As a result, price decline every year. However, the favorable environment for specialty drugs may be changing. In some cases, as recently pointed out by Express Scripts, there are enough drugs approved in a class that will allow pharmacy benefit managers (PBMs) to use formularies to rein in drug spending. There was also new pushback by doctors for excessively pricing at drug launch. One example was Bayer's colorectal cancer drug Stivaga. With pushback from prominent oncologists, Bayer had to backtrack on pricing and cut the price in half for patients.

Table 3 Difference in Growth Rates between Traditional and Specialty Medicine

	2012	2013E	2014E	2015E
Traditional medicine	-1.5%	-1.0%	-1.7%	-1.4%
Specialty medicine	18.4%	17.8%	19.6%	18.4%

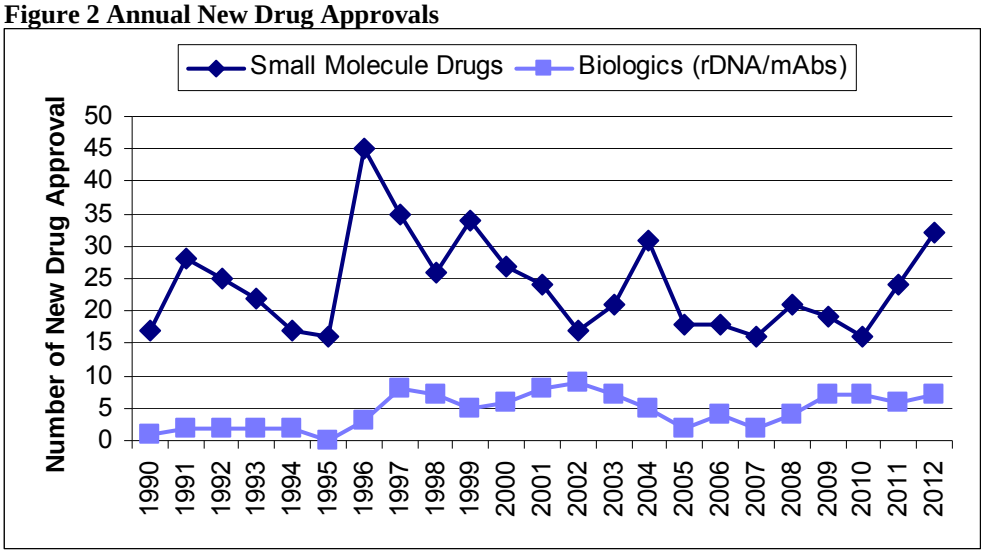
Source: Compiled by MHBK/IRD based on data from Express Scripts 2013 Drug Trend Report

C. Trends on New Drug Approval and the FDA

1. 2012 Drug Approvals

2012 saw the highest number of NCE approvals since 1997. In total, 32 new small molecule drugs and 7 new biologics were approved (Figure 2).

Figure 2 Annual New Drug Approvals



Source: Compiled by MHBK/IRD based on data from the FDA, and Tufts Center for the Study of Drug Development

The list of 2012 approvals included an impressive number of first-in-class drugs (see Table 4).

- Continued bumper crop of important anti-cancer drugs were approved, including Xtandi, Kyprolis, Iclusig and Perjeta.
- An important array of orphan drugs were approved, including Kalydeco, Justapid and Gattex.
- Primary care drugs with significant market potential included Eliquis, Linzess, Qsymia, Belviq and Vascepa.
- Anti-inflammatory drugs such as Xeljanz (RA), Aubagio (MS).

Table 4 NDA & BLA Approvals by the FDA in 2012

Drug Name	Indication	Manufacturer	Approval Date
CDER small molecules			
Picato	Topical treatment of actinic keratoses	LEO Pharma	23-Jan-12
Inlyta	Renal cell carcinoma	Pfizer	1/27/2012
Bydureon*	T2DM	Amylin/BMS/AZ	27-Jan-12
Erivedge (vismodegib)	Advanced BCC	Curis/Roche	30-Jan-12
Kalydeco	CF	Vertex	31-Jan-12
Zioptan	Glaucoma or Ocular hypertension	Merck	10-Feb-12
Surfaxin	Respiratory distress in premature infants	Discovery Laboratories	06-Mar-12
Omontys	Anemia in CKD	Affymax/Takeda	27-Mar-12
Amyvid	Radioactive label for PET diag. of AD	Eli Lilly	06-Apr-12
Stendra	ED	Vivus	27-Apr-12
Belviq	Obesity	Arena/Eisai	27-Jun-12
Myrbetriq	OAB	Astellas	28-Jun-12
Prepopik	Cbow el cleansing for colonoscopy	Ferring Pharms	16-Jul-12
Qsymia*	Obesity	Vivus	17-Jul-12
Kyprolis	Multiple myeloma	Onyx	20-Jul-12
Tudorza	COPD	Forest Lab	23-Jul-12
Stribild	HIV	Gilead	27-Aug-12
Linzess	IBS-c and chronic constipation	Ironw ood/Forest	30-Aug-12
Xtandi	Prostate cancer	Astellas	31-Aug-12
Bosulif	CML	Pfizer	04-Sep-12
Aubagio	Multiple sclerosis	Sanofi Aventis	12-Sep-12
Choline C 11	Radioactive diag. agent for PET imaging	Mayo Clinic	12-Sep-12
Stivarga	Colorectal cancer	Bayer	27-Sep-12
Fycompa	Epilepsy	Eisai	22-Oct-12
Synribo	CML	Teva	26-Oct-12
Vascepa*	Hypertriglyceridemia	Amarin	26-Jul-12
Xeljanz	RA	Pfizer	11/6/2012
Cometriq	Medullary thyroid cancer	Exelixis	11/29/2012
Inclusig	CML	Ariad	12/14/2012
Signifor	Cushing's syndrome	Novartis	14-Dec-12
Gattex	Short bow el syndrome	NPS Pharma	12/21/2012
Justapid	HoFH	Aegerion	12/21/2012
Eliquis	Prevent stroke and embolism in AF	BMS/Pfizer	28-Dec-12
Sirturo	TB	J&J	12/28/2012
Fulyzaq	Diarrhea in patients w ith AIDs	Salix	31-Dec-12
CDER Biologics			
Voraxaze	Methotrexate toxicity	BTG	17-Jan-12
Elelyso	Gaucher's disease	Protalix	01-May-12
Perjeta	Breast cancer	Roche	08-Jun-12
Zaltrap	Colorectal cancer	Sanofi Aventis	03-Aug-12
Tbo figrastim	Neutropenia	Teva	29-Aug-12
Jetrea	Vitreomacular adhesion	ThromboGenics	17-Oct-12
Raxibacumab	Anthrax	GSK	14-Dec-12

Source: Compiled by MHBK/IRD based on data from FDA and the Pink Sheet;
*Note: Bydureon, Qsymia and Vascepa haven't been considered NCE by CDER, but are listed in the table because of their importance.

2. Expected NCE Approvals in 2013

With more than 30 expected NME approvals, 2013 is likely to be another good year for drug approval (see Table 5). Already FDA has approved a number of drugs, including Kadcyla (T-DM1 for breast cancer), Nesina and Invokana for diabetes, Tecfidera for MS, Breo for COPD and Tafinlar/Mekinist for Melanoma.

Table 5 Expected NME Approvals in 2013

Drug Name	Indication	Manufacturer	Approval Date
Nesina	Diabetes	Takeda	25-Jan-13
Kynamro	HoFH	Sanofi / Isis	29-Jan-13
Pomalyst	Multiple myeloma	Celgene	08-Feb-13
Kadcyla	Breast cancer	Roche	22-Feb-13
Osphena	Vulvar and vaginal atrophy	Shionogi / AuatRx	26-Feb-13
Tecfidera	Multiple Sclerosis	Biogen Idec	27-Mar-13
Invokana	Diabetes	J&J	29-Mar-13
Breo	COPD	GSK / Theravance	12-May-13
Xofigo (Radium-223)	Prostate cancer	Bayer / Algeta	15-May-13
Tafinlar (Dabrafenib)	Melanoma	GSK	29-May-13
Mekinist (Trametinib)	Melanoma	GSK	29-May-13
Recombinant F IX	Hemophilia B	Baxter	
Levomilnacipran	Depression	Forest Lab / Pierre Fabre	
bazedoxifene conjugated estrogens	Menopausal symptoms	Pfizer / Ligand	
Rec F VIII	Hemophilia A	Novo Nordisk	
Opsumit	PAH	Actelion	
Cariprazine	Schizophrenia / bipolar	Forest Lab / Gedeon Richter	
UMEC/ VI LABA+LAMA	COPD	GSK / Theravance	
Dolutegravir	HIV	ViiV	
Metreleptin	Lipodystrophy	BMS / AZ	
Recombinant F IX	Hemophilia B	Inspiration Biopharma / Ipsen	
Sugammadex	Reverse neuromuscular	Merck	
Afatinib	NSCLC w ith mEGFR	Boehringer Ingelheim	
Suvorexant	Insomnia	Merck	
Lemtrada	Multiple Sclerosis	Sanofi / Bayer	
F IX fusion protein	Hemophilia B	Biogen Idec	
Vortioxetine	Depression	Takeda / Lundbeck	
F18 flutemetamol	PET imaging agent for AD	GE Healthcare	
Lyxumia	Diabetes	Sanofi / Zealand	
Albiglutide	Diabetes	GSK / Theravance	

Source: Compiled by MHBK/IRD based on public company reports

3. Trends in FDA's Regulatory Stance

It appears the tide has turned with regard to FDA's conservatism on safety. With the passage of time since the Vioxx withdrawal in 2004, the FDA has come under increasing industry, congressional and public pressure to approve new drugs. Last year's approval of two obesity drugs Belviq and Qsymia is a reflection of easing of approval hurdles in our view. The almost reversal of FDA's review on Avandia is another showcase of how overly cautious regulatory stance may prematurely impedes drug usage. In the Avandia case, FDA's advisory committee basically decided many of the initial alarms of Avandia risk were overblown.

As part of the PDUFA V authorization and FDASIA (Food and Drug Administration Safety and Innovation Act) passed into law in July 2012, a new breakthrough therapy designation is introduced. Its goal is to expedite the development and review of drugs for serious or life-threatening conditions. The criteria for breakthrough therapy designation require preliminary clinical evidence that demonstrates the investigational drug may offer substantial improvement on at least one clinically significant endpoint over available therapy in a serious medical condition. FDA is still working on the guidance for the industry. We understand the breakthrough designation allows sponsors to have frequent guidance from the FDA in designing and running clinical trials to ensure an expedited approval pathway.

Table 6 Some Notable Drugs That Won Breakthrough Designations from the FDA

Date Announced	Drug Name	Indication	Manufacturer
06-Jan-13	Ivacaftor (Kalydeco)	Cystic Fibrosis	Vertex
06-Jan-13	Ivacaftor / VX809 combo	Cystic Fibrosis	Vertex
13-Feb-13	Ibrutinib	R&R MCL, Waldenstrom's macroglobulinemia, CLL/SLL patients with 17p deletion	Janssen / Pharmacyclics
15-Mar-13	LDK378	Second line ALK+ NSCLC patients who had progressed or were intolerant to Xalkori	Novartis
10-Apr-13	Palbociclib	ER+, HER- breast cancer	Pfizer

Source: Compiled by MHBK/IRD based on Company Reports

4. Recent NCE Launch Experiences

As we observed in the past, biotech stocks often perform poorly following FDA approval (Table 7). This phenomenon was often indicative of limited market size, emerging side effect profile, or simply the current reality of slow new drug launches. For 2012 approval, the withdrawal of Omontys from the market was a prime example of unforeseen side effects showing up after the drug is launched into the broader population. For 2012 approvals, primary care drugs such as Vascepa and Qsymia are having very slow launch. Slow new product launch in the primary care market is a headwind in the pharmaceutical industry and we have cited this earlier as one of the reasons behind overall slow pharmaceutical market growth.

On the positive side, launch of specialty drugs is often brisk. Specialty drugs enjoy good pricing power as they often target big unmet medical need. Given the obvious clinical benefits, uptake by patients and insurance coverage are often fast. One hot area within specialty drugs is orphan drugs. Orphan diseases are rare diseases that affect less than 200,000 patients in the U.S. U.S. government provides substantial commercial (in terms of 7 years' market exclusivity) as well as tax incentives (R&D tax credits) for companies developing treatments for rare diseases. The idea is as the patient population is small, the economic incentive has to be big enough to attract drug developers. But as shown by leading orphan drug companies, orphan drugs can command very high pricing ($300-400,000 per year). Therefore, companies only need a few thousands patients to achieve very impressive financial results.

Stocks of orphan drug companies often significantly outperform following FDA approval. Examples include Alexion, Hyperion, Isis, Aegerion, NPS Pharma, Onyx and Vertex. We believe this is a result of initial underestimation of the market size for certain orphan diseases and under-appreciation of the medical value of the orphan drugs (more on orphan drugs later in this report).

Table 7 Share Price Performance Following Drug Approval

Company 10/10/2013	Drug	Indication	Approval date	Stock Performance Since Approval
Negative stock returns from approval				
Cumberland	Caldolor	Pain	11-Jun-09	-72.3%
Allos	Folotyn	PTCL	25-Sep-09	-76.9%
Auxilium	Xiaflex	Dupuytren's contracture	2-Feb-10	-39.0%
Dendreon	Provenge	HRPC	29-Apr-10	-94.9%
Savient	Krystexxa	Treatment refactory Gout	14-Sep-10	-96.2%
Cadence	Ofirmev	Pain and fevor	2-Nov-10	-37.9%
Depomed	GRALISE	Post-herpetic neurogia	31-Jan-11	-14.2%
Human Genome Sci.	Benlysta	Lupus	9-Mar-11	-44.5%
Xenoport	Horizant	RLS, PNH, DPN	7-Apr-11	-43.7%
Horizan Pharma	DUEXIS	Pain	25-Apr-11	-59.0%
Curis	Erivedge	Basal cell carcinoma	30-Jan-12	-19.6%
Affymax	Omontys	Anemia in dialysis patients	27-Mar-12	-91.6%
Arena	Belviq	Obesity	27-Jun-12	-62.5%
Vivus	Qsymia	Obesity	17-Jul-12	-61.8%
Amarin	Vascepa	Hypertriglyceridemia	26-Jul-12	-58.9%
Ariad	Iclusig	CML and Ph+ ALL	14-Dec-12	-75.6%
Positive stock returns from approval				
Vanda	Fanapt	Schizophrenia	7-May-09	20.5%
Alexion	Soliris	Paroxysmal nocturnal	16-Mar-07	950.9%
Acorda	Fampridine	Walking in MS patients	23-Jan-10	20.8%
Avanir Pharma	Nuedextra	Pseudobulbar affect	3-Nov-10	2.4%
Clinical Data	Viibryd	Depression	24-Jan-11	19.2%
Vertex	Incivek	HCV	23-May-11	25.7%
Seattle Genetics	Adcetris	Hodgkin's lymphoma	19-Aug-11	163.3%
Incyte	Jakafi	Myeloproliferative disease	17-Nov-11	176.8%
Regeneron	EYLEA	AMD, CRVO	18-Nov-11	465.3%
Amylin	Bydureon	Diabetes	27-Jan-12	155.4%
Onyx	Kyprolis	Multiple Myeloma	20-Jul-12	63.7%
Aegerion	Justapid	HoFH	21-Dec-12	197.2%
NPS Pharma	Gattex	Short bowel syndrome	21-Dec-12	238.0%
Isis	Kynamro	HoFH	29-Jan-13	141.0%
Hyperion	RAVICTI	Urea cycle disorder	1-Feb-13	61.4%

Source: Compiled by MHBK/IRD based on Capital IQ and public company reports.
Note: Highlighted companies had been acquired and the return is based on the takeover price over price on the date of FDA approval.

D. Current Status of Large Pharma Pipeline

1. Recent Pipeline Attrition

In 2012, large pharma's late-stage pipeline attrition continued unabated (as shown in Table 8). In addition, a number of late-stage licensing deals big pharma signed reported negative outcome (Table 9). Major setbacks include:

- Pfizer's Bapineuzumab and Lilly's Solanezumab failed phase III studies for Alzheimer's disease. Lilly further dropped its phase II BACE inhibitor for AD.
- In the atherosclerosis space, niacin-related drugs such as Tredaptive (HPS2-THRIVE) and Niaspan (AIM-HIGH) had disappointing data. Roche dropped Dalcetrapib after the disappointing dal-OUTCOMES trial. Despite the failures of torcetrapib and dalcetrapid from competitors, Merck and Eli Lilly are still pressing ahead with their CETP inhibitors in phase III trials.
- In Rheumatoid arthritis, AZ's syk inhibitor fostamatinib had poor data, Lilly dropped its anti-BAFF antibody and Pfizer's Xeljanz received negative opinion for approval in Europe.
- In the super hot HCV area, BMY's INX-189 failed due to safety issue, which will lead BMY to write off most of the $2.5bn it paid to acquire Inhibitex.
- In kidney disease area, Abbott and its partner Reata discontinued trial for the high-profile drug Bardoxolone.

