



Surveying Tomorrow's BioPharma Landscape

The NASDAQ Biotech Index Up Close

Welcome to the EvaluatePharma® Survey of Tomorrow's BioPharma Landscape

In this exclusive report, EvaluatePharma introduces a snapshot of the companies behind the widely-cited NASDAQ Biotechnology Index (NBI). This aggregate analysis of leading, publicly-traded biotech, pharma and tools companies that make up the NBI offers readers a window onto tomorrow's BioPharma landscape of products and pipelines. It also provides insight into this dynamic sector, by analyzing the changing number, rankings, composition and therapeutic area foci of the NBI's constituent companies. A pdf version of this report can be found at www.evaluatepharma.com/NBI2012.

EvaluatePharma has developed a reliable and consistent methodology to forecast product sales based on equity research analysts' projections. The key steps carried out for product sales forecasts by EvaluatePharma Analysts are as follows:

- Review company presentations to analysts, news flow and SEC filings, for key financial and operating drivers
- Collate forecasts of product sales, segment sales, costs and earnings per share from equity research analyst reports
- Create a consensus forecast based on the arithmetic average of most recent forecasts
- Build detailed group sales forecasts from consensus product and segment sales forecasts



Jonathan de Pass
CEO, EvaluatePharma LTD

The NASDAQ Biotech Index is cited all around the world but rarely do we see a detailed aggregate analysis of these leading, publicly traded biotechnology companies. This overview provides insight into the breadth and scope of today's biotech products and where this dynamic sector is heading.

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Executive Summary

In taking a snapshot of the top publicly-traded biotech companies listed in the NASDAQ Biotechnology Index, the report *Surveying Tomorrow's BioPharma Landscape: The NASDAQ Biotech Index Up Close* captures and highlights important trends and dynamics in the wider BioPharmaceutical industry. But it is not just painting a detailed picture of the sector today; it is also sketching out the industry landscape five or more years hence. The report maps out the continuing rise of biologic drugs. It captures the strong growth in oncology and anti-infectives, alongside the continued dominance of central nervous system (CNS) drugs. It tells the story of significant individual company successes – such as those of Gilead/Pharmasset, Celgene and others and their effects on the overall landscape. This is an objective overview analysis and is not an endorsement of the NASDAQ Biotech Index (NBI) or investment advice. Complimentary copies of the full report can be downloaded at: www.evaluatepharma.com/NBI2012.

Key Takeaways

- **Industry-Beating Sales Growth:** The compound annual sales growth of prescription drugs generated by companies in the NASDAQ Biotech Index is expected to reach 8.3% in the 2011-2018 period — well above the 3.1% forecasted for the wider pharmaceutical industry as stated in the *EvaluatePharma World Preview 2018: Embracing the Patent Cliff* report. Prescription sales from NBI companies are estimated to reach more than \$129 billion by 2018, almost double the \$74 billion generated in 2011.
- **Unexpected Product Winners:** By 2018, the highest-selling drug of any NBI company is expected to be Celgene's Revlimid — a small molecule compound derived from the controversial 1950s drug thalidomide and approved in 2006 to treat a rare cancer. Revlimid's sales could top \$6.7 billion by then, with Gilead's newly-acquired Phase II Hepatitis C therapy GS-7977 potentially a close second.
- **Pipeline Points to More Biologics; Growth of Oncology, Anti-Infectives and CNS products:** NBI companies have nearly 700 drugs in clinical trials, with 67% of the pipeline focused on cancer, anti-infectives and central nervous system diseases. Biologic drugs make up 42% of the NBI companies' pipelines, vs. only 8% of their marketed products today.

The report maps out the continuing rise of biologic drugs. It captures the strong growth in oncology and anti-infectives, alongside the continued dominance of CNS drugs. It tells the story of significant individual company successes – such as those of Gilead/Pharmasset, Celgene and others and their effects on the overall landscape.

NBI Companies and Products

Introduction

Biotechnology leaders read about it and biotech investors use it as a performance benchmark but what is the NASDAQ Biotech Index? What does its changing composition tell us about the present – and future – state of the BioPharmaceutical industry? This report takes a look under the hood and reveals the diversity of biotechnology companies listed in the NASDAQ Biotech Index. Marketed products, pipeline breadth and forecast sales are examined.

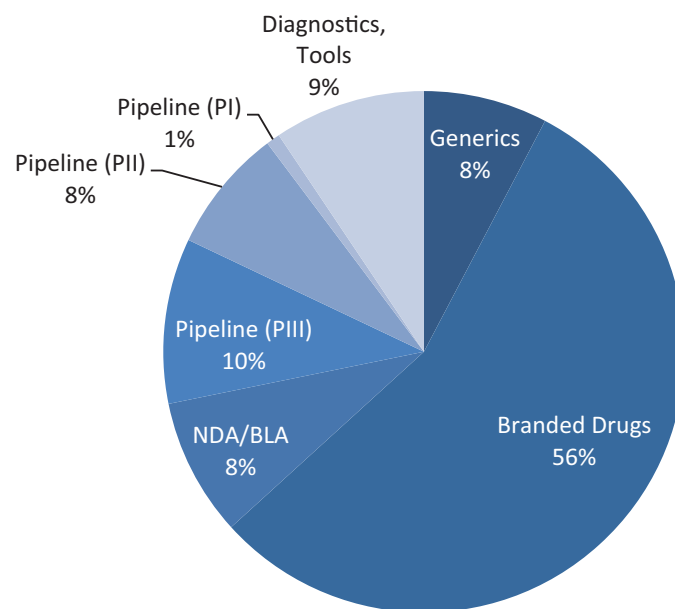
The NASDAQ Biotech Index represents a composite of 117 companies that trade on the NASDAQ Stock Exchange. To be included in the index, company securities must meet certain standards such as a minimum market valuation and trading volume and must be categorized as operating in the pharmaceutical or biotechnology industry. The Methodology section at the end of this report outlines the specific criteria for inclusion and maintenance of the index.

Most NBI companies have products on the market

Almost three quarters (73%) of NBI companies had marketed products, as of May 2012, compared with just 35% of those in the broader universe of publically traded US biotechnology companies. As such, the index captures a far more mature set of companies than those in the wider biotech sector. Furthermore, 91% of the NBI companies were focused on developing and marketing therapeutics, with just 9% in diagnostics and laboratory instruments.