Table 8 Notable Late-stage Development Failures from Large Pharma

	2009	2010	2011	2012	2013
Pfizer	Axitinib (adv. Pancreatic cancer), Sutent (Colon cancer) esreboxetine (fibromyalgia), PD 332,334 (GAD)	Dimebon (Alzheimer's); Figitumumab (lung cancer); Sutent (breast, liver, lung, prostate cancer); Tanezumab (OA), Thelin agonist (PAH)	Neratinib (breast cancer)	Bapineuzumab (ApoE4 Alzeimer's disease)	inotuzumab (NHL)
Merck	Rolofylline (CHF)	Vicriviroc (HIV); Acadesine (Ischemia-Reperfusion Injury)	Vorapaxar (anti-platelet); telcagepant (Migraine);	vernakalant (AF); Ridaforolimus (Sarcoma); Tredaptive (Atherosclerosis)	Preladenant (PD)
Bristol-Myers Squibb				Brivanib (HCC), INX-189 (HCV), γ secretase inhibitor (AD)	
Eli Lilly	Dirucotide (RRMS)	Semagacestat (Alzheimer's disease), Tasisulam (melanoma), Teplizumab (T1DM)	Arxxant (DR); Sollpura (liprotamase panreatic enzyme replacement)	pomaglumetad (mGluR2/3) for Schizophrenia, tabalumab (RA), Solanezumab (AD)	Enzastaurin (DLBCL); BACE inhibitor (AD)
Astra Zeneca	Zactima (lung cancer)	Recentin (Colon cancer), Motavizumab (RSV vaccine), Zibotentan (CRPC), Certriad	TC-5214 (depression), Olaparib (ovarian cancer)	fostamatinib (RA)	
Novartis	QAB 149 (COPD)		elinogrel (anti-platelet) Agomelatine (depression), SMC021 (osteoarthritis)	Tekturna (hypertension),	Dovetinib (kidney cancer)
Roche	Avastin (Adjuvant CRC); Tarceva (NSCLC maintenance)	Avastin (breast, prostate, gastric, colon adjuvant); Ocrelizumab (RA); Taspoglutide (Diabetes)		Dalcetrapib (atherosclerosis)	Aleglitazar (T2DM with ACS)
Sanofi-Aventis	Ciltyri (insomnia); Idrabiotaparinux (DVT, PE, AF); Xaliproden (neuropathy); Larotaxel (cancer) Satavaptan (hyponatremia); Saredutant (depression); AVE5530 (cholesterol); TroVax (cancer vaccine)	NV1FGF (Critical limb ischemia)	iniparib (triple-negative breast cancer); Prochymal (GvHD)	Over 2011-2012, under the new leadership of Zerhouni, Sanofi substantially pruned its late-stage portfolio by discontinuing 10 phase III programs.	Otamixaban (Factor Xa inhibitor)
GlaxoSmithKline	Rezonic (nausea); Mepolizumab (HES)	Simplirix (Herpes vaccine)	Almorexant (insomnia), otelixizumab (T1DM)		vercirnon (Crohn's disease); MAGE-A3 (melanoma); drisapersen (DMD)
Abbvie				Bardoxolone (CKD), Niaspan	

Source: Compiled by MHBK/IRD based on public company reports

Table 9 Setbacks of Pharma's Major Licensing/MA Deals in 2012

Acquirer / licenser	Target / licensee	Ann. Date	Deal Details ($mm)	Upfront ($mm)	Equity ($mm)	Stage
Bristol-Myers Squibb	Inhibitex	Jan-12	$2,500mn acquisition		$2,500	Phase II
Abbott	Reata	Dec-11	$400mn licensing fee for second-generation oral antioxidant inflammation modulators (AIMs).	$400		II
Abbott	Reata	Sep-10	$450mn near-term payments for OUS licensing rights to bardoxolone and a minority investment in the company , $350 in dev. and reg. MS, plus royalties.	$450		II
J&J*	Elan	Jul-09	Acquired all Elan's AD immunotherapy program including half of Elan's share in Bapineuzumab.		$1,000	III

Source: Compiled by MHBK/IRD based on public company reports.
*Note: Despite the failure of Bapineuzumab, J&J's loss is offset as its investment in Elan was made at a low valuation ($9.32 per share)

2. Overall Sizes of Pharma's pipelines are healthy

Despite the high-profile late-stage pipeline failures, some pharma's R&D pipelines look very healthy. Comparing the size of pharma's current pipeline to that of six years ago reveals the number of compounds in the clinic hasn't changed a lot and the slight decrease can be mostly attributed to pharma mergers (Table 10 and Table 11). Some pharma's pipelines are even as healthy as they have ever been. For example, Novartis, Roche, BMS and Eli Lilly all have very strong R&D pipelines. Although there is still a shortage of phase III projects, some companies such as AZ are quickly replenishing the phase III portfolio by advancing its mid-stage portfolio and pursuing late-stage acquisitions.

Mega pharma such as Pfizer, Sanofi and GSK have cut R&D portfolios substantially in recent years, mostly consciously rationalizing early-mid. stage projects. This has created opportunities for small biotech companies to outlicense deprioritized compounds from pharma (more on this point later in the report). Of major pharma, Pfizer took the lead in reducing R&D budget, which declined from $9.3bn in 2010 post Wyeth merger to $7.3bn in 2012 (13.7% of sales to 10.5% of sales). Pfizer saw its R&D portfolio shrink substantially over this time period. Despite the presumed increase in portfolio quality, Pfizer pipeline still appears meager given its size. Sanofi Aventis has dramatically cut its R&D portfolio from the legacy pipeline. Genzyme acquisition has helped its pipeline. GSK has a large number of important late-stage compounds, including the two novel drugs for melanoma that just received FDA approval.

Merck has suffered a number of high-profile setbacks in recent years. Its pipeline needs more rebuilding. Merck has changed the head of R&D this year with Roger Perlmutter returning to Merck after a long stint as the head of R&D at Amgen.

Table 10 Large Pharma Pipeline in 2013

	Phase I	Phase II	Phase I + II	Phase III	Filed	Total NMEs in clinic	Time of Company Update
BMY			40	6	1	47	Feb. 2013 website
PFE + Wyeth	29	19	48	6	4	58	Feb. 28th 2013 update
LLY	22	24	46	12	2	60	April 2013 website update
MRK + SGP*	30	22	52	12	4	68	Feb. 2013 update
Roche	36	23	59	9	3	71	Jan. 2013 FY12 result update
AZN	26	21	47	5	1	53	March 2013 Investor Day
NVS	22	20	42	10	1	73	Nov. 2012 R&D Day
GSK			50	10	6	66	Jan. 2013 pipeline update
Sanofi-Aventis	29	18	47	7	2	56	Feb. 2013 update
Sector			431	77	24	532	

Source: Compiled by MHBK/IRD based on public company reports.
Note: Merck didn't disclose the size of its phase I portfolio. To get to an industry total, an estimate of 30 phase I projects is used.

Table 11 Large Pharma Pipeline in 2007

2007	Phase I	Phase II	Phase I + II	Phase III	Filed	Total NMEs in clinic	Time of Company Update
BMY			13	6	0	19	Feb 2007
PFE	51	38	89	6	4	99	Nov 2006
WYE	18	13	31	2	6	39	Oct 2006
LLY	8	11	19	5	0	24	Dec 2006
MRK	28	21	49	5	3	57	Dec 2006
SGP	6	8	14	3	1	18	Feb 2007
Roche	25	18	43	3	2	48	Feb 2007
AZN	22	18	40	5	0	45	Present
NVS	20	20	40	7	3	50	Feb 2006
GSK	38	50	88	13	9	110	Feb 2007
Sanofi-Aventis	24	29	53	14	2	69	Feb 2007
Sector			479	69	30	578	

Source: Compiled by MHBK/IRD based on public company reports.

Table 12 lists late-stage pipeline of western large pharmaceutical companies.

Table 12 Late-stage R&D Pipeline of U.S. and European Large-cap Pharma

Company	Source	Pipeline Compounds (Indication)	Phases	Est. Filing Date	Est. Peak Sales Range ($bn)	
ABBV		Duopa (Parkinson's disease)	Filed	2012	0.0	0.5
ABBV		HCV IFN-free combination	III		2.0	3.0
ABBV	Biogen Idec	Daclizumab (MS)	III	2014	1.0	2.0
ABBV	Neurocrine	Elagolix (endometriosis)	III		0.5	1.0
ABBV	Facet Bio	Elotuzumab (multiple myeloma)	III		1.0	2.0
BMY	Amylin	Metreleptin (Lipodystrophy)	Filed	2012	0.5	1.0
BMY	Facet Bio	Elotuzumab (multiple myeloma)	III	2013	0.0	0.5
BMY		Asunaprevir (NS3 inhibitor for Hep C)	III	2014		
BMY		Daclatasvir (NS5A inhibitor for Hep C)	III	2014	0.5	1.0
BMY	Medarex	Nivolumab (PD-1 mAb for melanoma)	III	2015	1.0	2.0
BMY	ZymoGenetics	PEG-Interferon lamda (Hep C)	III	2015	0.5	1.0
LLY	Alnara Pharma	Liprotamase (exocrine pancreatic insufficiency)	CRL	2010	0.5	1.0
LLY	BI	Empagliflozin / BI 10773 (SGLT2 inhibitor for diabetes)	Filed	2013	0.5	1.0
LLY		Enzastaurin (DLBCL)	III	2013	0.5	1.0
LLY		Dulaglutide / GLP-1 Fc (Diabetes)	III	2013	0.5	1.0
LLY		Ixekizumab (Anti-IL17 Mab for Psoriasis)	III	2014	0.5	1.0
LLY		Edivoxetine (depression)	III	2014	1.0	2.0
LLY	Incyte	Baricitinib (RA)	III	2014	1.0	2.0
LLY		Tabalumab (BAFF antibody for Lupus)	III	2014	1.0	2.0
LLY	ImClone	Necitumumab / IMC-11F8 (NSCLC)	III	2015	0.5	1.0
LLY	ImClone	Ramucirumab / IMC-1121B (breast / gastric)	III	2015	0.5	1.0
LLY		Evacetrapib (CETP inhibitor for CV event prevention in high risk pts)	III	2015	0.5	1.0
LLY		Insulin glargine (diabetes)	III	2015	1.0	2.0
LLY		Novel Basal insulin (diabetes)	III	2015	1.0	2.0
LLY		Solanezumab (Aß Mab for Alzheimer's disease)	III	2016	1.0	2.0
MRK		Suvorexant / MK-4305 (Orexin receptor inhibitor for insomnia)	Filed	2012	0.5	1.0
MRK	Endocyte	Vintafolide (platinum-resistant ovarian cancer)	Filed (EU)	2012	0.5	1.0
MRK		MK-0653c (Lipitor-Zetia combo for atherosclerosis)	Filed (US)	2012	0.0	0.5
MRK	SGP	Sugammadex (reversal of neuromuscular blockade)	Filed (US)	2012	0.5	1.0
MRK	SGP	Corifollitropin Alfa (infertility)	III	2013	0.0	0.5
MRK	SGP	vorapaxar / TRA (Thrombosis)	III	2013	0.5	1.0
MRK	ALK-Abello	Grazax/MK-3641 (ragweed allergy)	III	2013	0.0	0.5
MRK	ALK-Abello	MK-7243 (grass pollen allergy)	III	2013	0.0	0.5
MRK	MBL & Medarex	Actoxumab/bezlotoxumab (MK-3415A for C. Diff infection)	III		0.5	1.0
MRK	SGP	NOMAC/E2 (Oral Contraceptive, U.S.)	III		0.5	1.0
MRK		MK-3102 (once weekly DPP IV inhibitor)	III		1.0	2.0
MRK		Preladenant (A2A receptor inhibitor for Parkinson's disease)	III	2014	0.5	1.0
MRK		Vaniprevir/ MK-7009 (Hep C)	III		0.0	0.5
MRK		Odanacatib (MK-0822 for Osteoporosis)	III	2014	1.0	2.0
MRK		MK-3222 (Mab against IL-23 for Psoriasis)	III		0.5	1.0
MRK		Anacetrapib (CETP inhibitor for obesity)	III	2015	1.0	2.0
PFE	WYE	Viviant (SERM for Osteoporosis)	Filed	2006	1.0	2.0
PFE	WYE	bazedoxifene conjugated estrogens (Menopause Symptoms)	Filed		0.5	1.0
PFE	King Pharma	Remoxy (temper-resistant opioid)	CRL	2010	0.5	1.0
PFE	FoldRx	Vyndaqel/Tafamidis meglumine (TTR familial amyloid polyneuropathy)	Filed		0.0	0.5
PFE	King Pharma	ALO-02 (Oxycodone-naltrexone core)	III		0.0	0.5
PFE		dacomitinib / PF-299804 (pan-HER inhibitor for lung cancer)	III		0.5	1.0
PFE		Tanezumab (nerve growth factor inhibitor for OA)	III		0.5	1.0
PFE		MnB rLP2086 (Adolescent and Young Adult Meningitis B)	III		0.5	1.0
PFE		Zithromax-Chloroquine (Malaria)	III		0.0	0.5

Company	Source	Pipeline Compounds (Indication)	Phases	Est. Filing Date	Est. Peak Sales Range ($bn)	
AZN	Amylin	Metreleptin (Lipodystrophy)	Filed	2012	0.5	1.0
AZN	Omthera	Epanova (high triglycerides)	III	2013	0.5	1.0
AZN	Pearl Therapeutics	PT003 (COPD)	III		0.5	1.0
AZN	Nektar	Naloxigol / NKTR-118 (opioid induced constipation)	III	2013	1.0	2.0
AZN	Ardea	Lesinurad (Gaut)	III	2014	1.0	2.0
AZN	Novexel	CAZ AVI (Pneumonia, skin infection)	III	2014	0.5	1.0
AZN	Amgen	Brodalumab (anti IL17 Mab for Psoriasis)	III	2015	1.0	2.0
NVS	Sosei R&D	QVA 149 (NVA237 + QAB149 for Asthma, COPD)	Filed	2012	1	2
NVS		LBH 589 (panobinostat, HDAC inhibitor forMM, hematological cancers)	III	2013	0	0.5
NVS		AIN457 (Psoriasis, autoimmune)	III	2013	0.5	1
NVS	Cothera	RLX030 (recombinant relaxin for heart failure)	III	2013	1	2
NVS		TKI258/Dovitinib (TKI, renal cell carcinoma)	III	2013	0.5	1
NVS		LCQ908 (Familial chylomicronemia syndrome)	III	2014	0.5	1
NVS		AFQ056 (Fragile X syndrome)	III	2014	0	0.5
NVS		LCZ696 (ARB for heart failure)	III	2014	0.5	1
NVS		LDE225 (SMO inhibitor for basal cell carcinoma)	III	2014	0	0.5
NVS		LDK378 (ALK inhibitor for NSCLC)	II	2014	1	2
NVS		PKC412 (PKC, FLT3, multi TKIs for AML, systemic mastocytosis)	III	2015	0	0.5
NVS		PKM120 / buparlisib (PI3K inhibitor for Breast cancer)	III	2015	0.5	1
NVS	Array	MEK 162 (MEK inhibitor for melanoma)	II	2015	0.5	1
Roche	Glycart	obinutuzumab / GA101 (CLL)	III	2013	0.5	1
Roche		bitopertin / Glycine reuptake inhibitor (Schiz. negative symptoms)	III	2013	1	2
Roche		Ocrelizumab (PPMS)	III	2014	0.5	1
Roche	Chugai	Tofogliflozin (diabetes)	III	2014	1	2
Roche		onartuzumab / MetMab (mNSCLC)	III	2015	0.5	1
Roche		Gentenerumab (AD)	III			
Roche		MEKi (melanoma)	III			
Roche		Aleglitazar (CV high risk in T2DM)	III	2015	0.5	1
SNY	Genzyme	Lemtrada (alemtuzumab for MS)	Filed	2012	1	2
SNY	Zealand Pharma	Lyxumia / Lixisenatide (GLP1 agonist for diabetes)	Filed	2012	0.5	1
SNY	TargeGen	SAR302503 (JAK2 inhibitor for myelofibrosis)	III	2013	0.5	1
SNY	Genzyme	Eliglustat tartrate (Gaucher disease)	III	2013	0.5	1
SNY	Regeneron	Alirocumab (anti-PCSK9 mAb for hypercholesterolemia)	III	2014	2	3
SNY		Otamixaban (Direct Xa inhibitor for ACS)	III	2013	1	2
SNY		Dengue (Dengue fever vaccine)	III	2014	0.5	1
SNY	Regeneron	Sarilumab (Anti-IL6 Mab for RA and autoimmune)	III		0.5	1
GSK	GSK/Theravance	Relovair / Breo (COPD, asthma)	Approved	2012	>2	
GSK		dabrafenib / 2118436 (BRAF inhibitor for metatatic melanoma)	Approved	2012	0.5	1
GSK		trametinib / 1120212 (MEK inhibitor for metastatic melanoma)	Approved	2012	0.5	1
GSK	Shionogi	Dolutegravir (HIV integrase inhibitor)	Filed	2012	1	2
GSK	GSK/Theravance	UMEC/ VI LABA+LAMA (COPD)	Filed	2012	1	2
GSK	HGS	Syncria / albiglutide (GLIP-1 analog for Type 1 diabetes)	Filed	2013	0.5	1
GSK		mepolizumab (anti-IL5 Mab forAsthma)	III	2013	0.5	1
GSK		MAGE-A3 (NSCLC)	III	2013	0.5	1
GSK	Chemocentryx	Vercirnon / Traficet (Crohn's disease)	III	2013	0.5	1
GSK	Amicus	Amigal / migalastat HCL (Fabry disease)	III	2013	0.5	1
GSK	Prosensa	drisapersen (Duchenne muscular dystrophy)	III	2013	0.5	1
GSK		Dolutegravir-Trii(HIV integrase inhibitor + abacavir + lamivudine)	III	2013	1	2
GSK	Impax	Patrome/IPX066 (Europe)	III	2013	0	0.5
GSK		Mosquirix (malaria vaccine)	III	2013	0	0.5
GSK	GSK/HGS	darapladib (LpPLA2 inhibitor for atherosclerosis)	III	2014	1	2
GSK		Herpes zoster vaccine	III	2014	0.5	1

Source: Compiled by MHBK/IRD based on public company reports

E. Patent Expiry and Generics Opportunities

2012 represented the peak of loss of exclusivities (LOEs) of big pharma. Large pharma will suffer residual impact of the LOE in 2013 but will look at the bulk of LOEs in the rear-view mirror. Going forward, we will still see some continued loss of patent exclusivity, although their impact will be modest.

Table 13 lists for each global pharma the percentage of 2012 sales that will be subject to generic erosion for the two specified time frames. In 2013, recent patent expiries will continue to hit several pharma, contributing to significant sales declines (Table 14). The major generic hit to 2012 revenues come from Plavix and Avapro (BMS), Zyprexa (Eli Lilly), Singulair (Merck), Lipitor (Pfizer), Seroquel (AZ). In the medium term (2012-2014), AstraZeneca and BMS have the highest exposure.