Figure 1. Percentage of NBI companies whose latest-stage asset is marketed vs. pipeline

Source: EvaluatePharma® (May 30, 2012)



Of the pre-commercial companies in the NBI, most are in Phase II or III, with only one company, Maxygen, in Phase I. These 21 Phase II and Phase III companies account for 18% of the companies in the NBI – and almost half of those have filed products with regulators.

Companies that focus primarily on biologics make up only 30% of the index. It is a common misconception when referring to the biotech sector, that “biotech” implies R&D companies working on biologic therapeutics. In practice, most drug companies identified as “biotech” actually work on traditional, small molecule approaches to medicine. For example, BIO estimates that 65% of biotech companies in the United States conduct small molecule research and 35% develop cell-derived biologic drugs.¹

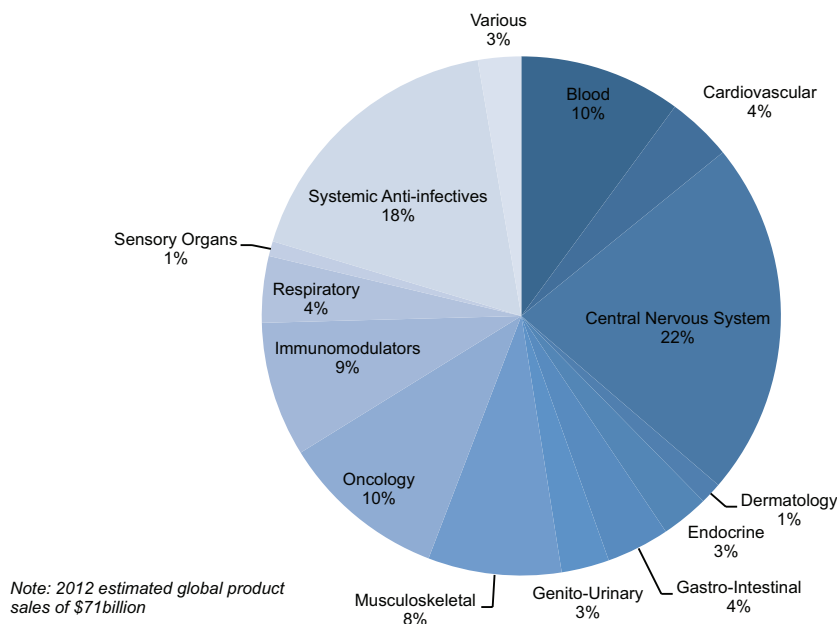
The 9% of companies classified as diagnostics/tools are engaged in DNA sequencing, clinical testing, laboratory assays and equipment that support the broader R&D of biotechnology worldwide. A more detailed analysis of their company focus will be outlined in the marketed products section below.

NBI Marketed Drugs: CNS, Anti-Infectives Dominate

Figure 2 shows that CNS therapies make up the largest portion (22%) of NBI product sales, dominated by multiple sclerosis treatments Copaxone, Avonex and Tysabri (Table 1). The next-largest category is anti-infectives (18%), driven by Gilead’s Atripla and Truvada. Product sales from oncology and blood segments contribute 10% each to total sales as shown in Figure 2.

Figure 2. Estimated 2012 product sales by therapeutic area

Source: EvaluatePharma® (May 30, 2012)



Nearly a quarter of 2012 NBI product sales will be generics, reflecting the impact of the host of patent expiries that have hit pharma and continue to do so. Generics are expected to contribute 24% to the \$85 billion in total 2012 prescription sales. Generics make up nearly 64% of the NBI’s 1823 marketed products, while generics firms, including most prominently Teva and Mylan, make up just 8% of NBI companies. These companies’ broad drug portfolios are skewed away from oncology and anti-infectives (which dominate biotech pipelines) toward CNS, GI and cardiovascular markets. Although cardiovascular therapies account for 13% of the currently marketed products from NBI companies, as a percentage of sales they make up only 4%.

1. BIO Industry Analysis 2011.

Table 1. Top 20 NBI marketed products ranked by estimated 2012 sales

Source: EvaluatePharma® (May 30, 2012)

Sales data are for sales made by the NBI company and do not include sales revenue of partners

Rank	Product	Company	Therapeutic Category	2012E (\$M)	Phase (Current)
1	Neulasta	Amgen	Oncology & Immunomodulators	\$4,172	Marketed
2	Copaxone	Teva Pharmaceutical Industries	Central Nervous System	\$3,968	Marketed
3	Enbrel	Amgen	Musculoskeletal	\$3,810	Marketed
4	Revlimid	Celgene	Oncology & Immunomodulators	\$3,795	Marketed
5	Atripla	Gilead Sciences	Systemic Anti-infectives	\$3,485	Marketed
6	Truvada	Gilead Sciences	Systemic Anti-infectives	\$2,979	Marketed
7	Avonex	Biogen Idec	Central Nervous System	\$2,813	Marketed
8	Aranesp	Amgen	Blood	\$2,081	Marketed
9	Epogen	Amgen	Blood	\$1,798	Marketed
10	Incivek	Vertex Pharmaceuticals	Systemic Anti-infectives	\$1,496	Marketed
11	Neupogen	Amgen	Oncology & Immunomodulators	\$1,260	Marketed
12	Soliris	Alexion Pharmaceuticals	Blood	\$1,073	Marketed
13	Vyvanse	Shire	Central Nervous System	\$1,004	Marketed
14	Lidoderm	Endo Pharmaceuticals	Central Nervous System	\$927	Marketed
15	Gamunex IGIV	Grifols	Systemic Anti-infectives	\$908	Marketed
16	Sensipar	Amgen	Endocrine	\$907	Marketed
17	Tysabri	Biogen Idec	Central Nervous System	\$839	Marketed
18	Cubicin	Cubist Pharmaceuticals	Systemic Anti-infectives	\$795	Marketed
19	Asacol	Warner Chilcott	Gastro-Intestinal	\$782	Marketed
20	Xgeva	Amgen	Musculoskeletal	\$773	Marketed

CNS therapies account for a quarter of this year's top-grossing NBI drugs, with three treatments for multiple sclerosis (MS) expected to generate \$6 billion in global sales. Other top selling products in CNS include therapies such as Shire's Vyvanse for ADHD and Endo's Lidoderm for pain.

Amgen's chemotherapy companion drug Neulasta takes the top slot, with projected 2012 sales of \$4.2 billion. Amgen products hold seven of the top 20 drugs in Table 1, with four of those drugs actually in the top 10. Gilead Sciences and Biogen Idec are the only other NBI companies to have more than one drug billed as a 2012 top-seller.