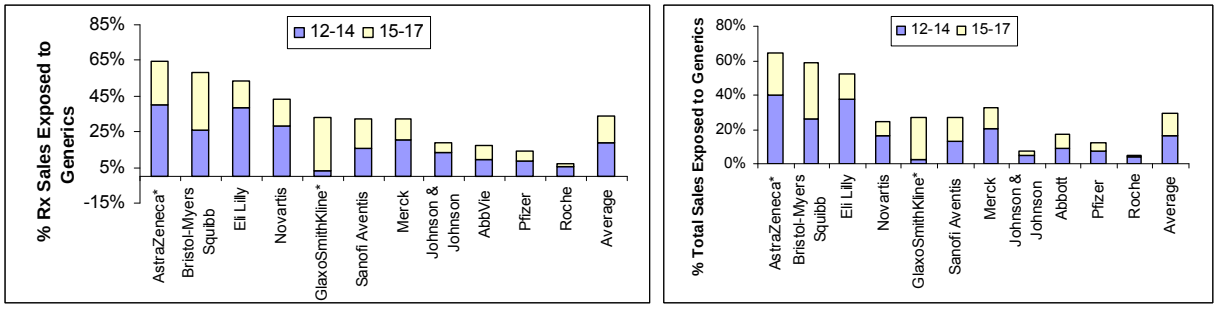
Table 13 Percentage of 2012 Sales Exposed to Generic Erosion

% Pharma Sales	12-14	15-17	Total
AstraZeneca*	40%	25%	64%
Bristol-Myers Squibb	26%	33%	59%
Eli Lilly	38%	15%	54%
Novartis	28%	15%	43%
GlaxoSmithKline*	3%	30%	33%
Sanofi Aventis	15%	17%	33%
Merck	21%	12%	32%
Johnson & Johnson	13%	6%	19%
AbbVie	9%	8%	17%
Pfizer	9%	5%	14%
Roche	5%	2%	7%
Average	19%	15%	34%

% Total Sales	12-14	15-17	Total
AstraZeneca*	40%	25%	64%
Bristol-Myers Squibb	26%	33%	59%
Eli Lilly	37%	15%	52%
Novartis	16%	8%	24%
GlaxoSmithKline*	3%	24%	27%
Sanofi Aventis	13%	14%	27%
Merck	21%	12%	32%
Johnson & Johnson	5%	2%	7%
Abbott	9%	8%	17%
Pfizer	7%	5%	12%
Roche	4%	1%	5%
Average	16%	13%	30%

Source: Compiled by MHBK/IRD based on public company reports.
Note1: biologics are excluded from the calculation.
Note2: Table on the left is as % pharma sales and table on the right is as % total company sales

Figure 3 Cumulative Patent Expiries for three time frames



Source: Compiled by MHBK/IRD based on public company reports.
Note: Figure on the left is as % pharma sales and figure on the right is as % total company sales

Table 14 Large Pharma's Financial Guidance for 2013

Outlook for 2013	Roche	AbbVie	Johnson & Johnson	GSK	Merck	Novartis	Pfizer *	BMS	Eli Lilly	Astra-Zeneca	Sanofi - Aventis
Sales Growth	Low to mid single-digit	Over $18bn (2012 of $18.4bn)	5-6% growth (CER)	1% growth (CER)	(6%) - (5%)	Low single-digit growth at CER	(6%) - (3%)	(11%) - (7%)	0 - 4%	Mid to high single-digit decline (CER)	
Gross Margins							Down ~1%	Down ~1%	Flat		
SG&A Growth							(4%) - 2%	Mid single digit growth for A&P; flat for G&A	(7%) - (4%)		
R&D Growth					Below 2012 level		(11%) - (4%)	low single-digit growth	0% - 4%		
Operating income						Decline low single digits					
EPS Growth	Ahead of sales growth	(17%) - (15%)	6-7%	3-4% growth CER	(10%) - (7%)		(2%) - 2%	(15%) - (11%)	19% - 22%	Decline significantly more than sales decline	7-10% lower at CER

Source: Compiled by MHBK/IRD based on public company reports.
Note: Pfizer data is as of 1Q2013.

F. Pharma M&A Environment

Because of deficiencies in pipeline, Pharma have been aggressive in in-licensing promising compounds (see Table 15). Several observations can be made:

- High deal valuation is not so important in determining the merit of the deal. The success of the clinical compound is ultimately the most important factor. We have seen this theme played out over the last couple of years. A good clinical compound can justify enormous price, while a bad compound carries significant negative value. Oftentimes there is enormous opportunity cost. Buying a good compound would diminish buyer's financial dry powder so it won't make mistakes in buying bad compound. The reverse is also true, i.e., missing out on a good compound will expose the buyer to the risk of buying bad compound. One prominent example is Bristol-Myers Squibb, which upon being outbid on the acquisition of Pharmasset by Gilead, acquired a similar company Inhibitex for $2.5bn. Although the valuation is a lot cheaper than Pharmasset, the compound failed and BMS had to write off most of the acquisition price. In comparison, although Gilead spent a breath-taking $11bn to buy a phase II asset, it is able to dodge the safety issues plaguing the class and generate exciting clinical data.
- Pharma who had aggressive acquired assets over 2011-2012 got good deals as price has gone up substantially in 2013. Examples include Gilead's acquisition of Calistoga ($375mn upfront in contrast to Infinity Pharma's $1bn current public valuation) and Celgene's acquisition of Avila ($350mn upfront compared to Pharmacyclics's $6bn current public valuation).
- Pharma-pharma alliances are on the rise and have delivered value in the industry. Phase II/III pipeline is not distributed evenly among pharma companies. This asymmetry combined with pressure on R&D expenditure and rich deal valuation from biotech companies have led to increased alliance among pharma peers (see Table 16). In areas where there is a scarcity of pipeline (e.g., Neurology) or where the development cost is very high (e.g., CV and Metabolic), pharma-pharma alliance is especially valuable. Some companies have created new entities that are category leader in a given field (e.g., ViiV in HIV; merged BMS/AZ U.S. operation in diabetes). Beneficiaries of such deals such as AZ have publicly indicated their intention to do more, especially at the phase II stage (before phase III start).

Table 15 Recent Biopharma Deals for Mid-Late Stage Compounds

Acquirer / licenser	Target / licensee	Ann. Date	Deal Value ($mm)	Upfront ($mm)	Equity ($mm)	Stage
Astellas	Fibrogen	Jul-13	$350mn in upfront and other pmts, eligible to $465mn in development milestones. Covered U.S. Canada, China, and other countries Astellas doesn't have right			III
Johnson & Johnson	Aragon	Jun-13	$650mn upfront and $350mn milestones		$650	II
Astra Zeneca	Pearl Therapeutics	Jun-13	$560mn upfront and $590mn milestones		$560	III
AstraZeneca PLC	Omthera	May-13	$323mn upfront and $120mn milestones		$323	NDA ready
Gilead	YM Biosciences	Dec-12	$510		$510	II
J & J	Genmab	Aug-12	Licensed Genmab's anti-CD38 Mab in phase I/II study in MM for $55mn upfront, $80mn equity investment and up to $1bn future milestone payments.	$55	$80	I/II
GSK	Human Genome Sciences	Jul-12	$3,000		$3,000	Approved
BMS / AstraZeneca	Amylin	Jul-12	BMS and AstraZeneca acquired Amylin for $7bn.		$7,000	Approved
AstraZeneca PLC	Ardea	Apr-12	$1,260		$1,260	III
Merck	Endocyte	Apr-12	Licensed phase III ovarian cancer compound EC145 for $120mn upfront, and up to $880mn developmental, regulatory and commercial milestones. Equal profit share in the U.S., double-digit royalty in international markets.	$120		Phase III
Dainippon Sumitomo	Boston Biomedical	Mar-12	Acquired the 30-people company for $200mn upfront, $540mn in dev. MS and $1.9bn in sales MS.		$200	II
Abbott	Galapagos	Feb-12	$150mn upfront, additional $200mn milestone if a mid-stage trial is successful, additional $1bn development and sales milestone	$150		II
Celgene	Avila Therapeutics	Jan-12	$350mn upfront, $295mn development and regulatory milestone for AVL-292 and $380mn development and approval milestone for other programs		$350	III
Amgen	Micromet	Jan-12	$1,160		$1,160	II
Bristol-Myers Squibb	Inhibitex	Jan-12	$2,500		$2,500	II
Alexion	Enobia	Dec-11	$610mn upfront and $470mn milestone payments		$610	II
J & J	Pharmacyclics	Dec-11	$150mn upfront, up to an additional $825 million in development and regulatory milestone payments. PCYC shares 40% costs but books 50% of the commercial P&L. Oncology only.	$150		II
Gilead	Pharmasset	Nov-11	$11,000		$11,000	II
Mundipharma	Allos	May-11	Commercial rights to Folotyn OUS for $50mn upfront, $310.5mn in reg. and commercial milestone and dd royalties	$50		Filed
Cephalon	GeminX	Mar-11	Acquired the company for $225mn upfront and $300mn in cash earn-out		$225	II
Astellas	AVEO	Feb-11	Licensed Tivozanib for $125mn upfront, $1.3bn in development, regulatory and sales milestones. Global 50-50 profit share.	$125		III
Gilead	Calistoga	Feb-11	$375mn upfront and $225mn earn-out		$375	II
Forest Lab	Clinical Data	Feb-11	Acquired Viibryd for depression for $928.6mn upfront and $185.7mn in cash earn-outs		$929	Approved
Salix	Progenics	Feb-11	Rights to Relistor for $60mn upfront, $90mn in U.S. reg. MS, up to $200mn in sales MS, plus royalties on U.S. sales and 60% of revenues from OUS sublicenses.	60		Approved

Source: Compiled by MHBK/IRD based on public company reports

Table 16 Pharma-Pharma Alliance

Partner I Licensor	Partner II Licensee	Upfront payments ($mn)	Deal	Year
Servier	Amgen	$50	Amgen gains U.S. right to heart failure drug ivabradine and a phase II compound also for CHF. Servier gains EU rights to omecamtiv mecarbil for heart failure.	2013
Merck	Pfizer	$60	Merck and Pfizer will collaborate on SGLT2 inhibitor Ertugliflozin and fixed dose combos with Januvia. Ertugliflozin will enter into phase III in 2013. Profit split 60-40.	2013
Lundbeck	Otsuka	$150	Otsuka further expanded alliance with Lundbeck by co-developing Lu AE58054 for Alzheimer's disease.	2013
Otsuka	Lundbeck	$200	Global collaboration including injectable Abilify and OPC-34712 from Otsuka and three compounds from Lundbeck.	2011
Otsuka	Kyowa Hakko Kirin	¥3.0 billion; ¥8.2 billion at approval	Otsuka sub-licensed Saxagliptin to KHK. Strategic alliance to develop KHK's oncology portfolio in Japan and Asia.	2012
BMS	Astra Zeneca	$100	Entered into an alliance to co-develop BMS's DPPIV inhibitor and SGLT-2 inhibitor; jointly acquired Amylin; Merged their U.S. commercial operation in diabetes in January 2013.	2007 2012
Amgen	Astra Zeneca	$50	Jointly develop and commercialize five inflammatory disease treatments in Amgen's portfolio.	2012
Boehringer Ingelheim	Eli Lilly	€ 300	Entered into an alliance to co-develop and market four mid-late stage diabetes assets, including BI's DPPIV and SGLT2 inhibitors, and two insulins from Lilly (dropped later on)	2011
GSK	Pfizer / Shionogi		Pooled HIV franchise under ViiV Healthcare. GSK owns 76.5%, Pfizer owns 13.5% and Shinogi owns 10%.	2009
Amgen	Takeda	$300	Licensed rights of 13 clinical candidates in Japan, global co-development right to TKI motesanib	2008
Lundbeck	Takeda	$40	Alliance to develop several compounds in Lundbeck's pipeline for depression and anxiety	2007
BMS	Pfizer	$250	Co-development and marketing of Factor Xa inhibitor Eliquis	2007
Bayer	J&J	$290 upfront & milestone	Co-development and marketing of Factor Xa inhibitor Xarelto	2005

Source: Compiled by MHBK/IRD based on public company reports

Table 17 and Table 18 list notable pharma acquisitions announced since the beginning of 2011. In terms of therapeutic areas that are in the spot light, dermatology has been hot (Obagi, DUSA, Fougera and Medicis). On the private side (Table 18), the deal flow has been a trickle than a torrent and also tends to involve early stage companies, probably a reflection of the lack of mature, private companies.

Table 17 Recent Biopharma M&As with Public Targets

Aquirer	Target	Ann. Date	Value ($mm)	Premium 1 Day	Premium 1 Month	Target Sales ($mm)	EV/Sales	P/E	EV/EBITDA prior yr
Otsuka	Astex	04-Sep-2013	$886	27%	52%	83	10.7		
Akorn	Hi-tech Pharmacal	27-Aug-2013	$539	24%	21%	232	2.3		11.1
Amgen, Inc.	Onyx	26-Aug-2013	$9,700		44%	516	18.8		
Cubist	Optimer	30-Jul-2013	$535	-19%		107	5.0		
Cubist	Trius	30-Jul-2013	$707	15%	63%				
Perrigo	Elan	29-Jul-2013	$6,700	11%		1,203	5.6		30.5
Spectrum Pharma	Talon Therapeutics	17-Jul-2013	$11						
Mitsubishi Tanabe	Medicago	12-Jul-2013	$357	22%	59%				
AstraZeneca PLC	Omthera	28-May-2013	$323	88%	92%				
Actavis	Warner Chilcott	20-May-2013	$8,500	5%	45%	2,400	3.5		
Valeant	Obagi Medical	20-Mar-2013	$360	28%	41%	121	3.0		15.2
Perrigo	Rosemont	11-Feb-2013	$283			63	4.5		
Allergan	MAP Pharma	23-Jan-2013	$958	60%	64%				
Gilead	YM Biosciences	12-Dec-2012	$510	81%	74%				
Sun Pharma	DUSA Pharma	08-Nov-2012	$230	38%	17%	50	4.6		
Valeant	Medicis	03-Sep-2012	$2,600	39%	33%	721	3.6		11.1
GSK	Human Genome Sciences	16-Jul-2012	$3,000		99%	131	22.9		
TPG	Par Pharma	16-Jul-2012	$1,900	37%	52%	926	2.1		9.0
BMS/AZ	Amylin	02-Jul-2012	$7,000	10%	101%	651	10.8		
AstraZeneca PLC	Ardea	23-Apr-2012	$1,260	54%	40%				
Spectrum Pharma	Allos	05-Apr-2012	$206	27%	30%	73	2.8		
Bausch + Lomb	Ista	27-Mar-2012	$500	9%	134%	160	3.1		
Amgen, Inc.	Micromet	26-Jan-2012	$1,160	33%					
Bristol-Myers Squibb	Inhibitex	07-Jan-2012	$2,500	163%	86%				
Gilead	Pharmasset	21-Nov-2011	$11,000	89%	74%				
Cubist	Caldolor	24-Oct-2011	$415						
Roche	Anadys	17-Oct-2011	$230	256%	289%				
Santen	Novagli Pharma	28-Sep-2011	€ 100	71%	71%				
Pfizer	Icagen	20-Jul-2011	$56		146%				
Teva	Cephalon	01-May-2011	$6,800	6%	39%	2,811	2.4	10.0	7.2
Endo Pharma	American Medical Systems	11-Apr-2011	$2,900	34%	43%	642	4.5	23.1	16.4
Merck	Inspire Pharma	06-Apr-2011	$340	25%	25%	106	3.2		
Cephalon	ChemGenex	29-Mar-2011	$232	59%	65%				
Forest Lab	Clinical Data	22-Feb-2011	$929	-8%	100%				
Kyow a Hakko Kirin	ProStrakan	21-Feb-2011	$477	19%	33%	155	3.1		
Sanofi Aventis	Genzyme	16-Feb-2011	$20,100		48%	4,049	5.0		

Source: Compiled by MHBK/IRD based on Capital IQ and public company reports

Table 18 Recent Biopharma M&As with Private Targets

Aquirer	Target	Ann. Date	Value ($mm)	Target Sales LTM ($mm)	P/Sales LTM
Actelion	Ceptaris Therapeutics	31-Jul-2013	$250		
Astra Zeneca	Amplimmune	27-Aug-2013	$225		
Celgene	Acetylon	30-Jul-2013	$100		
Johnson & Johnson	Aragon	17-Jun-2013	$650		
Astra Zeneca	Pearl Therapeutics	10-Jun-2013	$560		
Valeant	Bausch & Lomb	27-May-2013	$8,700	3,300	2.6
Novo A/S	Xellia Pharma	21-May-2013	$700	220	3.2
Takeda	Inviragen	08-May-2013	$35		
Auxilium	Actient	29-Apr-2013	$585	125	4.7
Shire	SARcode	25-Mar-2013	$160		
Mylan	Agila	27-Feb-2013	$1,600	255	6.3
Perrigo	Rosemont	11-Feb-2013	$283	63	4.5
Perrigo	Velcera	01-Feb-2013	$160		
Watson	Uteron	23-Jan-2013	$150		
Opko Health	Cytochroma	09-Jan-2013	$100		
The Medicines Company	Incline Therapeutics	12-Dec-2012	$185		
Takeda	Envoy Pharma	06-Nov-2012	$140		
Pfizer	NextWave	22-Oct-2012	$255		
Takeda	LigoCyte	03-Oct-2012	$60		
Dainippon Sumitomo	Elevation Pharma	31-Aug-2012	$100		
Valeant	OraPharma	15-Jun-2012	$312	95	3.3
Takeda	Multilab Industria	25-May-2012	$248	69	3.6
Cornerstone Therpeutics	EKR Therapeutics	15-May-2012	$125	58	2.2
Novartis	Fougera Pharma	02-May-2012	$1,500	429	3.5
Jazz Pharma	Eusa	26-Apr-2012	$650	170	3.8
Amgen	Mustafa Nevzat Pharmaceuticals	25-Apr-2012	$700	200	3.5
Shire	Pervasis	12-Apr-2012			
Takeda	URL Pharma	11-Apr-2012	$800	600	1.3
Amgen	KAI Pharma	10-Apr-2012	$315		
Shire	Ferrokin	15-Mar-2012	$100		
Dainippon Sumitomo	Boston Biomedical	02-Mar-2012	$200		
Biogen-Idec	Stromedix	14-Feb-2012	$75		
Celgene	Avila	26-Jan-2012	$350		

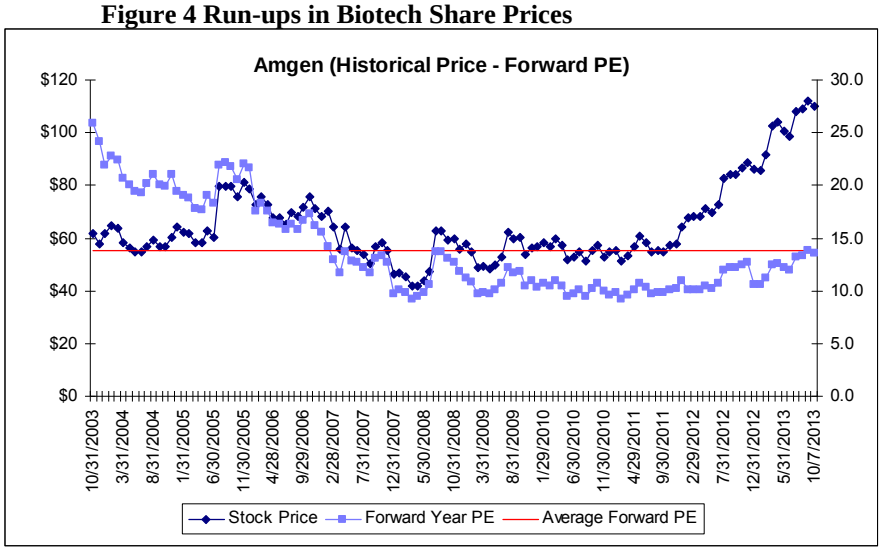
Source: Compiled by MHBK/IRD based on Capital IQ and public company reports
Note: Comment marks denote additional milestone payments