Product competition may re-shuffle the rankings

Teva's patented MS therapy Copaxone is the second-largest NBI drug with nearly \$4 billion in sales projected for 2012. It will have to fight to retain its ranking, though, given competition from Novartis' oral Gilenya and a further threat from Biogen Idec's BG-12, which could be approved by the end of the year. Copaxone also faces generic challenges from a host of drug developers that have pushed the company into ongoing litigation (Copaxone loses patent protection in 2014). Indeed, generics will soon effect four of the top 10 NBI drugs, that face patent expiry over the next three years. Amgen's Epogen loses exclusivity in 2012, followed by top selling Neulasta in 2015. Biogen Idec's Avonex loses patent protection in 2013. Gilead's top-grossing products, both HIV treatments, have longer patent lives, with Atripla and Truvada both patent-protected until 2021. However, as we shall see in the pipeline discussion, Gilead's new HIV therapy is expected to cannibalize some of these sales.

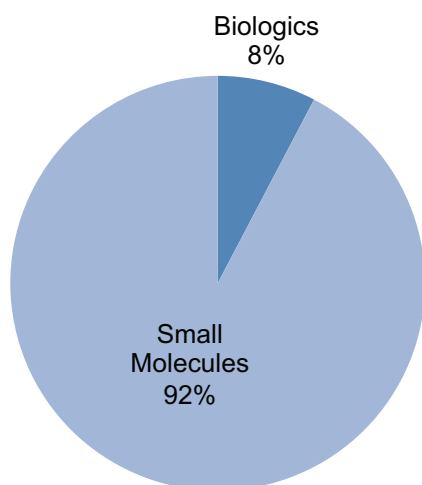
NBI Pipeline Drugs: Driven by Biologics, Oncology

As shown in Figure 3, biologics account for just 8% of currently marketed products, while the pipeline tells a different story. Biologics comprise 42% of the NBI pipeline drugs, an increase of over fourfold relative to the share of biologics among today's marketed products. This shift reflects increased focus on the development of biologics, where barriers to entry are higher than for small molecules but where revenues can nevertheless reach blockbuster proportions.

Figure 3. Percentage of biologics vs. small molecules on the market and in the pipeline

Source: EvaluatePharma® (May 30, 2012)

Marketed & Approved Products



Pipeline Products

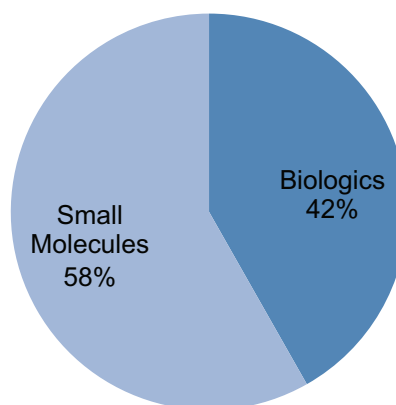
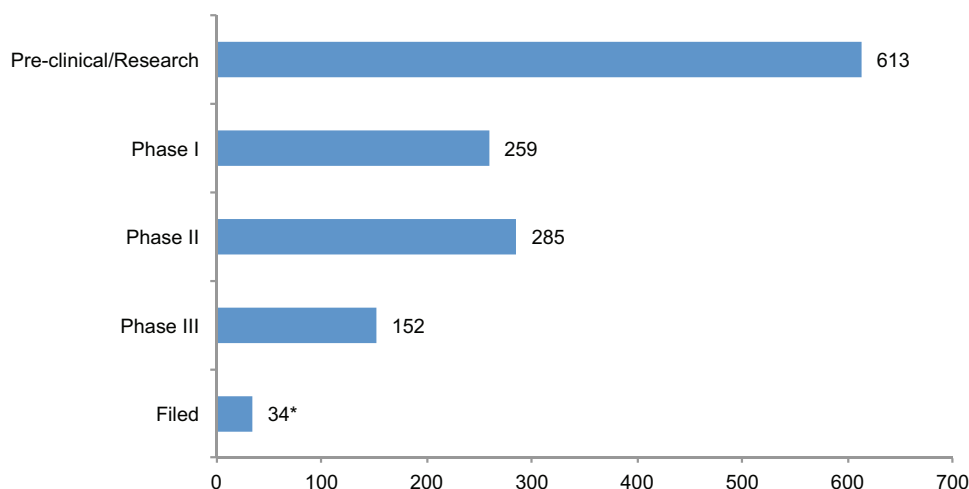


Figure 4 of this analysis shows 613 projects/compounds or 40% of the total pipeline is in the pre-clinical/research stage. The pipeline for the NBI also shows that of the three clinical development phases, most compounds are found in Phase II or proof-of-concept stage. Phase II is a critical juncture in development before expensive Phase III trials begin and where many compounds may fail. An example of the large attrition rate can be seen by looking at the NBI pipeline, where the number of Phase III candidates drops by over 47%; however, those late-stage programs are still expected to represent more than \$11 billion in sales by 2018. A healthy 34 NDA and BLAs have been filed and an additional 159 generic drugs and two biosimilars have also been filed for approval. Filed compounds are expected to contribute more than \$8.9 billion of the top 20 pipeline drug sales in 2018 (sales of the top 20 pipeline drugs in Table 2).

Figure 4. Breakdown of the NBI R&D pipeline by phase

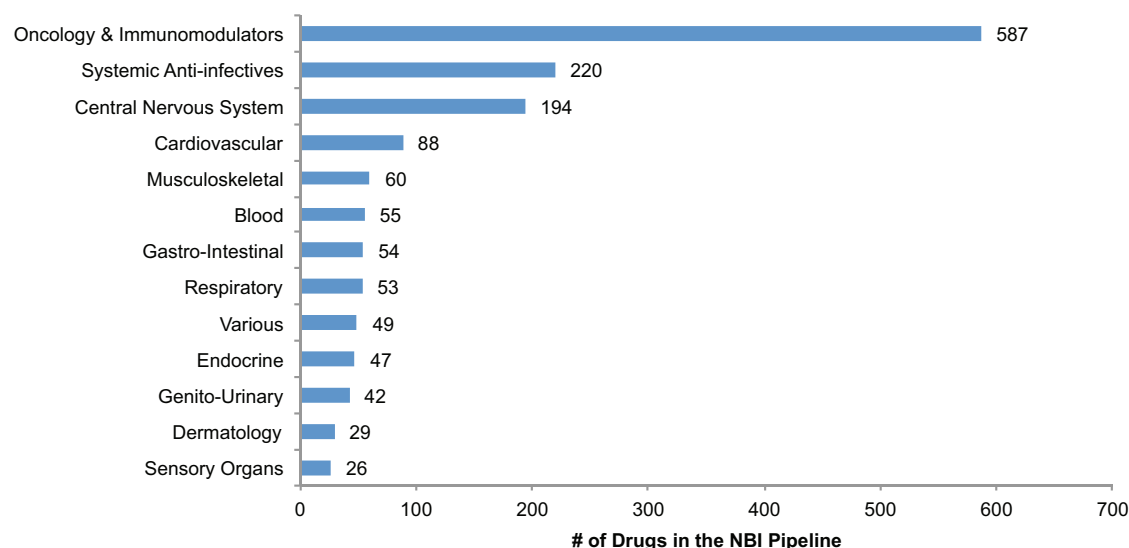
*Note: 34 NDA and BLAs and an additional 159 generic drugs and two biosimilars have been filed for approval.
Source: EvaluatePharma® (May 30, 2012)