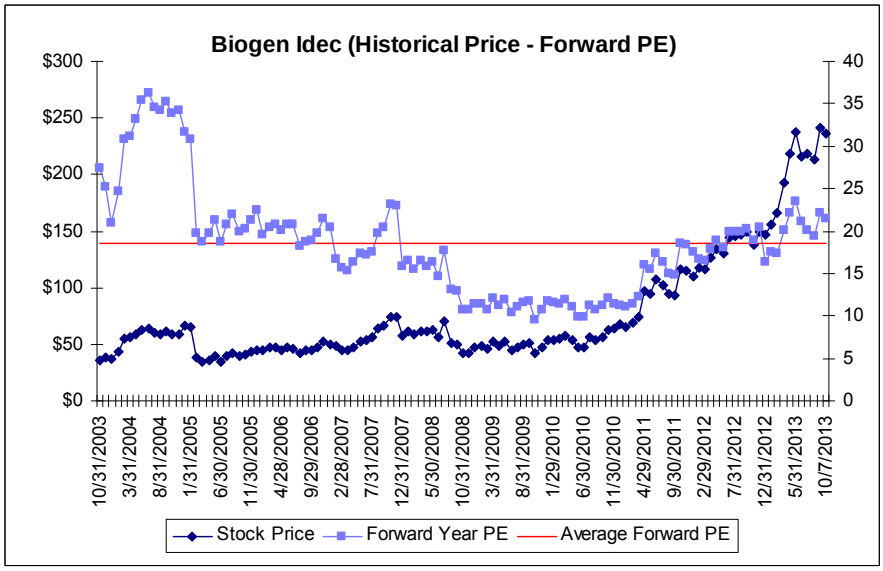
II. U.S. Biotech Industry Updates

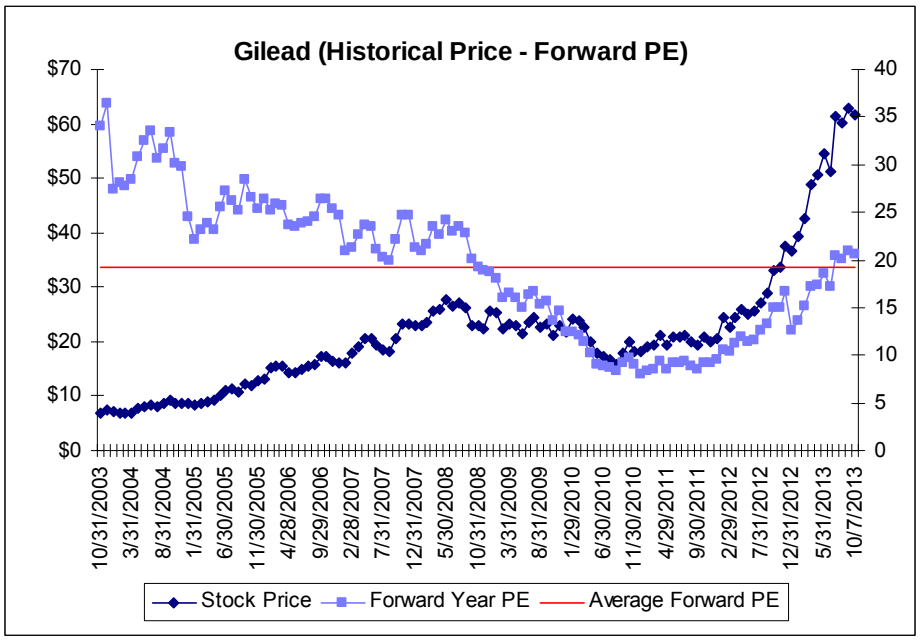
Over the last year, major biotech companies have witnessed a significant surge in their share prices (see charts below). The rising share price is a result of excitement over new drugs, specifically HCV therapies (Gilead), Multiple Sclerosis (Biogen Idec), oncology (Celgene), atherosclerosis and cancer therapy (Amgen). Leading biotech companies have enjoyed rising earnings estimates and a modest PE multiple expansions (or more precisely a recovery from historical lows).

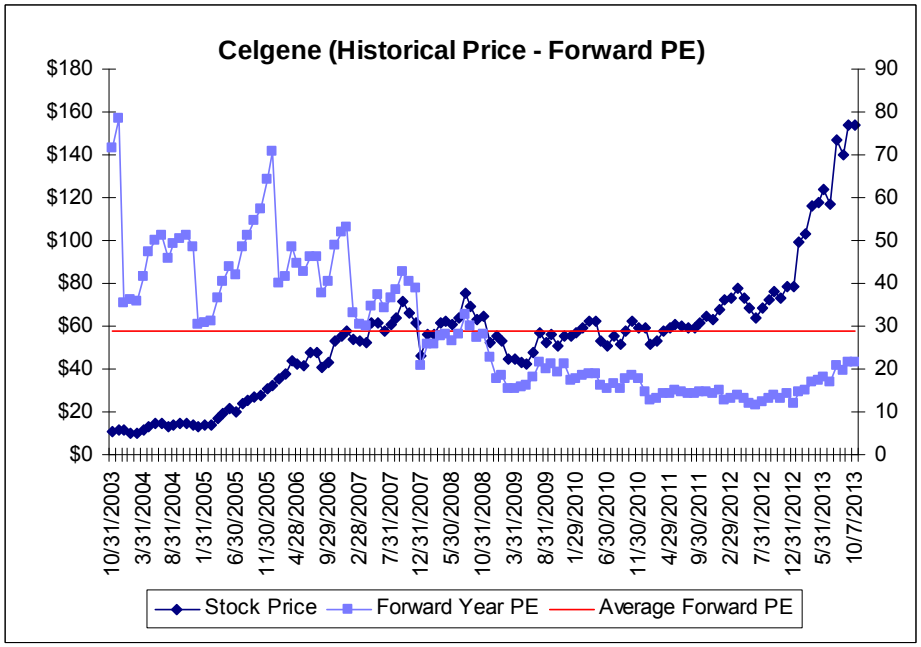
Major biotech companies have found great use of their cash. Gilead's expensive $11bn acquisition of Pharmasset in retrospect turned out to be a big winner. Celgene's acquisitions of Abraxis and Avila were major positives for the company.

Figure 4 Run-ups in Biotech Share Prices





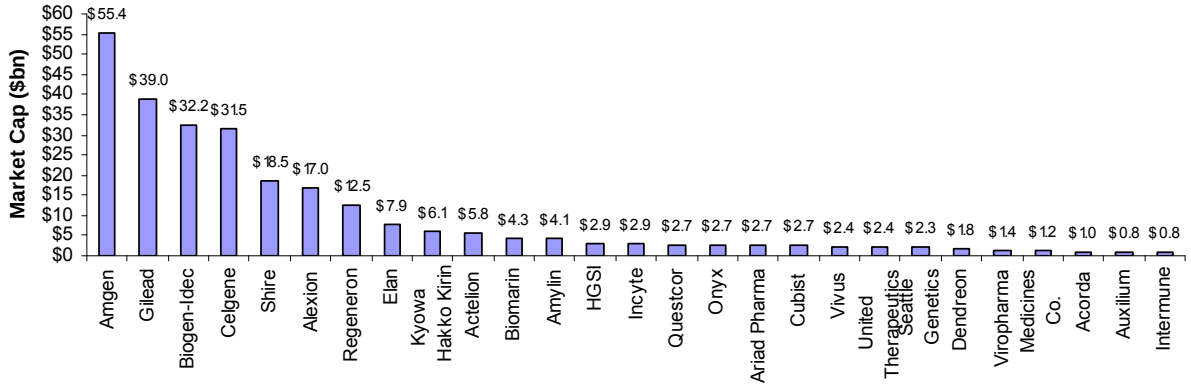




Source: Compiled by MHBK/IRD based on data from Capital IQ

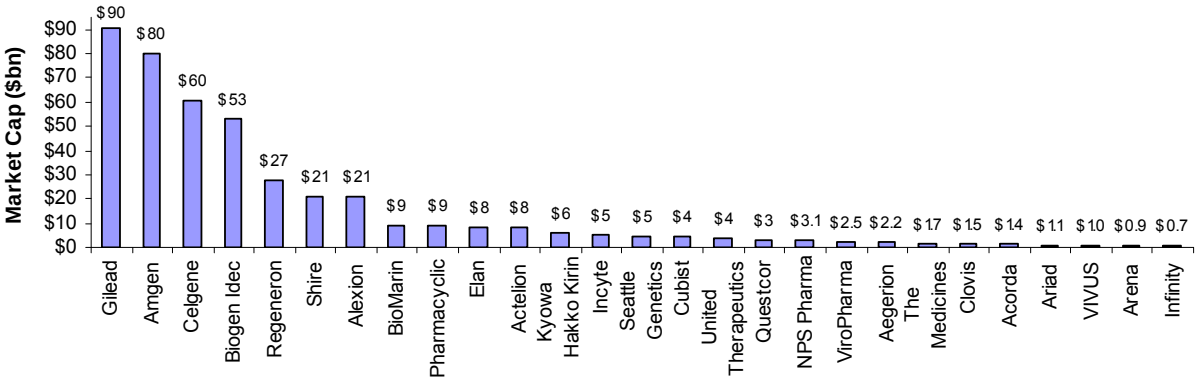
Comparing Figure 5 and Figure 6 again tells the story of broad-based rally in biotech shares. Following drug approvals Amylin and Human Genome Sciences were acquired last year. Several mid-cap biotech companies have seen their valuation increase significantly, including Regeneron, BioMarin, Onyx, Seattle Genetics, etc. Several companies have risen to fill the depleted rank of mid-cap biotech rank (which is a result of pharma acquisitions). These companies are often orphan drug companies, including NPS Pharma and Aegerion.

Figure 5 Biotech Ranking by Market Cap (as of May 2012)



Source: Compiled by MHBK/IRD based on data from Capital IQ

Figure 6 Biotech Ranking by Market Cap (Current)



Source: Compiled by MHBK/IRD based on data from Capital IQ

Table 19 is a list of biotech companies that either have or will be soon to have commercial products. These companies are likely to be the most dynamic and attract the highest interest from large pharma.

Table 19 Commercial or Near-Commercial Biotech Companies

10/10/2013		Market	EV	% 52-wk	Sales	Sales	EV/Sales		EPS		P/E	
Company name	Ticker	Cap (USD in mn)	(USD in mn)	High	2012A	2013E	2012A	2013E	2012A	2013E	2012A	2013E
Acorda Therapeutics, Inc.	ACOR	$1,383	$1,084	86%	$304	$341	3.6	3.2	0.92	0.77	46.1	37.9
Aegerion	AEGR	$2,214	$2,094	81%	$0	$41	NA	50.5	-2.39	-2.15		
Alexion Pharmaceuticals, Inc.	ALXN	$20,627	$19,652	85%	$1,118	$1,531	17.6	12.8	2.02	2.96	117.5	53.1
AMAG Pharmaceuticals, Inc.	AMAG	$413	$200	72%	$87	$79	2.3	2.5	-0.63	-0.56		
Amarin Corporation plc	AMRN	$1,087	$1,175	49%	$0	$49	NA	24.0	-1.22	-1.38		
Ariad Pharmaceuticals Inc.	ARIA	$1,079	$737	22%	$1	$58	1174.8	12.6	-1.33	-1.64	-6.0	-4.2
Auxilium Pharmaceuticals Inc.	AUXL	$844	$1,270	74%	$394	$381	3.2	3.3	1.47	0.48		11.6
AVEO Pharmaceuticals, Inc.	AVEO	$107	-$25	24%	$17	$3	-1.5	-7.6	-3.00	-1.30	2.9	-0.7
BioMarin Pharmaceutical Inc.	BMRN	$9,243	$8,953	82%	$500	$551	17.9	16.2	-0.68	-1.10		
Cadence Pharmaceuticals Inc.	CADX	$479	$452	69%	$50	$106	9.1	4.3	-0.86	-0.33		
Cubist Pharmaceuticals Inc.	CBST	$4,206	$3,694	95%	$926	$1,034	4.0	3.6	2.78	1.96	124.2	23.2
Cumberland Pharmaceuticals, Inc.	CPIX	$86	$23	74%	$49	$33	0.5	0.7	0.34	0.07	17.0	14.1
Dendreon Corp.	DNDN	$404	$788	36%	$325	$299	2.4	2.6	-2.48	-1.66		
Dyax Corp.	DYAX	$696	$732	91%	$54	$55	13.6	13.3	-0.30	-0.28		
Enzon Pharmaceuticals Inc.	ENZN	$73	$58	22%	$42	$36	1.4	1.6	0.11	0.37		16.0
Incyte Corporation	INCY	$5,313	$5,259	86%	$270	$349	19.5	15.1	-0.49	-0.30		
InterMune Inc.	ITMN	$1,083	$959	85%	$29	$63	33.0	15.3	-2.66	-2.81		
Jazz Pharmaceuticals Public Limited Co	JAZZ	$4,901	$4,949	90%	$591	$871	8.4	5.7	4.58	6.25	31.6	18.4
NPS Pharmaceuticals, Inc.	NPSP	$3,120	$3,103	90%	$134	$145	23.2	21.4	-0.21	-0.18		
Optimer Pharmaceuticals, Inc.	OPTR	$618	$540	75%	$100	$88	5.4	6.1	-1.19	-2.24	74.2	
Questcor Pharmaceuticals, Inc.	QCOR	$3,153	$3,078	78%	$493	$732	6.2	4.2	3.04	4.26	48.1	19.2
Regeneron Pharmaceuticals, Inc.	REGN	$27,391	$27,326	90%	$1,291	$1,931	21.2	14.2	4.12	7.00		69.7
Savient Pharmaceuticals, Inc.	SVNT	42	222	23%	19	26	11.6	8.5	-1.92	-1.27		
Seattle Genetics Inc.	SGEN	$4,825	$4,487	82%	$205	$246	21.8	18.3	-0.48	-0.64		
The Medicines Company	MDCO	$1,679	$1,609	87%	$503	$690	3.2	2.3	1.30	1.75	13.9	25.1
United Therapeutics Corporation	UTHR	$3,995	$3,579	96%	$904	$1,075	4.0	3.3	5.16	5.99	22.5	16.0
Vertex Pharmaceuticals Incorporated	VRTX	$16,332	$15,525	78%	$1,538	$1,174	10.1	13.2	1.32	-0.50	499.0	53.0
VIVUS Inc.	VVUS	$1,021	$869	44%	$3	$43	320.6	20.0	-1.27	-1.95		
ViroPharma Inc.	VPHM	$2,502	$2,412	93%	$440	$446	5.5	5.4	0.70	0.69	22.7	54.4
Average				71%								

Source: Compiled by MHBK/IRD based on public reports and Capital IQ

A. Biotech Product Launches and Current Landscape

Looking at drug approval history by major biotech (Table 20), there are a number of important drugs approved in 2012 and so far in 2013. From major biotech companies the list includes Stribild, Kyprolis, Tecfidera and Pomalyst. In 2013 we could see approvals of important drugs such as Sofosbuvir from Gilead.

Table 20 U.S. Biotech Drug Approvals by Company by Year

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Gilead	Viread	Hepsera	Emtriva	Truvada		Atripla	Letairis	Viread (HBV)*,		Cayston	Complera	Stribild	Sofosbuvir
Amgen	Aranesp, Kineret	Neulasta		Sensipar	Kepivance	Vectibix		Nplate (ITP)		Prolia Xgeva			
Celgene					Revlimid	Revlimid (MM)							Pomalyst, Apremilast, Abraxane (PC)
Biogen Idec		Zevalin	Amevive	Tysabri		Tysabri relaunch							Tecfidera
Regeneron								Arcalyst			Eylea	Zaltrap	
Alexion							Soliris						
Vertex			Lexiva								Incivek	Kalydeco	
Onyx					Nexavar							Kyprolis, Stivarga	
Seattle Genetics											Adcetris		
Medivation												Xtandi	
United Therapeutics		Inj. Remodulin							Tyvaso				
Incyte											Jakafi		
Ariad												Iclusig	
Arena												Belviq	
Acorda										Ampyra			
NPS Pharma												Justapid	
Aegerion												Gattex	
Vivus												Qsymia, Stendra	
Amarin												Vascepa	
Auxilium										Xiaflex			
Dendreon										Provenge			
Protalix												Elelyso	
Savient										Krystexxa			
Genentech			Raptiva Xolair	Avastin Tarceva		Lucentis		Avastin (BC)*					
Genzyme	Campath		Fabrazyme Aldurazyme	Clolar		Myozyme	Renvela*	Mozobil					
MedImmune			Flumist				CAIV-T^						
OSI Pharma				Tarceva									
Millennium			Velcade										
ImClone				Erbitux									
Amylin					Byetta Symlin							Bydureon	
Human Genome Sciences											Benlysta		
Plexxikon											Zelboraf		

Source: Compiled by MHBK/IRD based on public company reports.
Note: highlighted companies had been acquired.

Major biotech's late-stage portfolios have expanded, thanks to productive internal R&D engine and acquisitions (see Table 21). Large biotech companies have successfully acquired a number of late-stage assets including:

- Talimogene laherparepvec (T-Vec) and Blinatumomab for Amgen.
- Abraxane for Celgene.
- Sofosbuvir and Idelalisib for Gilead.

Table 21 Late-stage Pipeline of Leading Biotech Companies

Company	Compound	Indication	Phase	Mechanism of Action
Amgen	AMG 145	Hyperlipidemia	III	Anti PCSK9 Mab
	Romosozumab (AMG 785)	Postmenopausal osteoporosis	III	Anti Sclerostin Mab
	Brodalumab (AMG 827)	Psoriasis	III	Anti IL17RA Mab
	Talimogene laherparepvec / T-Vex (GM-CSF)	Metastatic melanoma	III	Oncolytic virus
	Trebananib (AMG - 386)	Ovarian cancer	III	Angiopoeitin peptibody
	Rilotumumab (AMG 102)	Gastric cancer	III	HGF Mab
	Blinatumomab (AMG 103)	ALL	II	BiTE targeting CD19 expressing cancer cells
Biogen-Idec	Long acting rFactor IX	Hemophilia B	Filed	
	Long acting rFactor VIII	Hemophilia A	III	
	Plegridy	MS	III	PEG IFNβ 1A
	Daclizumab	MS	III	Mab targets IL-2 receptor
	GA101	NHL/CLL	III	Next generation anti-CD20 Mab
	Dexpramipexole	ALS	III	Neuroprotection through improving mitochondra function
Celgene	Revlimid	NHL/CLL/MDS	III	IMiDs
	Abraxane	Lung, pancreatic, melanoma, etc.	III	Albumin bound paclitaxel nanoparticle
	Pomalidomide	Myelofibrosis, MM	III	IMiDs
	Apremilast	Psoriasis, PsA, AS	III	PDE4 inhibitor
	Amrubicin	SCLC	III	DNA intercalator
	Oral Vidaza	MDS / AML	II	DNA hypomethylating agent
Gilead	Elvitegravir	HIV	Filed	HIV Integrase inhibitor
	cobicistat (GS 9350)	PK enhancer	Filed	p450 enzyme inhibitor
	Sofosbuvir	HCV NS5B inhibitor	Filed	HCV nucleoside inhibitor
	Idelalisib	CLL / Indolent NHL	III	PI3Kδ inhibitor

Source: Compiled by MHBK/IRD based on public company reports

B. 2013 Milestones for Biotech Companies

In 2013, we again will see pivotal clinical data or regulatory decision for a large number of biotech companies (see Table 22).