An analysis of NBI pipeline drugs paints a very different story to that of the marketed portfolio. Oncology and Immunomodulator drugs dominate the collective pipeline, accounting for nearly 40% of the over 1500 R&D candidates, pushing CNS and anti-infectives, which top the marketed list, into distant second and third place (Figure 5). This reflects the growing prevalence and earlier detection of cancer as well as an advancing scientific understanding of the mechanisms behind this complex, diverse disease. The global oncology market is expected to top \$100 billion annually in 2018 according to the EvaluatePharma *World Preview 2018* report. There is also a strong anti-infectives pipeline, with Gilead's GS-7977 leading the pack and expected to be a blockbuster, having a significant impact on the overall R&D pipeline forecast.

Figure 5. Breakdown of the NBI R&D pipeline by therapeutic area

Source: EvaluatePharma® (May 30, 2012)



Indeed, by 2018, Gilead Sciences' anti-viral therapies, GS-7977 and Quad, are expected to be the top sellers from today's pipeline (Table 2). GS-7977 sales, at over \$5 billion, are forecast to overshadow those of all the other pipeline candidates. This example helps support Gilead's recent \$11.1 billion acquisition of Pharmasset – the highest price ever paid for a clinical-stage biotech. GS-7977 is a hepatitis C polymerase inhibitor developed by Pharmasset that recently advanced into two Phase III studies in genotype 2 and 3 patients and into Phase IIb for genotype 1 patients. Recent data released by Gilead revealed strong efficacy data for the treatment in combination with a mechanistically-different HCV drug candidate (Bristol-Myers Squibb's daclatasvir, an NS5A inhibitor).

Table 2. Top 20 NBI pipeline products (Phase I,II,III, or Filed) ranked by estimated 2018 sales

Source: EvaluatePharma® (May 30, 2012)

Sales data are for sales made by the NBI company and do not include sales revenue of partners

Rank	Product	Company	Therapeutic Category	2018E (\$M)	Phase (Current)
1	GS-7977	Gilead Sciences	Systemic Anti-infectives	\$5,359	Phase III
2	BG-12	Biogen Idec	Central Nervous System	\$3,400	Filed
3	Quad	Gilead Sciences	Systemic Anti-infectives	\$2,793	Filed
4	Qnexa	VIVUS	Gastro-Intestinal	\$983	Filed
5	Kyprolis	Onyx Pharmaceuticals	Oncology & Immunomodulators	\$897	Filed
6	Ponatinib	ARIAD Pharmaceuticals	Oncology & Immunomodulators	\$884	Phase II
7	AV-951	AVEO Oncology	Oncology & Immunomodulators	\$515	Phase III
8	AMR101	Amarin	Cardiovascular	\$510	Filed
9	VX-809	Vertex Pharmaceuticals	Respiratory	\$490	Phase II
10	GRN163L	Geron	Oncology & Immunomodulators	\$468	Phase II
11	Seasonal Flu VLP Vaccine	Novavax	Systemic Anti-infectives	\$462	Phase II
12	Ganetespib	Synta Pharmaceuticals	Oncology & Immunomodulators	\$449	Phase III
13	GALNS	BioMarin Pharmaceutical	Various	\$429	Phase III
14	Allovetin-7	Vical	Oncology & Immunomodulators	\$419	Phase III
15	ALN-TTR01	Alnylam Pharmaceuticals	Various	\$385	Phase I
16	Elvitegravir	Gilead Sciences	Systemic Anti-infectives	\$367	Phase III
17	Cabozantinib	Exelixis	Oncology & Immunomodulators	\$327	Phase III
18	Gattex	NPS Pharmaceuticals	Gastro-Intestinal	\$310	Filed
19	PEGylated-IFN β -1a	Biogen Idec	Central Nervous System	\$308	Phase III
20	ENB-0040	Alexion Pharmaceuticals	Musculoskeletal	\$302	Phase III

That said, GS-7977 is not alone. Nasdaq-listed Idenix has a Phase II nucleoside polymerase inhibitor, and so does Bristol, having bought out Nasdaq-listed Inhibitex in January 2012 for \$2.5 billion.

Gilead has another shot on goal and one much closer than GS-7977. Quad, which combines four therapies (tenofovir (Viread), emtricitabine (Emtriva), elvitegravir and boosting agent cobicistat) into a single tablet HIV regimen, was recently recommended by an FDA advisory committee and is expected to generate more than \$2.8 billion in 2018. In addition, the company has shown strong clinical trial results for a single component of Quad, HIV integrase inhibitor elvitegravir, showing that it may also be an effective option for patients as a once-daily dosing to treat HIV.

EvaluatePharma consensus estimates show strong sales projections for Biogen Idec's BG-12 (dimethyl fumarate), a small molecule immune modulator for relapsing forms of multiple sclerosis, which was acquired through its deal with the Swiss company Fumapharm AG in 2006. BG-12 has an advantage over most established competitor products as it is an oral treatment. It also has a reasonably benign safety profile, potentially offering it an edge over Gilenya, and is projected to be a go-to first line treatment.