- In the cancer vaccine field, late 2012 saw the failure of Oncothyreon/Merck KGaA's Stimuvax. In 2013, we will se phase III data for Amgen's T-Vec (already reported at ASCO), GSK's MAGE-A3 and Vical's Allovectin.
- In other areas of oncology, Onconova and Tesaro will report phase III data for their compounds.
- Several companies will report phase III data for new antibiotics. The risk is low for these clinical trials.

Historically for the biotech industry, negative clinical or regulatory news was more the norm. Consistently with the historical pattern, there have been many clinical trial failures over the last year (see Table 23).

Table 22 Important Milestones for Biotech Companies in 2013

Company	Product	Indication	Key Events	Time Frame
AcelRx Pharma	ARX-01	Post-operative pain	Phase III data	1Q13; 3Q13
Actelion / Nippon Shinyaku	Selexipag	PAH	Interim Phase III data	Mid-2013
Amgen	Talimogene laherparepvec	Metastatic melanoma	Phase III data	2013
Amgen	AMG386	Ovarian cancer	Phase III data	2013
Biogen Idec	PEGylated IFNβ 1a	MS	Phase III data	2013
Celgene	Apremilast	Psoriasis / Psoriatic arthritis	Submit NDA	2H13; 1H13
Cubist	CXA-201	cIAI; cUTI	Submit NDA	YE2013
Durata	IV dalbavancin	ABSSSI	Phase III data, NDA	2013
Gilead	Sofosbuvir	HCV	Submit NDA, MAA	Mid-2013
GSK	MAGE-A3	NSCLC	Phase III data	2013
GTx	Ostarine	Muscle wasting in NSCLC	Phase III data	2Q13
Kythera / Bayer	ATX-101	Reduce submental fat	Phase III data	Mid-2013
Nektar	Naloxegol	Opioid-induced constipation	Submit NDA, MAA	3Q13
NPS Pharma	Natpara	Hypoparathyroidism	Submit BLA	Mid-2013
OncoGenex	Custirsen	Metastatic CRPC	Phase III data	YE2013
Onconova	Estybon	MDS	Phase III data	2H2013
Tesaro	Rolapitant	CINV	Phase III data	2H2013
Orexigen	Contrave	Obesity	Interim Phase III data; submit NDA	2013
QRx Pharma	MoxDuo	Pain	Submit NDA, MAA	2013
Rigel	Fostamatinib	RA	Phase III data	2013
Rockwell Medical	Ferric	Iron deficiency in CKD	Submit NDA	2H13
The Medicines Co.	IV oritavancin	ABSSSI	Phase III data	2013
Tioga/ Ono	Asimadoline	IBS-D	Phase III data	Mid-2013
Trius	Tedozolid	ABSSSI	Phase III data	2013
Vical	Allovectin	Metatatic melanoma	Phase III data	Mid-2013

Source: Compiled by MHBK/IRD based on Capital IQ and public company reports

Table 23 Negative Clinical and Regulatory News for Biotech Companies

Company	Date of Announcement	Share Price Decline in a Day	Clinical Trial Failed
Ariad	Oct-13	-66%	FDA put a clinical hold on Iclusig clinical trial due to CV safety concerns
Achillion	Sep-13	-58%	FDA refused to life a clinical hold on Achillion's HCV protease inhibitor.
Prosensa	Sep-13	-70%	Drisapersen failed to meet primary endpoint in phase III study.
Acura Pharma	Aug-13	-20%	Pain drug Vucavert missed primary endpoint in a phase II study.
ChemoCentryx	Aug-13	-29%	Phase III trial for vercirnon in Crohn's disease failed to show efficacy.
GTx	Aug-13	-66%	Phase III trial in NSCLC muscle wasting failed to show significant efficacy improvement.
Vical	Aug-13	-57%	Phase III trial of Allovectin failed to show efficacy in melanoma.
Resverlogix	Jun-13	-93%	Phase IIb ASSURE trial failed to show significant reduction in atheroma volume.
AVEO Pharma	May-13	-50%	FDA AdComm recommended against approval of tivozanib for renal cell carcinoma.
Titan Pharma	May-13	-74%	FDA gave a CRL to Probuphine for treating opioid dependence, asking for more efficacy data.
Delcath	Apr-13	-40%	FDA Adcom recommended approval of Melblez for liver metastasis of ocular melanoma.
Clavis Pharma	Apr-13	-82%	Phase III trial of elacytarabine in AML failed to show survival benefit.
Ziopharm	Mar-13	-65%	Palifosfamide failed to show PFS benefits in phase III soft tissue sarcoma study.
Celsion	1/31/2013	-81%	Thermodox didn't meet the primary PFS end point in liver cancer.
Pharmaxis	1/30/2013	-40%	FDA AdCom voted against approval of Bronchitol for improving pulmonary function in CF pts
Amicus	12/20/2012	-47%	Amigal didn't meet primary end point in Fabry's disease study.
Oncothyreon	12/19/2012	-51%	Stimuvax didn't meet survival end point in phase III NSCLC study.
Rigel	12/13/2012	-35%	Fastamatinib was shown to be inferior to Humira in a phase II study.
Dynavax	11/16/2012	-46%	FDA Adcom had a negative vote for the safety of Heplisav due to its novel adjuvant.
Tranzyme	11/15/2012	-76%	Phase II study of oral Ghrelin agonist failed to show efficacy in diabetis gastroparesis.
Clovis Oncology	11/12/2012	-42%	A phase III study of CO-101 in pancreatic cancer failed to show efficacy.
Clavis Pharma	11/12/2012	-80%	A phase III study of CO-101 in pancreatic cancer failed to show efficacy.
Catalyst Pharma Partners	11/8/2012	-62%	Phase IIb study for cocaine addiction failed.
BioCryst	11/8/2012	-40%	Discontinued phase III trial of influenza drug peramivir due to futility
Wilex	10/16/2012	-62%	Rencarex missed efficacy endpoint in cell cell RCC.
ArQule	10/2/2012	-56%	Phase III MARQUEE trial in NSCLC failed to show efficacy at interim analysis.
Cornerstone Therapeutics	9/13/2012	-21%	FDA advisory panel voted against approval of Lixivaptan for hyponatremia.
Zalicus	9/10/2012	-43%	Dropped combination drug Synavive for RA due to lack of efficacy vs. Prednisolone.
Geron	9/10/2012	-56%	Imetelstat failed a couple of phase II trials in breast and NSCLC.
Idenix	8/16/2012	-30%	FDA placed a clinical hold on its HCV polymerase inhibitor due to CV signal seen in BMS's
Agennix	8/6/2012	-69%	Phase III study of talactoferrin failed to meet survival endpoint in NSCLC.
Halozyme	8/2/2012	-50%	FDA halted Halozyme trial with its rHuPH due to safety concern. CRL for HyQ.
Progenics	7/30/2012	-50%	FDA issued a CRL for injectable Relistor for OIC in non-cancer pain
Anthera	6/27/2012	-69%	Blisibimod misses Phase IIb SLE endpoint
Ventrus	6/25/2012	-59%	Phase III trial of 5HT antagonist to treat hemorrhoids failed.
Chealsea Therapeutics	5/31/2012	-31%	CH-4051 missed the co-primary endpoints vs. methotrexate in a Phase II RA trial
MediciNova	5/24/2012	-43%	MN221 failed a phase IIb study as an adjunctive therapy for athma.
Halozyme	4/16/2012	-24%	FDA requested additional data before the approval of HyQvia.
Keryx	4/2/2012	-65%	Perifosine phase III trial for CRC failed to show efficacy.
Aeterna Zentaris	4/2/2012	-66%	Perifosine phase III trial for CRC failed to show efficacy.
Chealsea Therapeutics	3/28/2012	-28%	FDA declined to approve Northera for NOH and requested more clinical data.
Tranzyme	3/12/2012	-43%	Ghrelin agonist failed a phase III study in POI. The company will discontinue the program.
Anthera	3/12/2012	-45%	Phase III study of sPLA2 inhibitor varespladib failed to show efficacy in ASC patients.
Karo Bio	2/14/2012	-68%	Discontinued Eprotirome for HeFH due to toxicity seen in dog
Infinity Pharma	1/27/2012	-40%	Hedgehog inhibitor Saridegib failed to show survival benefits in pancreatic cancer.
Columbia Laboratories	1/20/2012	-56%	FDA refusesd to approve Prochieve for preterm birth

Source: Compiled by MHBK/IRD based on Capital IQ and public company reports

C. Biotech Companies Focused on Oncology

Oncology companies have always been a key corner stone of the biotech industry. As we discussed earlier, the center of gravity in terms of innovation in oncology seems to have shifted from the biotech industry to the pharmaceutical industry. Part of this shift may be because many cancer biotech companies had already been acquired by pharma (see Table 24). As we noted earlier, large biopharma are currently reaping the rewards from past acquisitions in oncology. Because of the depleted rank of cancer-focused biotech companies, currently there is a limited set of publicly traded biotech companies. Correspondingly, private-help cancer biotechs also have dwindled in number. In addition, many independent oncology biotech companies are of poor quality, making them unattractive acquisition targets. One recent phenomenon is for former CEOs of successful oncology companies to found new companies, i.e., a second or third act by proven management team. These companies base their business model on in-licensing early-stage compounds from big pharma or other sources and developing them using management team's expertise. As there has been a pipeline rationalization among pharma, pharma often have early-stage compounds to out-license. This kind of "reverse licensing" has created substantial values for the serial entrepreneurs and investors who backed them. A partial list is shown in Table 26.

Table 24 Historical Acquisitions in Oncology

Aquirer	Target	Announcement Date	Value ($mm)	Premium 1 Day	Premium 1 Month	Target Sales LTM ($mm)	P/Sales LTM
Johnson & Johnson	Aragon	17-Jun-2013	$650				
Gilead	YM Biosciences	12-Dec-2012	$510	81%	74%		
Jazz Pharma	Eusa	26-Apr-2012	$650			170	3.8
Spectrum Pharma	Allos	05-Apr-2012	$206	27%	30%	73	2.8
Dainippon Sumitomo	Boston Biomedical	02-Mar-2012	$200				
Amgen, Inc.	Micromet	26-Jan-2012	$1,160	33%			
Celgene	Avila	26-Jan-2012	$350				
Takeda	Intellikine	21-Dec-2011	$190				
Supergen	Astex	07-Apr-2011	$113				
Cephalon	ChemGenex	30-Mar-2011	$230				
Cephalon	GeminX	22-Mar-2011	$225				
Daiichi Sankyo	Plexxikon	01-Mar-2011	$805				
Gilead	Calistoga	22-Feb-2011	$375				
Amgen	Biovex	24-Jan-2011	$425				
Sanofi Aventis	Targegen	30-Jun-2010	$75 upfront				
Gilead	CGI Pharma	25-Jun-2010	$120				
Celgene	Abraxis	30-Jun-2010	2,900	17%	62%	359	8.1
Astellas	OSI Pharma	01-Mar-2010	4,000	55%	68%	428	9.3
Celgene	Gloucester	07-Dec-2009	$340				
Onyx	Proteolix	12-Oct-2009	$276				
Bristol-Myers Squibb	Medarex	22-Jul-2009	$2,100	90%	93%	52	
Johnson & Johnson	Cougar Biotech	21-May-2009	1,000	16%	19%		
Sanofi Aventis	BiPar	15-Apr-2009	$500				
Eli Lilly & Co.	ImClone	31-Jul-2008	6,585	51%	73%	591	11.1
Roche	Genentech	21-Jul-2008	46,800	16%	27%	13,403	7.9
Daiichi Sankyo	U3 Pharma	21-May-2008	$235				
Takeda	Millennium Pharma	10-Apr-2008	8,800	53%	91%	528	16.7
Eisai	MGI Pharma	10-Dec-2007	3,923	23%	37%	369	10.6
Celgene	Pharmion	19-Nov-2007	2,900	46%	53%	256	11.3
Astellas	Agensys	27-Nov-2007	$537				
Eisai	Morphotec	21-Mar-2007	$325				

Source: Compiled by MHBK/IRD based on data from Capital IQ.
Note: comment marks denote additional milestone payments.

Table 25 Publicly-traded, North America-based Oncology Companies

10/10/2013 Company name	Ticker	Market Cap (USD in mn)	EV (USD in mn)	Price ($USD)	% 52-wk High	Sales 2012	Sales 2013E	Net Income 2012	Net Income 2013E	Net Cash
S&P 500 Index	^SPX			1678	97%					
NASDAQ Composite Index	^COMP			3731	98%					
Celgene Corporation	CELG	$60,404	$59,989	151.46	96%	$5,515	$6,353	1,456	2,555	415
Incyte Corporation	INCY	$5,313	$5,259	36.05	86%	$270	$349	-44	-49	54
Seattle Genetics Inc.	SGEN	$4,825	$4,487	40.30	82%	$205	$246	-54	-81	338
Medivation, Inc.	MDVN	$3,751	$3,707	51.60	84%	$175	$241	-41	-58	44
Dendreon Corp.	DNDN	$404	$788	2.63	36%	$325	$299	-394	-247	-384
Ariad Pharmaceuticals Inc.	ARIA	$1,079	$737	$5.69	22%	$1	$58	-221	-300	342
Spectrum Pharmaceuticals, Inc.	SPPI	$513	$439	8.34	63%	$267	$155	95	-13	74
Curis, Inc.	CRIS	$312	$285	3.83	81%	$18	$15	-16	-13	27
Æterna Zentaris Inc.	TSX:AEZ	$46	$20	1.46	44%	$32	$56	-20	-3	25
Agios Pharmaceuticals, Inc.	AGIO	$782	$798	26.30	78%	$0	$25	-20	-36	99
Ambit Biosciences Corporation	AMBI	$292	$209	17.49	82%	$0	$28	-27	-12	83
ArQule Inc.	ARQL	$142	$64	2.33	73%	$36	$15	-11	-30	78
Array BioPharma, Inc.	ARRY	$623	$614	5.57	78%	$86	$60	-24	-59	9
Astex Pharmaceuticals, Inc.	ASTX	$807	$673	8.49	90%	$82	$61	8	-28	134
BIND Therapeutics, Inc.	BIND	$229	$212	14.95	98%	$0	$0	-19	0	17
bluebird bio, Inc.	BLUE	$543	$314	22.97	63%	$0	$21	-24	-24	229
Cell Therapeutics, Inc.	CTIC	$198	$176	1.82	93%	$1	$11	-101	0	20
Celldex Therapeutics, Inc.	CLDX	$2,081	$1,926	27.70	71%	$10	$3	-59	-77	155
Clovis Oncology, Inc.	CLVS	$1,492	$1,120	50.86	59%	$0	$0	-74	-79	372
Cyclacel Pharmaceuticals, Inc.	CYCC	$62	$28	3.71	45%	$0	$0	-13	-16	34
CytRx Corporation	CYTR	$68	$40	2.23	61%	$0	$0	-18	-23	28
Endocyte, Inc.	ECYT	$478	$368	13.29	70%	$34	$62	-17	-16	111
Epizyme, Inc.	EPZM	$995	$846	35.45	78%	$0	$45	-1	0	149
Exelixis, Inc.	EXEL	$959	$943	5.29	89%	$50	$33	-148	-230	16
Fate Therapeutics, Inc.	FATE	$128	$187	6.83	74%	$0	$0	-14	0	-2
Five Prime Therapeutics, Inc.	FPRX	$209	$180	13.15	82%	$0	$0	-28	0	28
Halozyme Therapeutics, Inc.	HALO	$1,085	$1,041	10.17	84%	$28	$53	-54	-78	44
Heat Biologics, Inc.	HTBX	$74	$72	12.37	81%	$0	$0	-2	-8	2
GTX Inc.	GTXI	$97	$66	1.60	22%	$3	$0	-27	-52	32
ImmunoGen, Inc.	IMGN	$1,335	$1,140	16.03	79%	$19	$36	-73	-76	195
Infinity Pharmaceuticals, Inc.	INFI	$728	$452	14.85	29%	$47	$0	-54	-139	277
Merrimack Pharmaceuticals, Inc.	MACK	$352	$330	3.53	46%	$46	$64	-91	-124	22
Nektar Therapeutics	NKTR	$1,111	$1,044	9.88	68%	$79	$192	-172	-129	67
OncoGenex Pharmaceuticals, Inc.	OGXI	$125	$68	8.59	61%	$18	$24	-21	-34	57
Oncolytics Biotech Inc.	TSX:ONC	$234	$197	2.84	60%	$0	$0	-36	-24	36
OncoMed Pharmaceuticals, Inc.	OMED	$388	$515	14.59	47%	$0	$45	-22	-12	56
Oncothyreon Inc	ONTY	$115	$64	1.83	33%	$0	$0	-3	-34	51
Puma Biotechnology, Inc.	PBYI	$1,162	$1,055	41.87	67%	$0	$0	-74	-52	108
Pharmacyclics Inc.	PCYC	$8,817	$8,312	118.19	82%	$83	$185	88	90	505
Sunesis Pharmaceuticals, Inc.	SNSS	$241	$213	4.72	72%	$2	$7	-44	-41	28
Synta Pharmaceuticals Corp.	SNTA	$423	$376	6.12	52%	$0	$0	-63	-88	46
TG Therapeutics, Inc.	TGTX	$136	$126	4.15	54%	$0	$0	-18	-27	10
Tesaro, Inc.	TSRO	$1,168	$990	36.76	71%	$0	$0	-62	-84	178
Threshold Pharmaceuticals Inc.	THLD	$251	$153	4.46	73%	$7	$12	-71	-37	98
ZIOPHARM Oncology, Inc.	ZIOP	$356	$318	4.43	74%	$1	$1	-96	-72	39
Average					67%					

Source: Compiled by MHBK/IRD based on data from Capital IQ.

Table 26 Public Oncology Companies Founded by Former Biotech CEOs

6/25/2013 Company name	Ticker	Year Founded	Market Cap $mn	Price ($USD)	% 52-wk High	Source of the compounds	CEO founder	CEO's former company
Clovis Oncology, Inc.	CLVS	2009	$1,859	63.77	74%	Avila, Pfizer	Patrick J. Mahaffy	Pharmion
Tesaro, Inc.	TSRO	2010	$1,010	32.03	62%	Schering-Plough, Merck, Amgen	Lonnie Moulder	MGI Pharma
Puma Biotechnology, Inc.	PBYI	2010	$1,282	41.56	93%	Pfizer	Alan Auerbach	Cougar
TG Therapeutics, Inc.	TGTX	2012	$166	6.08	78%	GTC Biotherapeutics; Rhizen Pharmaceuticals	Michael S. Weiss	Keryx

Source: Compiled by MHBK/IRD based on data from Capital IQ.

D. Orphan Drug Companies Are Becoming More Prominent

As we discussed previously, orphan drug companies are becoming a more prominent and critical constituent of biotech industry. Following oncology companies, orphan drug companies represent the second largest block of biotech industry. Their importance is increasingly appreciated by the stock market as well as large pharma companies.