Also among the top ten 2018 NBI product candidates are a trio of oncology drugs whose combined sales may top \$2 billion. Of the two kinase inhibitors in that trio, ARIAD's second oncology product candidate, ponatinib,

is an oral multi-targeted kinase inhibitor with potentially broad applications in cancer. Ponatinib has fully enrolled its pivotal Phase 2 registration trial in patients with resistant or intolerant chronic myeloid leukemia (CML) and Philadelphia positive acute lymphoblastic leukemia (Ph+ ALL). According to EvaluatePharma consensus estimates, ponatinib could reach over \$800 million in sales by 2018. If successful, it will join a very busy class with GlaxoSmithKline's Votrient (pazopanib) among the most recent entrants. Onyx's Kyprolis (carfilzomib), which is a proteasome inhibitor in the same class as Takeda's Velcade (bortezomib), has been filed for accelerated approval with an expected PDUFA date of July 27, 2012 for the treatment of late-stage multiple myeloma. Onyx acquired the drug in 2009 when the company bought privately-held Proteolix.

Vivus' Qnexa, a low dose combination of two previously approved drugs (phentermine and topiramate), is awaiting approval from the FDA for the treatment of obesity. The FDA has set a very high safety and efficacy bar for obesity treatments, which has tripped up many candidates. However, if approved, consensus forecasts have Qnexa generating over \$900 million in revenue by 2018.

Table 3. Top 40 NBI products ranked by estimated 2018 sales

Source: EvaluatePharma® (May 30, 2012)

Sales data are for sales made by the NBI company and do not include sales revenue of partners

Rank	Product	Company	Therapeutic Category	2018E (\$M)	Phase (Current)
1	Revlimid	Celgene	Oncology & Immunomodulators	\$6,751	Marketed
2	GS-7977	Gilead Sciences	Systemic Anti-infectives	\$5,359	Phase III
3	Soliris	Alexion Pharmaceuticals	Blood	\$3,782	Marketed
4	BG-12	Biogen Idec	Central Nervous System	\$3,400	Filed
5	Enbrel	Amgen	Musculoskeletal	\$3,103	Marketed
6	Neulasta	Amgen	Oncology & Immunomodulators	\$2,810	Marketed
7	Quad	Gilead Sciences	Systemic Anti-infectives	\$2,793	Filed
8	Xgeva	Amgen	Musculoskeletal	\$2,323	Marketed
9	Vyvanse	Shire	Central Nervous System	\$2,067	Marketed
10	Kalydeco	Vertex Pharmaceuticals	Respiratory	\$2,020	Marketed
11	Avonex	Biogen Idec	Central Nervous System	\$1,924	Marketed
12	Eylea	Regeneron Pharmaceuticals	Sensory Organs	\$1,848	Marketed
13	Complera	Gilead Sciences	Systemic Anti-infectives	\$1,547	Marketed
14	Aranesp	Amgen	Blood	\$1,543	Marketed
15	Truvada	Gilead Sciences	Systemic Anti-infectives	\$1,501	Marketed
16	Atripla	Gilead Sciences	Systemic Anti-infectives	\$1,395	Marketed
17	Gamunex IGIV	Grifols	Systemic Anti-infectives	\$1,290	Marketed
18	Benlysta	Human Genome Sciences	Oncology & Immunomodulators	\$1,230	Marketed
19	Copaxone	Teva Pharmaceutical Industries	Central Nervous System	\$1,185	Marketed
20	Jakafi	Incyte	Oncology & Immunomodulators	\$1,134	Marketed
21	Bydureon	Amylin Pharmaceuticals	Endocrine	\$1,103	Marketed
22	EpiPen	Mylan	Respiratory	\$1,097	Marketed
23	Provence	Dendreon	Oncology & Immunomodulators	\$1,056	Marketed
24	Tysabri	Biogen Idec	Central Nervous System	\$1,054	Marketed
25	Prolia	Amgen	Musculoskeletal	\$1,032	Marketed
26	Epogen	Amgen	Blood	\$999	Marketed
27	Xifaxan	Salix Pharmaceuticals	Gastro-Intestinal	\$986	Marketed
28	Qnexa	VIVUS	Gastro-Intestinal	\$983	Filed
29	H.P. Acthar Gel	Questcor Pharmaceuticals	Central Nervous System	\$924	Marketed
30	Kyprolis	Onyx Pharmaceuticals	Oncology & Immunomodulators	\$897	Filed
31	Vidaza	Celgene	Oncology & Immunomodulators	\$888	Marketed
32	Ponatinib	ARIAD Pharmaceuticals	Oncology & Immunomodulators	\$884	Phase II
33	Cubicin	Cubist Pharmaceuticals	Systemic Anti-infectives	\$882	Marketed
34	Flebogamma	Grifols	Systemic Anti-infectives	\$829	Marketed
35	Abraxane	Celgene	Oncology & Immunomodulators	\$815	Marketed
36	Cinryze	ViroPharma	Blood	\$789	Marketed
37	Elaprase	Shire	Various	\$775	Marketed
38	ProAir HFA	Teva Pharmaceutical Industries	Respiratory	\$703	Marketed
39	Esbriet	InterMune	Respiratory	\$694	Marketed
40	Prolastin-CA1P1	Grifols	Respiratory	\$674	Marketed

Table 3 lists the top 40 NBI products by estimated 2018 sales attributable to specific NBI companies. The list combines consensus sales projections for both pipeline and marketed products. Reflecting the growing importance of oncology, Celgene's Revlimid is forecast to head the 2018 top 40 product list. Its sales could reach \$6.7 billion, an increase of nearly \$3 billion over the drug's expected 2012 sales. A further eight drugs within oncology & immuno-modulators feature in this group and, in addition, the systemic anti-infectives also have eight of the top 40 drugs. Twenty-five of the top 40 are expected to each generate sales over \$1 billion. Alexion's Soliris, which prevents the destruction of white blood cells in people with ultra-rare paroxysmal nocturnal hemoglobinuria (PNH) and hemolytic-uremic (HUS) syndromes, is estimated to grow from \$1.1 billion in 2012 to \$3.7 billion by 2018.

Amgen's marketed products still figure prominently, with three of its drugs holding a top five spot for marketed products. However, analysts project Neulasta's sales to fall after its 2015 patent expiry, taking the drug from its top seller spot.

Gilead's two potential blockbusters are expected to help push Neulasta, Copaxone and Gilead's own Atripla out of their current top-five sales slots shown in Table 1. In addition, Copaxone is facing generic competition from an expiring patent.

Several recent FDA approvals are likely to make the 2018 top 40 list. These include Incyte's JAK-inhibitor Jakafi, approved for myelofibrosis, Vertex's cystic fibrosis drug, Kalydeco and Human Genome Science's lupus treatment Benlysta, each expected to top \$1 billion in sales by 2018.

The bottom quartile of the top 40 have sales projections in the \$675-\$900 million range and are primarily marketed drugs in a range of therapeutic areas.

NBI Diagnostics and R&D Tools

Tools companies contribute more to the NBI than clinical diagnostics

Barely 10% of the NBI's 117 companies are focused on diagnostics and R&D tools that support clinical and bench science in biotechnology. Within that group, diagnostics are overshadowed by tools – reflecting both the appeal of reliable and low-risk revenues generated by companies in the laboratory assay and instrument businesses, and that the diagnostics business model remains uncertain, despite the growing role for diagnostics in personalized medicine.

Table 4. NBI diagnostics and tools companies by total 2011 revenue

Source: Company Filings

	Company	Product Type	Revenue (\$M)	Mcap
1	Life Technologies Corp	Assay Kits, MicroArrays/Chips, Instruments, Synthetics	\$3,820	\$8,334
2	Qiagen N.V.	Assay Kits, MicroArrays/Chips, Instruments	\$1,170	\$4,033
3	Illumina Inc	MicroArrays/Chips, Sequencing	\$1,056	\$5,732
4	Gen-Probe Inc.	Assay Kits, Instruments	\$576	\$3,699
5	Myriad Genetics Inc.	Sequencing	\$402	\$2,229
6	Affymetrix Inc	Assay Kits, MicroArrays/Chips, Instruments	\$267	\$301
7	Genomic Health Inc	Sequencing	\$206	\$878
8	Luminex Copr	Assay Kits, Instruments	\$184	\$1,029
9	Sequenom Inc	Sequencing	\$56	\$615
10	Pacific Biosciences	Sequencing	\$34	\$140

Thus most of the \$7.8 billion in total revenue from these 10 companies comes from the tools side. The top three companies, with large stakes in the laboratory assay and instrument businesses, account for 78% of the total revenue for the group. They also account for 67% of the total market capitalization of the diagnostic and tools segment.

Life Technologies is the largest company in this category by a wide margin based on sales, or market capitalization. Life Technologies' revenue comes from molecular biology and cell-based products for research, which account for 71% of its \$3.8 billion in 2011 revenue. Approximately 27% is from the genetic systems division, which focuses on sequencing technologies.

Qiagen and Illumina follow Life Technologies by revenue and market capitalization, with \$1.17 billion and \$1.05 billion in 2011 sales, respectively. The majority of Qiagen's revenues came from the sales of consumable products such as packaged diagnostic kits and prepared assays, with sales of automated machines and laboratory equipment bringing in the remainder. Illumina's main revenue stream is also product-based, with approximately 60% coming from the sale of sample preparation and sequencing kits and 40% from the sale of their larger sequencing instruments.

Despite the challenges facing companies seeking to commercialize diagnostics – not least limited IP protection and low pricing – the sale of rapid molecular diagnostic tests in women's health and infectious disease indications accounted for nearly all of Gen-Probe's \$402 million revenue in 2011, while the majority of Myriad Genetics' \$576 million revenue came from the company's molecular diagnostic testing and analysis services, particularly their breast cancer BRACAnalysis test. As of May 2012, Gen-Probe was in the process of being acquired by Hologic for \$3.7 billion.

The bottom five companies each generated revenues below \$300 million in 2011, and are split between diagnostics and tools. Affymetrix and Luminex focus more on tools for the lab, whereas Genomic Health, Sequenom and Pacific Biosciences have been more focused on the clinical diagnostics market with new DNA sequencing technologies.

Aggregate Sales Projection to 2018

Total prescription sales from NBI companies are expected to rise from \$74 billion in 2011 to \$129 billion in 2018 – a compound annual growth rate (CAGR) of 8.3% that overshadows the global pharmaceutical CAGR of 3.1%, according to the EvaluatePharma *World Preview 2018* report. By then, NBI companies will be contributing 14.6% of worldwide pharma sales, forecast to reach \$885 billion by 2018 as revealed in the EvaluatePharma *World Preview 2018* report.

Figure 6. Aggregate prescription sales for the NBI companies 2011-2018

CAGR: Compound Annual Growth Rate
Source: EvaluatePharma® (May 30, 2012)

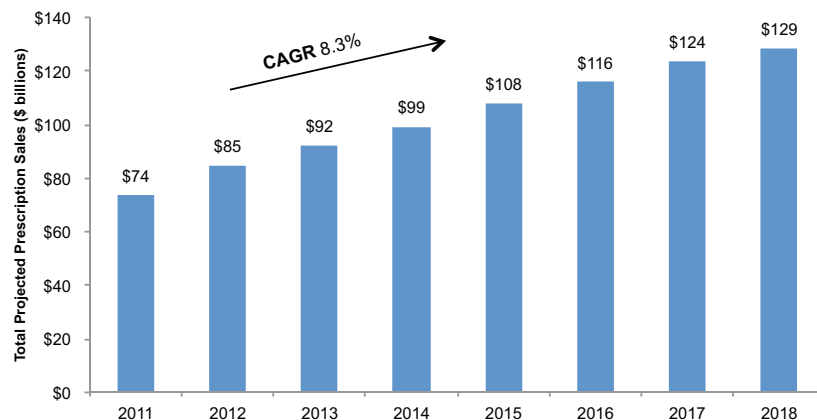


Table 5 shows that by 2018, generics firm Teva will still be the largest single prescription revenue-contributor to the NBI index. But big biotech is where most of the growth is coming from: Gilead is expected to rise to the second spot with \$15 billion in prescription sales, as new products emerge, and Celgene's prescription sales are expected to double to \$9.3 billion placing it just behind Amgen, which is estimated to reach \$14.5 billion.

Teva's \$15.6 billion 2011 prescription sales made up 21% of the total \$74 billion for NBI companies. Teva's prescription sales are expected to grow to over \$19 billion by 2018, but will comprise only 14.7% of the total \$129 billion in 2018 prescription sales. Similarly, Amgen was second in the group for 2011, with 20% of total sales, but is estimated to make up only 11% of the total in 2018. Gilead and Celgene sales are expected to grow substantially, but will remain near 12% and 7%, respectively, in terms of total NBI sales over the next six years. Collectively, these top four companies will bring in 45% of NBI total prescription sales by 2018.

Eight companies are expected to move above \$1 billion in prescription sales by 2018: Regeneron, Salix, Amylin, Human Genome Sciences (currently facing a hostile acquisition bid from GlaxoSmithKline), United Therapeutics, Cubist, Incyte, and Dendreon.