There are estimated 6,000-7,000 rare diseases in the world, only 10% of which have approved therapy. Although the incidence of each disease is low, combined together, 30mn Americans and 30mn Europeans currently suffer from rare diseases. The high commercial potential of rare diseases has been proven by a number of important drugs on the market (see Table 27). Companies such as Genzyme and Alexion have reached the top-echelon of the biotech industry on the back of successfully marketing orphan drugs. Consistent with the popularity of orphan drugs, the equity market has rewarded rich valuations for leading companies in this field. There are now an impressive group of orphan drug companies in the public equity market (see Table 28).

Table 27 Major Orphan Drugs (outside of Oncology) Currently on the Market

Drug	Manufacturer	Indication	Estimated U.S. WAC	Patient Population	2010 sales ($mn)	2012 Sales ($mn)	2013 Guidance
Soliris	Alexion	PNH (paroxymal nocturnal hemoglobinuria)	$410K	8-10K	$541	$1,134	$1,490-$1,505
	Alexion	aHUS (atypical hemolytic uremic syndrome)					
Cerezyme	Genzyme	Gaucher disease	$216K	10K	$1,239	$817	
Myozyme / Lumizyme	Genzyme	Pompe Disease	$355K	5-10K	$412	$596	
Elaprase	Shire	Hunter Syndrome	$410K	2K	$404	$498	
Replagal	Shire	Fabry Disease	$200K	5-10K	$351	$498	
Fabrazyme	Genzyme	Fabry Disease	$234K	5-10K	$494	$377	
Cinryze	Viropharma	HAE prophylaxis	$406K	6.2K in U.S.	$177	$327	$390 to $400mn U.S.
VPRIV	Shire	Gaucher disease	$170K	10K	$143	$307	
Naglazyme	Biomarin	MPS-VI	$608K	1K	$193	$257	
Kalydeco	Vertex	CF	$294K	1,200 in U.S.		$172	
Kuvan	Biomarin	Phenylketonuria	$100K	50K	$99	$143	
Firazyr	Shire	Acute attack of HAE		6.2K in U.S.	$11	$116	
Kalbitor	Dyax	Acute attack of HAE		6.2K in U.S.	$9	$40	$52-56
Aldurazyme	Genzyme	MPS-I	$282K	3K	$167		
Justapid	Aegerion	HoFH	$295K	6K			
Gattex	NPS Pharma	Short Bowel Syndrome	$295K	3-5K in U.S.			
RAVICTI	Hyperion	Urea cycle disorders	$277K	2K in U.S.			

Source: Compiled by MHBK/IRD based on public company reports.
*Note: 2010 revenues were shown alongside of 2012 sales because a number of drugs from Genzyme achieved peak sales in 2010 before the manufacturing constraints.

Table 28 Publicly-traded Orphan Drug Companies

10/8/2013 Company name	Market Cap (USD in mn)	EV (USD in mn)	Price (USD)	52-wk Hi	52-wk Low	Sales 2012A	Sales 2013E	EV/Sales 2012A	EV/Sales 2013E	P/E 2012A	P/E 2013E
Aegerion	$2,462	$2,342	$84.98	$99.00	$13.50	$0	$41	NA	56.5		
Biomarin	$9,563	$9,273	$67.25	80.67	36.28	$500	$551	18.5	16.8		
bluebird bio, Inc.	$557	$329	$23.50	36.25	23.76	$0	$21	NA	15.9		
Dyax Corp.	$728	$763	$6.65	7.28	2.24	$54	$55	14.2	13.9		
Hyperion	$531	$432	$26.42	29.50	10.00	$0	$36	NA	12.0		
Intercept Pharma	$1,245	$1,083	$64.65	77.53	17.96	$3	$2	348.9	671.9		
NPS Pharmaceuticals, Inc.	$3,166	$3,148	$31.21	35.72	7.35	$134	$145	23.5	21.7		
Questcor Pharmaceuticals, Inc.	$3,180	$3,105	$55.06	74.76	19.90	$493	$732	6.3	4.2	45.5	18.1
Raptor	$814	$789	$13.64	15.29	4.35	$0	$9	NA	89.8		
Sarepta	$1,678	$1,524	$50.05	55.61	21.21	$36	$16	42.2	92.8		
Synageva	1,873	1,588	$61.91	70.50	38.58	13	15	125.3	108.6		
United Therapeutics Corporation	$4,067	$3,651	$81.47	85.92	44.51	$904	$1,075	4.0	3.4	22.3	15.8
ViroPharma Inc.	$2,602	$2,511	$39.71	41.14	22.12	$440	$446	5.7	5.6	23.6	56.7
Total	**$32,466**	**$30,538**				**$2,577**	**$3,143**				

Source: Compiled by MHBK/IRD based on data from Capital IQ

Orphan diseases have attracted drug developers' interest for a number of reasons:

- Life threatening nature of the disease makes any clinically proven therapy a medical necessity. Therefore, pricing and reimbursement has been very favorable (see Table 27).
- Orphan drugs enjoy a variety of incentives from exclusivity (7 years in the U.S. and 10 years in Europe), tax credits, fee waivers, to expedited regulatory review.
- Only a small sales force is needed, thus orphan drug carries small SG&A overhead.

As shown in Table 29, pharma have changed their mindset and embraced rare diseases. Their focus has been to acquire late-stage assets that have significantly reduced clinical risk. Some pharma such as GSK have also teamed up with venture funds to provide seed financing for start-up orphan drug developers. This way, they can ensure there is a continued and growing supply of orphan drugs in development.

Table 29 Pharma's Initiatives in Orphan Diseases

Company	Strategies	Deals
Sanofi-Aventis	Established a platform for rare disease through Genzyme	Acquired Genzyme for $20bn in 2011.
Alexion	Selected acquisition of orphan disease products	- Acquired Enobia for up to $1.08bn in 2011. - Acquired Taligen for $111mn in January 2011
Pfizer	Established rare disease unit in June 2010	- Licensed orphan drug for sickle cell disease from Glycomimetics in 2011 - Licensed UPLYSO from Protalix in 2009 - Acquired FoldRx in 2010 - Partnered with Zacharon Pharma for LSD MPS
GSK	Established a stand-alone unit for the development and commercialization of rare diseases in February 2010	- Partnered with Angiochem for CNS LSD. - Licensed DMD compound from Prosensa in 2009 - Licesned several ERTs from JCR - Partnered with Amicus in 2010
Eli Lilly		-Acquired Alnara in 2010
Shire	Through acquisitions and internal development, Shire Human Genetic Therapies Inc. has been a bright star within Shire.	-Acquired Premacure (retinopathy of infants) - Acquired Lotus Tissue Repair in 2013. - Acquired TKT in 2005 - Entered into partnership with Amicus in 2007 - Acquired Jerini in 2008 - Signed deal with Acceleron in 2010
Viropharma	Acquired a major asset at a bargain price.	-Acquired Lev Pharma in 2008
Chiesi	Entered into rare disease market through acquisition of Zymenex. Considering setting up a rare disease unit.	-Acquired Zymenex in 2013 -Licensed from UniQure Glybera and Hemophilia B gene therapies in 2013

Source: Compiled by MHBK/IRD based on public company reports

Currently a number of compounds for orphan disease are in late-stage development. A number of orphan diseases such as Cystic Fibrosis, Familial hypercholesterolemia, and Duchenne muscular dystrophy (DMD) are on the edge of major breakthroughs.

Table 30 Selected Compounds in Development for Orphan Indications (excl. oncology)

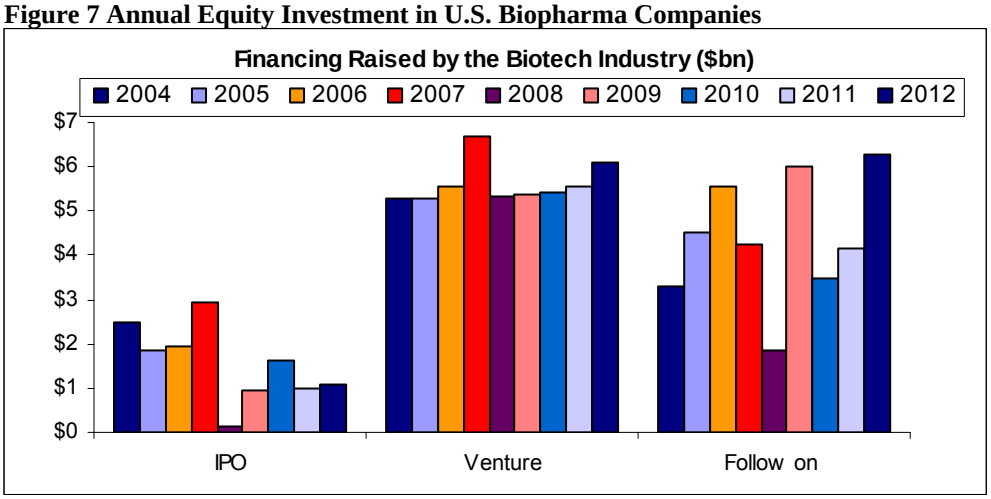
Drug candidate	Manufacturer	Indication	Status
Alipogene (Glybera)	uniQure	Lipoprotein lipase deficiency	Approved in Europe
Esbriet (Perfenidone)	InterMune	Idiopathic Pulmonary Fibrosis (IPF)	Phase III in U.S., approved in Europe
Liprotamase	Alnara / Eli Lilly	exocrine pancreatic insufficiency (EPI)	Received CRL from FDA
Tafamidis meglumine	FoldRx / Pfizer	Familial amyloid polyneuropathy (FAP)	Received RTF letter from FDA
Vimizim (GALNS)	Biomarin	MPS IVa (Morquio Syndrome)	Filed
Natpara / NPSP 558	NPS Pharma	Hypoparathyroidism	Phase III
Eliglustat (GENZ-112638)	Genzyme	Gaucher disease	Phase III
Ataluren	PTC / Genzyme	Cystic Fibrosis / Duchenne muscular dystrophy	Phase III
Obeticholic Acid / OCA	Intercept	PBC	Phase III
PEG-PAL	Biomarin	PKU (Phenylketonuria)	Phase II
Eteplirsen	Sarepta	Duchenne muscular dystrophy	Phase II
Drisapersen (PRO 044)	Prosensa / GSK	Duchenne muscular dystrophy	Phase I/II
UX001	Ultragenyx	Hereditary inclusion body myopathy	Phase II
UX007	Ultragenyx	Fatty acid oxidation disorder	Phase II in 2H2013
UX003	Ultragenyx	MPS VII	Phase I/II
Lenti-D	Bluebird Bio	Childhood Cerebral ALD (Adrenoleukodystrophy)	Phase II
LentiGlobin	Bluebird Bio	Beta Thalassemia /Sickle cell anemia	Phase I
Sebelipase (SBC-102)	Synageva	Lysosome acid lipase/LAL deficiency	Phase II
ENB-0040	Alexion/Enobia	Hypophosphatasia (HPP)	Phase II

Source: Compiled by MHBK/IRD based on public company reports

E. Financing Trends for Biotech Companies

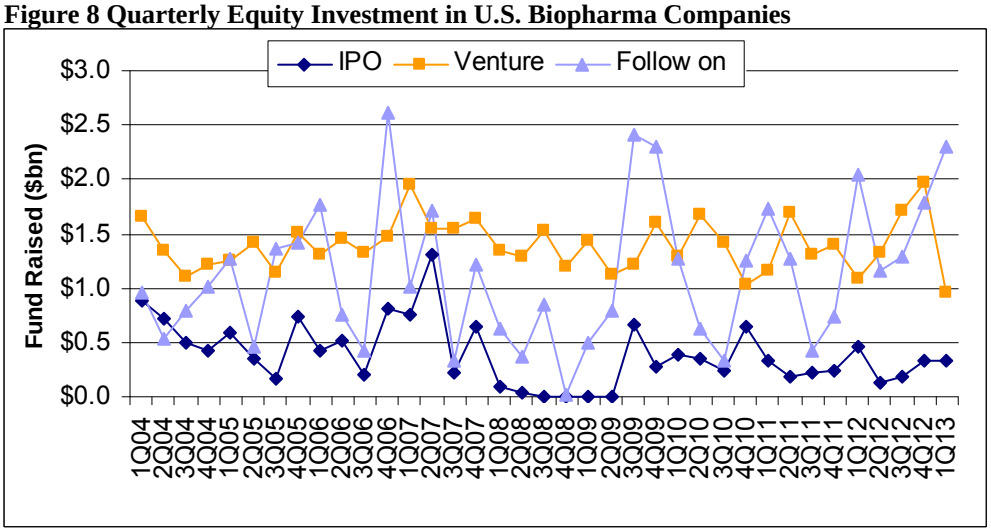
In 2012, strong biotech stock performance and healthy flow of clinical data paved the way for U.S. biotech industry to raise a record amount of follow-on offerings (see Figure 7 and Figure 8). Venture financing remains stable. Although not a torrent by any measure, there has been a steady stream of biotech IPOs. Aftermarket IPO performance has been stellar. Companies in hot spaces such as orphan drugs, oncology, anti-viral have seen very strong post-IPO performance. In lukewarm areas such as specialty pharma and CV/metabolic, IPO aftermarket performance has been poor (see Table 31). The strong after-market performance of recent biotech IPOs have led to a bigger opening of IPO window. For the first 9 months of 2013, 42 companies have gone public globally.

Figure 7 Annual Equity Investment in U.S. Biopharma Companies



Source: Compiled by MHBK/IRD based on data from BioCentury

Figure 8 Quarterly Equity Investment in U.S. Biopharma Companies



Source: Compiled by MHBK/IRD based on data from BioCentury

Table 31 NASDAQ Biopharma IPO and Aftermarket Performance

Company Symbol	Company Name	IPO Date	IPO Price Range Low	IPO Price Range High	IPO Price	IPO Open Price	Total Shares Offered	Total Fund Raised	1 day return	Return by YE	Current Market Cap	Return To Date 10/10/2013
FATE	Fate Therapeutics	10/1/2013	14.0	16.0	6.0	6.56	6.7	40.2	10%		163	32%
ENZY	Enzymotec	9/27/2013	16.0	18.0	14.0	14.25	4.4	61.6	30%		354	20%
FMI	Foundation Medicine	9/25/2013			18.0	31.50	5.9	106.2	96%		884	76%
OPHT	Ophthotech	9/25/2013	16.0	19.0	22.0	23.06	7.6	167.2	20%		933	32%
EVOK	Evoke Pharma	9/25/2013	12.0	14.0	12.0	11.15	2.1	25.2	-2%		80	4%
BIND	Bind Therapeutics	9/20/2013	14.0	16.0	15.0	15.00	4.7	70.5	-6%		238	-2%
XLRN	Accleron	9/19/2013	13.0	15.0	15.0	18.50	5.6	84.0	-13%		705	55%
FPRX	Five Prime	9/19/2013	12.0	14.0	13.0	16.00	4.8	62.4	54%		211	0%
XON	Intrexon	7/25/2013	14.0	16.0	16.0	21.10	10.0	160.0	55%		2,243	39%
ICEL	Cellular Dynamics	7/25/2013	12.0	14.0	12.0	11.00	3.8	46.2	-21%		279	40%
CNAT	Conatus	7/25/2013	10.0	12.0	11.0	11.00	6.0	66.0	-14%		158	-14%
AGIO	Agios	7/24/2013	14.0	16.0	18.0	29.00	5.9	106.2	74%		957	61%
HTBX	Heat Biologics	7/23/2013	10.0	12.0	10.0	10.00	2.5	25.0	-19%		83	30%
OMED	OncoMed	7/17/2013	14.0	16.0	17.0	28.10	4.8	81.6	60%		440	-8%
RNA	Prosensa	6/27/2013	11.0	13.0	13.0	20.00	6.0	78.0	48%		217	-58%
PETX	Aratana Therapeutics	6/27/2013	11.0	13.0	6.0	7.00	5.8	34.8	38%		423	199%
NSTG	Nanostring	6/26/2013	13.0	15.0	10.0	9.90	5.4	54.0	-19%		171	9%
ESPR	Esperion	6/26/2013	13.0	15.0	14.0	17.00	5.0	70.0	4%		279	25%
PTCT	PTC Therapeutics	6/20/2013	13.0	16.0	15.0	15.51	8.4	126.0	8%		455	12%
BLUE	Bluebird Bio	6/18/2013	14.0	16.0	17.0	25.50	5.9	100.3	58%		612	38%
EPZM	Epizyme	5/30/2013	13.0	15.0	15.0	20.00	5.1	76.5	53%		1,115	153%
ADHD	Alcobra	5/22/2013	10.0	12.0	8.0	8.25	3.1	24.8	-6%		284	185%
PTLA	Portola	5/22/2013	13.0	16.0	14.5	15.25	8.4	121.8	4%		940	60%
AMBI	Ambit	5/16/2013	13.0	15.0	8.0	8.00	8.1	64.8	-8%		307	112%
RCPT	Receptos	5/8/2013	14.0	16.0	14.0	15.00	5.2	72.8	0%		550	98%
OMTH	Omthera	4/11/2013	12.0	14.0	8.0	7.40	8.0	64.0	-7%		260	59%
CMRX	Chimerix	4/11/2013	13.0	15.0	14.0	15.14	8.4	117.6	34%		565	32%
CGIX	Cancer Genetics Inc.	4/4/2013	10.0	12.0	10.0	10.00	6.9	69.0	13%		116	88%
ENTA	Enanta	3/20/2013	14.0	16.0	14.0	14.00	4.0	56.0	23%		388	49%
TTPH	Tetraphase	3/20/2013	10.0	12.0	7.0	7.00	10.7	74.9	1%		235	58%
KBIO	KaloBios	1/31/2013	12.0	14.0	8.0	8.16	8.8	70.0	0%		151	-43%
STML	Stemline Therapeutics	1/29/2013	10.0	12.0	10.0	11.00	3.8	38.0	18%		516	272%
LPDX	LipoScience	1/25/2013	13.0	15.0	9.0	9.8	5.0	45.0	16%		73	-46%
2013 Raised								**2,460.6**	**18%**			**51%**
KYTH	Kythera	10/11/2012	14.0	16.0	16.0	16.00	4.4	70.4	19%	90%	855	186%
ICPT	Intercept	10/11/2012	13.0	15.0	15.0	15.00	5.0	75.0	27%	128%	1,334	331%
RGLS	Regulus	10/4/2012	10.0	12.0	4.0	4.72	11.3	45.0	5%	58%	405	132%
HPTX	Hyperion	7/26/2012	11.0	13.0	10.0	10.00	5.0	50.0	2%	13%	571	164%
DRTX	Durata	7/19/2012	11.0	13.0	9.0	9.00	7.5	67.5	6%	-15%	238	-3%
TSRO	Tesaro	6/27/2012	12.0	15.0	13.5	13.50	6.0	81.0	4%	26%	1,265	169%
SUPN	Supernus	5/1/2012	12.0	14.0	5.0	6.50	10.0	50.0	15%	43%	224	44%
MACK	Merrimack	3/29/2012	8.0	10.0	7.0	6.25	14.3	100.1	-12%	-13%	397	-49%
CCXI	ChemoCentryx	2/8/2012	14.0	16.0	10.0	10.49	5.7	57.0	5%	9%	226	-46%
CEMP	Cempra	2/3/2012	11.0	13.0	6.0	6.2	8.4	50.4	4%	7%	394	96%
VSTM	Verastem	1/27/2011	9.0	11.0	10.0	11.0	5.5	55.0	14%	-12%	283	0%
2012 Raised								**701.4**	**8%**			**93%**
CLVS	Clovis Oncology	11/16/2011	13.0	15.0	13.0	13.0	10.0	130.0	-2%	8%	1,685	319%
NLNK	NewLink Genetics	11/11/2011	10.0	12.0	7.0	7.0	6.2	43.4	0%	1%	530	166%
HZNP	Horizon Pharma	7/28/2011	10.0	12.0	9.0	9.0	5.5	49.5	0%	-56%	250	-58%
SGNT	Sagent	4/20/2011	14.0	16.0	16.0	18.3	5.8	92.8	26%	31%	651	27%
TZYM	Tranzyme Inc.	4/04/2011	11.0	13.0	4.0	4.0	13.5	54.0	1%	-28%	0	-100%
ACRX	AcelRx Pharmaceuticals Inc.	2/11/2011	12.0	14.0	5.0	5.0	8.0	40.0	-12%	-62%	434	87%
ECYT	Endocyte Inc.	2/04/2011	13.0	15.0	6.0	6.4	12.5	75.0	25%	-21%	504	130%
PCRX	Pacira Pharmaceuticals Inc.	2/10/2011	14.0	16.0	7.0	7.0	6.0	42.0	0%	24%	1,784	639%
FLDM	Fluidigm	2/03/2011	13.5	15.5	13.5	13.5	5.6	75.6	4%	-3%	558	61%
BGMD	BG Medicine	2/2/2011	13.0	15.0	7.0	7.0	5.0	35.0	23%	-33%	23	-89%
2011 Raised								**637.3**	**6%**			**118%**
VTUS	Ventrus Biosciences Inc.	12/17/2010	6.0	7.0	6.0	7.7	2.9	17.4	5%	10%	63	-50%
ANAC	Anacor Pharmaceuticals Inc.	11/24/2010	16.0	18.0	5.0	5.0	12.0	60.0	2%	7%	479	134%
GNOM	Complete Genomics Inc.	11/11/2010	12.0	14.0	9.0	8.5	6.0	54.0	-15%	-17%	118	-65%
PACB	Pacific Biosciences of California Ir	10/27/2010	15.0	17.0	16.0	16.5	12.5	200.0	6%	-1%	350	-69%
AEGR	Aegerion Pharmaceuticals Inc.	10/22/2010	14.0	16.0	9.5	9.7	5.0	47.5	8%	49%	2,675	795%
SHP	ShangPharma Corp. ADS	10/19/2010	14.5	16.5	15.0	15.0	5.8	87.0	-15%	-23%	13,375	61%
PATH	NuPathe Inc.	8/06/2010	14.0	16.0	10.0	10.0	5.0	50.0	-9%	-9%	73	-77%
TSRX	Trius Therapeutics Inc.	8/03/2010	12.0	14.0	5.0	5.1	10.0	50.0	9%	-26%	707	170%
ALIM	Alimera Sciences Inc.	4/22/2010	15.0	17.0	11.00	11.00	6.6	72.1	0%	-6%	117	-69%
TNGN	Tengion Inc.	4/12/2010	8.0	10.0	5.00	5.00	6.0	30.0	916%	408%	3	-90%
AVEO	AVEO Pharma	3/12/2010	13.0	15.0	9.00	8.25	9.0	81.0	0%	62%	112	-77%
ANTH	Anthera	3/1/2010	13.0	15.0	7.00	7.01	6.0	42.0	2%	-30%	74	-46%
IRWD	Ironwood Pharma	2/3/2010	14.0	16.0	11.25	11.59	16.7	187.5	3%	-8%	1,381	-2%
2010 Raised								**978.5**	**70%**			**47%**