Table 5. Top 20 NBI companies ranked by estimated 2018 prescription sales

Source: EvaluatePharma® (May 30, 2012)

Rank	Company	2018E (\$M)
1	Teva Pharmaceutical Industries	\$19,168
2	Gilead Sciences	\$15,119
3	Amgen	\$14,520
4	Celgene	\$9,374
5	Mylan	\$8,587
6	Biogen Idec	\$7,201
7	Shire	\$6,786
8	Alexion Pharmaceuticals	\$4,083
9	Grifols	\$4,053
10	Vertex Pharmaceuticals	\$2,724
11	Endo Pharmaceuticals	\$2,240
12	Warner Chilcott	\$2,077
13	Regeneron Pharmaceuticals	\$2,065
14	Salix Pharmaceuticals	\$1,870
15	Amylin Pharmaceuticals	\$1,470
16	Cubist Pharmaceuticals	\$1,278
17	Human Genome Sciences	\$1,263
18	United Therapeutics	\$1,173
19	Incyte	\$1,134
20	Dendreon	\$1,056

Conclusions

With its wide variety of constituent companies – ranging from pre-commercial micro-cap biotechs to generics giants and revenue-generating tools groups – the NBI captures many of the characteristics of, and trends within, the industry at large. It is an industry snapshot of the top public BioPharma firms dominated today by large, well-established players with a mix of biologics and small molecule drugs and the top selling products of tomorrow.

But the index also captures the dynamic shifts in the top company rankings, relative share of biologic drugs, and rise to prominence of therapeutic areas such as oncology and infectious diseases. The size and breadth of the NBI pipeline, with over 1500 compounds in R&D today, has much to offer, and is well positioned to yield many great treatments for patients in the years to come.

For investors, this sector has offered diversity to their portfolios. Although the index today is concentrated in the larger companies, this could change in the future if market participants become more comfortable with pipeline risk, and the number of public companies increase when the IPO market gets healthier.

NBI Methodology

The NASDAQ Biotechnology Index (NBI) is a modified market capitalization-weighted index created on November 1, 1993.

Eligibility

To be eligible for inclusion in the Index, a security must be listed on The NASDAQ Global Stock Market and meet the following criteria:

- The initial market capitalization of at least \$200 million; and must meet the maintenance criteria of \$100 million in market capitalization
- The initial average daily trading volume of at least 100,000 shares; and must meet the maintenance criteria of 50,000 shares average daily trading volume
- The security may not be issued by an issuer currently in bankruptcy proceedings;
- The issuer of the security may not have entered into a definitive agreement or other arrangement which would likely result in the security no longer being Index eligible;
- The issuer of the security may not have annual financial statements with an audit opinion that is currently withdrawn; and
- The listed security must have “seasoned” on a recognized market (generally, at least six months).

Index evaluated semi-annually

Generally, the list of semi-annual additions and deletions is publicly announced via a press release in the early part of May and November. Replacements are made effective after the close of trading on the third Friday in May and November. Moreover, if at any time during the year other than the Evaluation, an Index Security no longer meets the Eligibility Criteria, or is otherwise determined to have become ineligible for continued inclusion in the Index, the security is removed from the Index and will not be replaced. The data used in the rankings include end of March and September market data and is updated for total shares outstanding submitted in a publicly filed SEC document via EDGAR through the end of April and October, respectively.

Index rebalanced quarterly

On a quarterly basis coinciding with the quarterly scheduled Index Share adjustment procedures, the Index will be rebalanced if it is determined that: (1) the current weight of the single largest market capitalization Index Security is greater than 24.0% and (2) the “collective weight” of those Index Securities whose individual current weights are in excess of 4.5%, when added together, exceed 48.0% of the Index.