Source: Compiled by MHBK/IRD based on Capital IQ and public company reports.
Note: Highlighted companies had been acquired.

III.Generic Industry Updates

For a number of years, generic industry has been in the sweet spot of pharmaceutical industry as high value of patent expiries, increasing penetration of generic drugs around the world, industry consolidation led to super-charged earnings growth.

However, the gravy train of large patent expiries has lost steam as large pharma have passed the peak of LOEs in 2012. Meanwhile competition for both new ANDAs and commodity generics is increasing. For paragraph IV challenges, there are often several companies sharing the first-to-file status. For commodity generics, there is intense pricing pressure from Asian and other players. On the litigation front, Teva and Sun were recently ordered to pay damage of $2.15bn to Pfizer and Takeda for their at-risk launch of Protonix. This outsized fine will no doubt dampen generic companies' appetite in at-risk launches. This will in turn tip the balance of power to brand companies in patent litigations and settlements. On the settlement front, in early June, SCOTUS ruled that pay-for-delay settlement can violate anti-trust laws, which gives FTC the green lights to challenge such settlements. In recent years, pay-for-delay practices have become a common tactic for U.S. generic players to extract value from brand players without going to the end of the litigation. From the brand company side, settlement is an important risk mitigation strategy. FTC has tried to stop such practices, but was often blocked by the ruling by U.S. Appeals Court. Now with FTC off the sidelines, brand companies and generic challengers will hesitate whether to settle vs. going through the full-length of the trial. They are likely to structure settlements so the brand's compensation to generics is smaller and can be justified on legal ground. How the future unfolds will have big impact on the affected companies. For example, Novartis is trying to extent patent of Gleevec beyond the composition of matter patent that expires in 2015 to the polymorph patent that expires in 2019. With the change in environment, challenging patent will not be lucrative as in the past. Generic players will increasingly pick the battles and may have to pick smaller targets.

Below are some notable developments for the generics industry:

- **Generics penetration is steadily on the rise**
  U.S. generic penetration by volume increased from 80% in 2011 to 84% in 2012 and is expected to increase to 87% in 2017. On a value basis, unbranded generics count for 15.7% of total drug spending and branded generics count for 12.8% of total drug spending. Globally, driven by economic pressure, generics penetration has also been on the rise.

- **Generic industry pipeline**

  Table 32 and Table 33 compare the size of generic company pipeline between 2010 and 2013. It appears the industry leader Teva has become more selective in developing new ANDAs. Other players have grown their pipeline substantially. Mylan, Sandoz, Actavis (used to be Watson) and Par Pharma made the most significant improvement. Mylan added 129 ANDAs through the recent acquisition of injectable generics manufacturer Agila.

Table 32 Summary of Pipeline Statistics of Leading Generic Companies 2013

Company	2012 Sales ($mn)	R&D ($mn)	R&D/ Sales	US ANDA filed	First To File
Teva	$20,317	$1,283	6.3%	143	63
Sandoz	$8,702	$695	8.0%	172	45
Mylan	$6,796	$389	5.7%	325	38
Actavis	$5,915	$393	6.6%	190	49
Ranbaxy	$2,271				
Dr. Reddy's	$1,893	$116	6.1%		
Impax	$582	$78	13.3%	44	7
Hi-Tech Pharmacal	$230	$12	5.3%	18	
Sagent	$184	$16	8.9%	63	
Par Pharma				72	23
Apotex				41	11
Total				**1,068**	

Source: Compiled by MHBK/IRD based public company reports.
Note: 2012 sales are according to data from Capital IQ

Table 33 Summary of Pipeline Statistics of Leading Generics Companies 2010

Company	2009 Sales ($mn)	R&D ($mn)	R&D/ Sales	US ANDA filed	Brand Value of ANDA ($bn)	Brand Value per ANDA ($mn)	Para IV challenges	First To File	Brand Value FTF ($bn)
Teva	$13,900	$802	5.8%	210	113	538	133	83	50
Sandoz	$7,493	$613	8.2%	108			54	15	
Mylan	$5,093	$275	5.4%	140	88	629		41	17
Watson	$2,793	$197	7.1%	100	50	500	29	15	
Hospira*	$2,775	$158	5.9%	11	4.5	409	2	2	4
Dr. Reddy's	$1,563	$84	5.4%	73			38	12	
Ranbaxy	$1,519	$102	6.7%	66	45	682		13	24
Par	$1,193	$39	3.3%	27	13	481	18	12	6.3
Impax	$358	$40	11.2%	32	17	531	15	6	
Total				**767**					

Source: Compiled by MHBK/IRD based on public company reports
*Note: As Hospira doesn't break out R&D expense for generics specifically; R&D expense for the generic division was allocated based on proportion of sales

- **Biosimilar is a huge opportunity; Despite slow start, it will eventually be a big business**
  Biosimilars represent a big opportunity for both generic and brand pharma companies. Total sales of biologics are approaching almost $100bn (see Table 34 for a list of top 12 biologics). Overall, development and adoption of biosimilars has been slower than people originally expected. For example, in 2007 IMS Health predicted that biosmilar sales would reach $16bn by 2011. Actual sales for 2012 were about $720mn. Reasons for the slow-coming of biosimilar are multifaceted. The regulatory process for biosimilars is so cumbersome that major players are pursuing the BLA pathways instead of the pathway established by ACA. Although there is huge cost pressure on payers worldwide, adoption of biosimilars has been gradual and it varies significantly between markets. For example overall volume penetration in Germany is close to 60% for biosimilar EPO and filgrastim. But the penetration is much lower in other European countries, especially southern Europe where there is a historically strong bias against generics. Payers would prefer a more substantial discount, e.g., 30-40%, rather than the 10-20% current discount to the brand to fully embrace biosimilars. While the regulatory process difficult and market acceptance variable, development of a biosimilar is quite costly ($100-200mn), much higher than the cost of developing a small molecule generic of $5mn. Recognizing the long road and substantial resources needed to develop biosimilars, many industry players have teamed up (see Table 35).

Increasingly, the biosimilar field is becoming dominated by large players that can bring huge resources. During its Analyst Day on February, 2013, Amgen announced it is developing six biosimilars targeting Humira, Remicade, Avastin, Herceptin, Rituxan and Erbitux, and plans to start launching from this portfolio in 2017. These six drugs have combined peak sales of $41bn. So Amgen has made a big investment going after the largest biosimilar opportunities. Recently, Sandoz (Novartis) launched global phase III trials for generic Enbrel (etanercept). In total Sandoz is running seven phase III programs for five biosimilar molecules.

In late June, European Medicines Agency (EMA) recommended approval of biosimilar infliximab (brand name Remicade) from Hospira and Celltrion. Remicade generated worldwide sales of ~$6bn, of which $2bn was generated from EU. The biosimilar Remicade will be marketed as Remsima by Celltrion and Inflectra by Hospira respectively in EU. The approval was a landmark as it was the first antibody biosimilar approved in the western world. Hospira and Celltrion have generated clinical data only in RA and ankylosing spondylitis, and none in gastrointestinal conditions. But EMA allowed bridging the clinical data to other indications so the approved indications include RA, Crohn's disease, ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis. This set an important precedent for future approval of other biosimilars. CHMP will let each individual member states to make their own decisions on interchangebility and substitution, which seems to be a win for the brand companies. Celltrion and Hospira have indicated it will offer at ~30% discount to Remicade. Of all the large pharmaceutical companies, Roche is the most exposed to biosimilar risks due to its portfolio of antibody drugs such as Avastin, Rituxan, Herceptin, Actemra, Xolair etc. Not all antibodies are easy to copy. Several biosimilar developers have encountered difficulties in developing biosimilar of Rituxan for example. However, most industry participants recognize the potential of biosmilars. Korea-based Celltrion reportedly is attracting acquirers for the company.

Table 34 Sales of Top Biologics

Brand Name	INN	Global Sales MAT* 09/2012 ($bn)	EU expiry date	US expiry date
Humira	Adalimumab	$8.1	2018	2016
Enbrel	Etanercept	$7.3	2015	2028 (extended)
Remicade	Infliximab	$7.1	2015	2018
Lantus	Insulin Glargine	$6.2	2014	2014
Rituxan/Mabthera	Rituximab	$5.9	2013	2016
Avastin	Bevacizumab	$5.3	2019	2017
Avonex, Rebif	Interferon Beta -1A	$5.0	2012	Expired
Herceptin	Trastuzumab	$5.0	2015	2015
Novomix, Novorapid	Insulin Aspart	$4.9	2014	2019
Copaxone	Glatiramer Acetate	$4.3	2017	2015
Neulasta	Pegfligrastim	$4.3	2015	2014
Lucentis	Ranibizumab	$4.0	2016	2016
Total		$67.4		

Source: Compiled by MHBK/IRD based on data from IMS Health.
Note: MAT= Moving Annual Total.

Table 35 Partnerships in Biosimilars

Partner I	Partner II
Watson	Amgen
Mylan	Biocon
Biogen-Idec	Samsung
Baxter	Momenta
Mochida	Gedeon Richter
Nichi-Iko	Aprogen (Korean)
Nichi-Iko	Sanofi-Aventis
Fujifilm	Kyowa Hakko Kirin
Merck Serono	Dr. Reddy's
Daiichi-Sankyo	Coherus
Hospira	Celltrion

Source: Compiled by MHBK/IRD based on public company reports

- **M&A in generic industry**
  How are generic companies coping with the changing dynamics in industry? Generic industry has been in the consolidation mode over the last several years. Room for further consolidation is limited and also there is increasing pressure inside the generic industry. To cope with the new environment, some generics companies are expanding into specialty pharmaceutical areas such as respiratory, CNS, dermatology, where they can use their formulation and manufacturing expertise to develop drugs with some barrier to entry. Teva has emphasized development of so called NTE (new therapeutic entities, as compared to NCE, new chemical entities). NTEs basically are known molecules enhanced with novel formulation, novel delivery, or unique way of use. NTEs will have some barrier to entry but also low development risk as the chemical entity is proven. Also hewing to the theme of expanding into specialty pharmaceuticals, Actavis acquired Warner Chilcott in a transformative deal. The Indian based Sun Pharma acquired U.S. dermatology company DUSA in 2012. Sandoz also acquired dermatology company Fourgera in 2012.

Table 36 Generic Industry M&As since 2010

Acquirer	Target	Announce Date	Deal Value (mn)	Revenues prior yr($mm)	EV / Sales	EV/EBITDA prior year	Country
Endo Pharma	Boca Pharmacal	28-Aug-2013	$225			4.5	U.S.
Akorn	Hi-tech Pharmacal	27-Aug-2013	$539	232	2.3	11.1	U.S.
Actavis	Warner Chilcott	20-May-2013	$8,500	2,400	3.5		Ireland
Mylan	Agila	27-Feb-2013	$1,600	$255	6.3	18.6	India
Sun Pharma	DUSA Pharma	08-Nov-2012	$230	50	4.6		U.S.
TPG	Par Pharmaceuticals	16-Jul-2012	$1,900	$926	2.1	9.0	U.S.
Novartis (Sandoz)	Fougera Pharma	02-May-2012	$1,500	$429	3.5		U.S.
Watson Pharmaceuticals	Actavis	25-Apr-2012	€ 4,500	€ 1,900	2.4	14.6	Europe
Watson Pharmaceuticals	Ascent	24-Jan-2012	AU$375	AU150	2.5		Australia
Teva	50% Teva-Kowa Japan	26-Sep-2011	$150	$100	1.5		Japan
Par Pharmaceuticals	Anchen	24-Aug-2011	$410	$125	3.3	11	U.S.
Watson Pharmaceuticals	Specifar	24-May-2011	€ 400	€ 85	4.7		Greece
Valeant	Sanitas	24-May-2011	€ 364	€ 95	3.8		Lithuania
Par Pharmaceuticals	Edict Pharma	23-May-2011	$25				India
Teva	Taiyo	09-May-2011	$1,300	$530	2.5		Japan
Endo Pharma	Qualitest	28-Oct-2010	$1,200	$350	3.4	16.7	U.S.
Mylan Laboratories	Bioniche	14-Jul-2010	$550	$130	4.2		Ireland
Novartis (Sandoz)	Oriel	01-Jun-2010	$74				U.S.
Perrigo	Paddock Laboratories	20-Jan-2010	$540	$270	2.0		U.S.
Abbott	Piramal Healthcare	21-May-2010	$3,388	$400	8.5	28	India
Teva	Ratiopharm	18-Mar-2010	$4,950	$2,300	2.3	11.8	Germany
Cephalon	Mepha	01-Feb-2010	$590	$379	1.6		Switzerland

Source: Compiled by MHBK/IRD based on Capital IQ and public company reports.
Note1: highlighted deals were acquisitions of dermatology-related companies by generic companies.
Note2: comment marks denote additional milestone payments.