NBI Company Listing

NASDAQ biotechnology holdings as of March 30, 2012²

Company Name	NASDAQ Ticker	Index Weight (%)	Market Cap (\$M)	Company Name	NASDAQ Ticker	Index Weight (%)	Market Cap (\$M)
Alexion Pharmaceuticals Inc.	ALXN	7.56%	\$17,271	Optimer Pharmaceuticals Inc.	OPTR	0.27%	\$650
Amgen Inc.	AMGN	7.14%	\$53,180	Rigel Pharmaceuticals Inc.	RIGL	0.27%	\$575
Regeneron Pharmaceuticals Inc.	REGN	6.61%	\$10,703	Alnylam Pharmaceuticals Inc.	ALNY	0.25%	\$574
Celgene Corp.	CELG	6.33%	\$34,017	NPS Pharmaceuticals Inc.	NPSP	0.23%	\$589
Gilead Sciences Inc.	GILD	5.35%	\$37,039	Affymax Inc.	AFFY	0.23%	\$420
Biogen Idec Inc.	BIIB	4.97%	\$30,079	AVEO Pharmaceuticals Inc.	AVEO	0.22%	\$541
Teva Pharmaceutical ADS	TEVA	4.55%	\$42,463	Hi-Tech Pharmacal Co. Inc.	HITK	0.21%	\$469
Perrigo Co.	PRGO	4.01%	\$9,639	Sagent Pharmaceuticals Inc.	SGNT	0.21%	\$499
Vertex Pharmaceuticals Inc.	VRTX	3.48%	\$8,626	Sequenom Inc.	SQNM	0.20%	\$466
Mylan Inc.	MYL	2.96%	\$10,012	MannKind Corp.	MNKD	0.20%	\$414
Illumina Inc.	ILMN	2.48%	\$6,484	MAP Pharmaceuticals Inc.	MAPP	0.19%	\$438
Shire PLC ADS	SHPGY	2.13%	\$17,767	Avanir Pharmaceuticals Inc.	AVNR	0.19%	\$454
BioMarin Pharmaceutical Inc.	BMRN	2.04%	\$3,960	Enzon Pharmaceuticals Inc.	ENZN	0.19%	\$330
Life Technologies Corp.	LIFE	1.60%	\$8,703	Arena Pharmaceuticals Inc.	ARNA	0.19%	\$555
Salix Pharmaceuticals Ltd.	SLXP	1.47%	\$3,120	Santarus Inc.	SNTS	0.17%	\$358
Onyx Pharmaceuticals Inc.	ONXX	1.42%	\$2,414	Progenics Pharmaceuticals Inc.	PGNX	0.16%	\$335
Cubist Pharmaceuticals Inc.	CBST	1.36%	\$2,723	Curis Inc.	CRIS	0.16%	\$374
United Therapeutics Corp.	UTHR	1.25%	\$2,527	Ligand Pharmaceuticals Inc.	LGND	0.16%	\$313
Incyte Corp.	INCY	1.24%	\$2,458	AMAG Pharmaceuticals Inc.	AMAG	0.15%	\$338
Medivation Inc.	MDVN	1.17%	\$2,691	Ista Pharmaceuticals Inc.	ISTA	0.15%	\$378
Questcor Pharmaceuticals Inc.	QCOR	1.14%	\$2,393	SciClone Pharmaceuticals Inc.	SCLN	0.15%	\$365
Warner Chilcott Plc	WCRX	1.11%	\$4,191	Depomed Inc.	DEPO	0.13%	\$348
Ariad Pharmaceuticals Inc.	ARIA	1.06%	\$2,540	Cadence Pharmaceuticals Inc.	CADX	0.13%	\$316
Endo Pharmaceuticals	ENDP	0.94%	\$4,520	QLT Inc.	QLTI	0.13%	\$343
Seattle Genetics Inc.	SGEN	0.94%	\$2,371	Vical Inc.	VICL	0.13%	\$292
Qiagen N.V.	QGEN	0.93%	\$3,647	Immunomedics Inc.	IMMU	0.12%	\$274
Alkermes PLC	ALKS	0.89%	\$2,414	Geron Corp.	GERN	0.12%	\$224
ViroPharma Inc.	VPHM	0.88%	\$2,127	Neurocrine Biosciences Inc.	NBIX	0.12%	\$528
Gen-Probe Inc.	GPRO	0.88%	\$3,004	Affymetrix Inc.	AFFX	0.12%	\$301
Myriad Genetics Inc.	MYGN	0.80%	\$1,994	Synta Pharmaceuticals Corp.	SNTA	0.12%	\$248
Impax Laboratories Inc.	IPXL	0.78%	\$1,642	Obagi Medical Products Inc.	OMPI	0.11%	\$250
Theravance Inc.	THRX	0.76%	\$1,686	ArQule Inc.	ARQL	0.11%	\$377
VIVUS Inc.	VVUS	0.73%	\$2,191	Sangamo BioSciences Inc.	SGMO	0.11%	\$258
Amylin Pharmaceuticals Inc.	AMLN	0.73%	\$4,014	GTx Inc.	GTXI	0.11%	\$242
Techne Corp.	TECH	0.72%	\$2,584	China Biologic Products Inc.	CBPO	0.10%	\$238
Dendreon Corp.	DNDN	0.68%	\$1,639	BioCryst Pharmaceuticals Inc.	BCRX	0.10%	\$239
Halozyne Therapeutics Inc.	HALO	0.62%	\$1,430	AVI BioPharma Inc.	AVII	0.09%	\$209
InterMune Inc.	ITMN	0.60%	\$958	Array BioPharma Inc.	ARRY	0.08%	\$278
Grifols S.A. ADS	GRFS	0.55%	\$1,750	SIGA Technologies Inc.	SIGA	0.08%	\$174
Akorn Inc.	AKRX	0.52%	\$1,112	Pacific Biosciences of California Inc.	PACB	0.08%	\$187
Amarin Corp. PLC	AMRN	0.52%	\$1,534	Targacept Inc.	TRGT	0.08%	\$171
Nektar Therapeutics	NKTR	0.50%	\$907	Osiris Therapeutics Inc.	OSIR	0.08%	\$168
Acorda Therapeutics Inc.	ACOR	0.44%	\$1,054	Astex Pharmaceuticals Inc.	ASTX	0.08%	\$173
Exelixis Inc.	EXEL	0.44%	\$769	Oncothyreon Inc.	ONTY	0.08%	\$241
Luminex Corp.	LMNX	0.42%	\$976	Dyax Corp.	DYAX	0.08%	\$154
Idenix Pharmaceuticals Inc.	IDIX	0.42%	\$1,053	Endocyte Inc.	ECYT	0.07%	\$178
Genomic Health Inc.	GHDX	0.41%	\$918	XenoPort Inc.	XNPT	0.07%	\$160
Ironwood Pharmaceuticals Inc.	IRWD	0.41%	\$903	Maxygen Inc.	MAXY	0.07%	\$159
Isis Pharmaceuticals Inc.	ISIS	0.38%	\$878	Novavax Inc.	NVAX	0.06%	\$153
Lexicon Pharmaceuticals Inc.	LXRX	0.38%	\$894	Savient Pharmaceuticals Inc.	SVNT	0.06%	\$156
Auxilium Pharmaceuticals Inc.	AUXL	0.37%	\$897	Vanda Pharmaceuticals Inc.	VNDA	0.06%	\$135
Human Genome Sciences Inc.	HGSI	0.36%	\$1,640	Cytori Therapeutics Inc.	CYTX	0.06%	\$144
Momenta Pharmaceuticals Inc.	MNTA	0.36%	\$786	Pain Therapeutics Inc.	PTIE	0.05%	\$162
Immunogen Inc.	IMGN	0.34%	\$1,104	Sinovac Biotech Ltd.	SVA	0.05%	\$111
Ardea Biosciences Inc.	RDEA	0.34%	\$799	BioSante Pharmaceuticals Inc.	BPAX	0.03%	\$82
Medicines Co.	MDCO	0.34%	\$1,091	Durect Corp.	DRRX	0.03%	\$70
Spectrum Pharmaceuticals Inc.	SPPI	0.32%	\$749	Columbia Laboratories Inc.	CBRX	0.03%	\$62
Achillion Pharmaceuticals Inc.	ACHN	0.30%	\$676	Cardiome Pharma Corp.	CRME	0.02%	\$43
PDL BioPharma Inc.	PDLI	0.29%	\$890				

2 As of May 21, 2012, the Nasdaq semi-annual rebalancing resulted in the addition of ten securities and the removal of five, for a net 122 companies. The ten added securities are: Cerus Corporation (CERS), Celldex Therapeutics, Inc. (CLDX), Amicus Therapeutics, Inc. (FOLD), Infinity Pharmaceuticals, Inc. (INFI), Jazz Pharmaceuticals plc (JAZZ), Omeros Corporation (OMER), Orexigen Therapeutics, Inc. (OREX), Pacira Pharmaceuticals, Inc. (PCRX), Raptor Pharmaceutical Corp. (RPTP) and Trius Therapeutics, Inc. (TSRX). The five removed are: BioSante Pharmaceuticals, Inc. (BPAX), China Biologic Products, Inc. (CBPO), Columbia Laboratories, Inc. (CBRX), Cardiome Pharma Corp (CRME) and DURECT Corporation (DRRX). Source: NASDAQ

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