IV. Appendix

Table 37 Patent Expiry Schedule for Global Pharma Companies

Company	Product	Patent Expiry [1]	2012 Revs	% of 2012 Pharma Sales Exposed 12-14	15-17
BMY	Avapro	Mar-12	503	2.9%	-
BMY	Plavix	May-12	2,547	14.5%	-
BMY	Sustiva	May-13	1,527	8.7%	-
BMY	Baraclude (hepatitis B)	Feb-15	1,388	-	7.9%
BMY	Abilify	April-15	2,827	-	16.0%
BMY	Reyataz	Jun-17	1,521	-	8.6%
BMY	Total BMY Pharma Sales Exposed		10,313	26.0%	32.6%
BMY	Total BMY Pharma Sales		17,621		
BMY	Total BMY Sales		17,621	26.0%	32.6%
LLY	Cymbalta	Dec-13	4,994	22.7%	-
LLY	Humalog	Feb-14	2,396	10.9%	-
LLY	Evista	Mar-14	1,010	4.6%	-
LLY	ReoPro	2015	143	-	0.7%
LLY	Alimta	Jul-16	2,594	-	11.8%
LLY	Strattera	May-17	621	-	2.8%
LLY	Total LLY Pharma Sales Exposed		14,019	38.2%	15.3%
LLY	Total LLY Pharma Sales		21,970		
LLY	Total LLY Sales		22,603	37.2%	14.9%
SGP	Clarinex	Jan-12	393	1.0%	-
MRK	Singulair	Aug-12	3,853	9.5%	-
MRK	Maxalt	Jul-12	638	1.6%	-
MRK	Nexium est. (est. MRK 32%)	2012	727	1.8%	-
MRK	Invanz	Feb-13	445	1.1%	-
MRK	Cancidas	Sep-13	619	1.5%	-
MRK	Propecia	Nov-13	424	1.0%	-
SGP	Temodar	Aug-13	817	2.0%	-
SGP	Avelox	2014	201	0.5%	-
SGP	Integrilin	Nov-14	211	0.5%	-
MRK	Emend	Apr-15	489	-	1.2%
SGP	Zetia	Dec-16	2,567	-	6.3%
SGP	Vytorin	Dec-16	1,747	-	4.3%
MRK	Total MRK Pharma Sales Exposed		13,131	20.5%	11.8%
MRK	Total MRK Pro Forma Pharma Sales (incl. 50% Vytorin, Zetia)		40,601		
MRK	Total MRK Pro Forma Sales (incl. 50% Vytorin, Zetia)		40,601	20.5%	11.8%
PFE	Detrol/LA	Sep-12	761	1.5%	-
PFE	Geodon	Sep-12	0	0.0%	-
WYE	Rapamune	2014	346	0.7%	-
WYE	ReFacto	2014	584	1.1%	-
PFE	Celebrex	May-14	2,719	5.3%	-
WYE	Premarin	2015	1,073	-	2.1%
WYE	Tygacil	Apr-16	335	-	0.7%
PFE	Zyvox	May-15	1,345	-	2.6%
PFE	Total PFE Pharma Sales Exposed		13,906	8.6%	5.4%
PFE	Total Pfizer Pharma Sales		51,214		
PFE	Total Pfizer Sales		58,986	7.5%	4.7%
JNJ	Aciphex	May-13	835	3.3%	-
JNJ	Velcade	2017	1,500	5.9%	-
JNJ	Zytiga	Apr-16	961	3.8%	-
JNJ	Prezista	2015	1,414	-	5.6%
JNJ	Total JNJ Pharma Sales Exposed		4,785	13.0%	5.6%
JNJ	Total JNJ Pharma Sales		25,351		
JNJ	Total JNJ Sales		67,224	4.9%	2.1%

(Continued)

Company	Product	Patent Expiry [1]	2012 Revs	% of 2012 Pharma Sales Exposed 12-14	15-17
ABBV	Tricor/Trilipix	2012	1,098	4.2%	-
ABBV	Niaspan	Sep-13	911	5.0%	-
ABBV	Norvir	Jan-15	455	-	2.5%
ABBV	Kaletra	Jun-16	1,013	-	5.5%
ABT	Total AbbVie Pharma Sales Exposed		3,477	9.1%	8.0%
ABBV	Total AbbVie Pharma Sales		18,389	-	-
ABBV	Total AbbVie Sales		18,389	9.1%	8.0%
AZN	Atacand	Dec-12	1,009	3.6%	-
AZN	Seroquel	Mar-12	2,803	10.0%	-
AZN	Symbicort	2010EU; 2014 US	3,194	11.4%	-
AZN	Zomig	May-13	182	0.7%	-
AZN	Nexium	May-14	3,944	14.1%	-
AZN	Crestor	Jul-16	6,253	-	22.4%
AZN	Iressa	Apr-16	611	-	2.2%
AZN	Total AZN Pharma Sales Exposed		21,350	39.8%	24.5%
AZN	Total AZN Pharma Sales		27,973		
AZN	Total AZN Sales		27,973	39.8%	24.5%
NVS	Diovan	Dec-12	4,417	13.7%	-
NVS	Exelon	Aug-12	1,050	3.3%	-
NVS	Zometa	Mar-13	1,288	4.0%	-
NVS	Comtan	Oct-13	530	1.6%	-
NVS	Sandostatin LAR	2014	1,512	4.7%	-
NVS	TOBI	2014	317	1.0%	-
NVS	Gleevec	Jul-15	4,675	-	14.5%
NVS	Exforge	Dec-17	1,352	-	4.2%
NVS	Total NVS Pharma Sales Exposed		14,227	28.3%	14.5%
NVS	Total NVS Pharma Sales		32,153		
NVS	Total NVS Sales		56,673	16.1%	8.2%
Roche	Cellcept	May-09	909	-	-
Roche	Boniva	Mar-12	323	0.9%	-
Roche	Xeloda	Dec-13	1,523	4.3%	-
Roche	Tamiflu	Jun-17	560	-	1.6%
Roche	Total Roche Pharma Sales Exposed (mn SF)		3,315	5.2%	1.6%
Roche	Total Roche Sales Exposed (mn SF)		35,232		
Roche	Total Roche Sales (mn SF)		45,499	4.1%	1.2%
SNY	Eloxatin	Aug-12	956	3.3%	-
SNY	Plavix	May-12	2,066	7.2%	-
SNY	Avapro (Aprovel)	Mar-12	1,151	4.0%	-
SNY	Actonel	Dec-13	134	0.5%	-
SNY	Xatral	Jun-14	130	0.5%	-
SNY	Lantus	Mar-15	4,960	-	17.2%
SNY	Total Sanofi-Aventis Pharma Sales Exposed (mn euro)		12,350	15.4%	17.2%
SNY	Total Sanofi-Aventis Pharma Sales (mn euro)		28,871		
SNY	Total Sanofi-Aventis Sales (mn euro)		34,947	12.7%	14.2%
GSK	Epzicom	Jun-12	665	3.1%	-
GSK	Avodart	Oct-15	790	-	3.7%
GSK	Seretide/Advair	2016	5,046	-	23.7%
GSK	Lovaza	Apr-17	607	-	2.8%
GSK	Total GSK Pharma Sales Exposed (mn GBP)		7,550	3.1%	30.2%
GSK	Total GSK Pharma Sales (mn GBP)		21,321		
GSK	Total GSK Sales (mn GBP)		26,431	2.5%	24.4%
Total	Total Industry Pharma Sales Exposed ($mn)		183,080	20.9%	6.3%
Total	Total Industry Pharma Sales ($mn)		300,244		
Total	Total Industry Sales ($mn)		366,738	17.1%	5.1%

Source: Compiled by MHBK/IRD based on public company reports
Note 1: U.S. patent expiry date is used as a proxy for patent expiry globally
Note 2: 2012 global sales are used to calculate total generic exposure in each time period

Table 38: U.S. Drug Industry Company Valuation

October 10, 2013						EPS (in mn)			P/E			Growth			PEG Ratio		
Company	Ticker	Price (USD)	52-wk Hi	52-wk Low	Market Cap (USD in mn)	2012	2013E	2014E	2012	2013E	2014E	'12-14 ST	'12-17 LT	Div. Yield	PE/ LT Grth	EV/ 012 Sales	EV/ 012 EBITDA
S&P 500	**^SPX**	**1680.9**	**1725.5**	**1353.3**		**102.6**	**109.6**	**119.3**	**16.4**	**15.3**	**14.1**						
U.S. Large-Cap Pharma																	
AbbVie Inc.	ABBV	45.07	48.42	32.51	71,043	3.84	3.13	3.22	11.7	14.4	14.0	-8.5%	1.6%	3.6%	2.77	4.2	10.3
Bristol-Myers Squibb Company	BMY	47.42	49.57	30.64	76,406	1.96	1.74	2.01	24.2	27.3	23.5	1.5%	5.9%	3.0%	3.10	4.6	15.2
Johnson & Johnson	JNJ	87.20	94.42	67.80	242,242	5.09	5.46	5.81	17.1	16.0	15.0	6.8%	6.0%	3.0%	1.77	3.4	10.9
Eli Lilly and Company	LLY	48.72	58.41	44.88	52,451	3.33	4.12	2.76	14.6	11.8	17.6	-8.9%	3.0%	4.0%		2.4	8.6
Merck & Co. Inc.	MRK	47.07	50.16	40.02	138,330	3.80	3.48	3.64	12.4	13.5	12.9	-2.2%	2.0%	3.7%	2.37	3.2	6.7
Pfizer Inc.	PFE	28.35	31.15	23.55	187,288	2.17	2.21	2.31	13.1	12.8	12.3	3.2%	4.3%	3.4%	1.68	3.3	6.5
U.S. Pharma Industry		**46.00**			**767,760**	**3.12**	**3.11**	**3.18**	**14.7**	**14.8**	**14.5**	**1.0%**	**4.0%**	**3.4%**	**2.01**	**3.4**	**8.5**
U.S. Large-Cap Biotech																	
Amgen Inc.	AMGN	108.00	117.91	81.56	80,067	6.55	7.33	8.10	16.5	14.7	13.3	11.2%	10.0%	1.7%	1.26	4.8	11.3
Biogen Idec Inc.	BIIB	230.39	248.95	134.00	53,203	6.57	8.56	11.00	35.1	26.9	20.9	29.4%	24.3%	0.0%	1.11	9.7	23.3
Celgene Corporation	CELG	151.59	157.95	71.23	60,404	4.88	5.93	7.12	31.0	25.6	21.3	20.8%	24.6%	0.0%	1.04	10.9	22.9
Gilead Sciences Inc.	GILD	61.77	64.74	32.07	90,154	1.92	1.96	3.01	32.1	31.5	20.6	25.0%	28.7%	0.0%	1.10	10.0	21.1
U.S. Large-Cap Biotech		**96.77**			**283,828**	**3.85**	**4.37**	**5.47**	**25.1**	**22.2**	**17.7**	**19.2%**	**20.5%**	**1.0%**	**1.03**	**7.7**	**17.5**
U.S. Mid-Cap Biotech																	
Alexion Pharmaceuticals, Inc.	ALXN	107.40	125.65	81.82	20,627	2.02	2.96	3.30	53.1	36.2	32.6					17.6	43.4
Ariad Pharmaceuticals Inc.	ARIA	5.49	25.40	4.00	1,079	-1.33	-1.64	-1.38	-	-	-						
United Therapeutics Corporation	UTHR	82.51	85.92	44.51	3,995	5.16	5.99	7.52	16.0	13.8	11.0					4.0	8.3
Acorda Therapeutics, Inc.	ACOR	35.06	40.87	22.37	1,383	0.92	0.77	1.24	38.0	45.6	28.2					3.6	-
InterMune Inc.	ITMN	13.77	16.00	7.80	1,083	-2.66	-2.81	-2.00	-	-	-					33.0	-
Infinity Pharmaceuticals, Inc.	INFI	14.71	50.51	14.36	728	-1.93	-2.89	-2.61	-	-	-					9.6	-
BioMarin Pharmaceutical Inc.	BMRN	66.02	80.67	36.28	9,243	-0.68	-1.10	-0.87	-	-	-					17.9	295.7
Pharmacyclics Inc.	PCYC	114.75	143.34	44.91	8,817	0.22	0.96	0.56	531.3	119.0	205.4					99.9	342.1
Regeneron Pharmaceuticals, Inc.	REGN	289.52	319.83	136.13	27,391	4.12	7.00	9.33	70.2	41.4	31.0					21.2	59.9
Vertex Pharmaceuticals Incorporated	VRTX	70.28	89.96	38.44	16,332	1.32	-0.50	-1.42	53.2	-	-					10.1	65.5
Dendreon Corp.	DNDN	2.59	7.22	2.48	404	-2.48	-1.66	-1.12	-	-	-					2.4	-
Auxilium Pharmaceuticals Inc.	AUXL	17.10	23.09	13.87	844	1.47	0.48	1.11	11.7	35.4	15.5					3.2	15.8
Cubist Pharmaceuticals Inc.	CBST	64.93	68.00	38.53	4,206	2.78	1.96	2.53	23.3	33.2	25.7					4.0	13.2
Incyte Corporation	INCY	36.15	41.95	15.43	5,313	-0.49	-0.30	0.34	-	-	106.3					19.5	
Seattle Genetics Inc.	SGEN	40.52	49.23	21.05	4,825	-0.48	-0.64	-0.64	-	-	-					21.8	
Questcor Pharmaceuticals, Inc.	QCOR	58.09	74.76	20.40	3,153	3.04	4.26	5.35	19.1	13.6	10.9					6.2	
ViroPharma Inc.	VPHM	38.32	41.14	22.12	2,502	0.70	0.69	1.29	54.7	55.4	29.7						
VIVUS Inc.	VVUS	10.19	23.59	9.11	1,021	-1.27	-1.95	-1.24	-	-	-						
U.S. Mid-Cap Biotech																**12.5**	

Source: Compiled by MHBK/IRD based on data from Capital IQ

Table 39: U.S. Drug Industry Key Company Financial Metrics

October 10, 2013		Enterprise	Sales (in mn)			Growth	EBITDA (USD in mn)			Growth	Net Income (in mn)			Growth	Net
Company	Ticker	Value	2012	2013E	2014E	'12-14	2012	2013E	2014E	'12-14	2012	2013E	2014E	'12-14	Cash
U.S. Large-Cap Pharma															
AbbVie Inc.	ABBV	77,443	18,380	18,727	19,074	1.9%	7,758	7,498	7,591	-1.1%	5,275	5,031	5,167	-1.0%	-6,400
Bristol-Myers Squibb Company	BMY	80,833	17,621	16,221	17,393	-0.6%	5,665	4,069	4,661	-9.3%	1,960	2,859	3,267	29.1%	-4,425
Johnson & Johnson	JNJ	232,095	67,224	70,696	73,792	4.8%	21,098	23,185	24,644	8.1%	10,853	15,577	16,489	23.3%	10,147
Eli Lilly and Company	LLY	53,051	22,603	22,964	19,647	-6.8%	6,478	6,665	4,742	-14.4%	4,089	4,496	2,951	-15.1%	-591
Merck & Co. Inc.	MRK	150,978	47,267	44,493	44,389	-3.1%	17,427	20,965	21,667	11.5%	6,168	10,411	10,540	30.7%	-10,043
Pfizer Inc.	PFE	190,911	58,986	51,505	50,173	-7.8%	26,222	24,054	23,741	-4.8%	14,570	14,882	14,718	0.5%	-3,157
U.S. Pharma Industry		**785,310**	**232,081**	**224,606**	**224,469**	**-1.7%**	**84,648**	**86,436**	**87,046**	**1.4%**	**42,915**	**53,255**	**53,131**	11.3%	**-14,469**
U.S. Large-Cap Biotech															
Amgen Inc.	AMGN	81,964	17,265	18,274	19,135	5.3%	7,072	7,685	8,534	9.8%	4,345	5,595	6,164	19.1%	-1,897
Biogen Idec Inc.	BIIB	53,265	5,516	6,808	8,083	21.0%	2,194	2,941	3,884	33.1%	1,380	2,052	2,662	38.9%	-62
Celgene Corporation	CELG	59,989	5,507	6,353	7,251	14.8%	2,321	3,214	3,816	28.2%	1,456	2,555	3,024	44.1%	415
Gilead Sciences Inc.	GILD	95,456	9,703	10,781	13,372	17.4%	4,314	4,924	7,054	27.9%	2,592	3,275	4,905	37.6%	-5,050
U.S. Large-Cap Biotech		**290,673**	**37,991**	**42,216**	**47,841**	**12.2%**	**15,901**	**18,764**	**23,289**	**21.0%**	**9,773**	**13,477**	**16,755**	**30.9%**	**-6,594**
U.S. Mid-Cap Biotech															
Alexion Pharmaceuticals, Inc.	ALXN	19,652	1,134	1,531	1,912	29.8%	417	671	914	48.1%	255	614	691	64.6%	976
Ariad Pharmaceuticals Inc.	ARIA	737	1	58	0		-197	-285	-233	8.8%	-221	-300	-249	6.1%	342
United Therapeutics Corporation	UTHR	3,579	914	1,075	1,145	11.9%	454	515	566	11.7%	304	314	366	9.6%	416
Acorda Therapeutics, Inc.	ACOR	1,084	306	341	386	12.3%	31	0	26	-8.3%	155	32	50	-43.2%	299
InterMune Inc.	ITMN	959	26	63	128	120.8%	-192	-210	-159	-9.1%	-150	-220	-159	3.0%	125
Infinity Pharmaceuticals, Inc.	INFI	452	47	0	76	27.2%	-97	-141	-104	3.8%	-54	-139	-135	57.9%	277
BioMarin Pharmaceutical Inc.	BMRN	8,953	501	551	677	16.3%	-57	-40	-27	-30.6%	-114	-157	-134	8.4%	291
Pharmacyclics Inc.	PCYC	8,312	165	185	315	38.4%	86				88	90	137	24.9%	505
Regeneron Pharmaceuticals, Inc.	REGN	27,326	1,378	1,931	2,475	34.0%	495	776	1,135	51.5%	750	844	1,170	24.9%	64
Vertex Pharmaceuticals Incorporated	VRTX	15,525	1,527	1,174	972	-20.2%	42	-244	-344	NA	-107	-125	-228	45.8%	1,033
Dendreon Corp.	DNDN	788	326	299	354	4.3%	-254	-150	-74	-46.0%	-394	-247	-171	-34.1%	-384
Auxilium Pharmaceuticals Inc.	AUXL	1,270	395	381	466	8.6%	104	41	84	-10.0%	86	25	55	-19.8%	-425
Cubist Pharmaceuticals Inc.	CBST	3,694	926	1,034	1,203	14.0%	280	175	244	-6.7%	154	155	206	15.8%	512
Incyte Corporation	INCY	5,259	297	349	512	31.3%	29	8	111	95.7%	-44	-49	60	NA	54
Seattle Genetics Inc.	SGEN	4,487	211	246	277	14.6%	-51	-74	-86	30.1%	-54	-81	-81	22.4%	338
Questcor Pharmaceuticals, Inc.	QCOR	3,078	509	732	908	33.5%	299	409	516	31.5%	198	287	361	35.1%	75
ViroPharma Inc.	VPHM	2,412	428	446	561	14.5%	76	-32	114	22.9%	6	50	98	317.6%	91
VIVUS Inc.	VVUS	869	2	43	193	878.8%	-140	-205	-116	-8.7%	-140	-204	-137	-0.9%	152
U.S. Mid-Cap Biotech															

Source: Compiled by MHBK/IRD based on data from Capital IQ

Abbreviations	
ABBV	Abbvie
ACA	Patient Protection and Affordable Care Act, aka Obamacare
ACO	Accountable Care Organization
AD	Alzheimer's Disease
AMGN	Amgen
ANDA	Abbreviated New Drug Applications
ASCO	American Society of Clinical Oncology
AZN/AZ	Astra-Zeneca
Biosimilars	Generic copies of brand biologic drugs such as proteins, antibodies.
BMY/BMS	Bristol-Myers Squibb
BLA	Biologic License Application
CBO	Congressional Budget Office
CDHP	Consumer-driven health plans
CMS	Centers for Medicare & Medicaid Services
EPO	Erythropoietin
FOB	Follow-on Biologics, aka biosimilars
GILD	Gilead Sciences
GSK	GlaxoSmithKline
HHS	U.S. Department of Health and Human Services
HMO	Health Maintenance Organization
INN	International Nonproprietary Names
IPO	Initial Public Offering
JNJ	Johnson & Johnson
LLY	Eli Lilly
LOEs	Loss of exclusivities
MRK	Merck
NDA	New Drug Applications
NME/NCE	New Molecular/Chemical Entities
NVS	Novartis
P IV Challenge	Paragraph IV Challenge. Patent challenge before the scheduled patent expiration date
PBM	Pharma Benefit Manager
PE Multiple	Price to Earnings Multiple
PFE	Pfizer
SCOTUS	Supreme Court of the United States
SGP	Schering-Plough
Specialty Medicine	Drugs that treat diseases which are not suffered by the general public and are prescribed by specialty doctors rather than by primary care physicians (PCPs). Disease conditions include inflammation, Multiple Sclerosis, Cancer, Blood cell deficiency, Growth deficiency, Hepatitis C and others.
WYE	Wyeth

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