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Pharma 50

Pharma 50 Insight:
The Accelerating Growth of Specialty Markets

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A highlight of the Pharma 50 ranking over the last few years is the steady upward trajectory of companies with a strong franchise in specialty medicines. Specialty markets are appealing to companies that have a strong research and development pipeline, are prioritizing serious unmet medical needs, and are taking a more personalized approach to the traditional relationship between physicians and patients. This is why we find it appropriate to examine in more detail the factors that drive success in the specialty drug market as well as likely key areas of growth in this segment over the next five years.

Overall, this market has experienced significant expansion since the turn of the decade, with steady gains

Rank	Company headquarters [website]	2013 Rx Sales (USD in mln)	2013 R&D spend (USD in mln)	2013 Top-selling Drugs [USD in mln]
1	**Novartis** Basel, Switzerland [novartis.com]	$46,017	$9,360.3	Gleevec [4,693] Diovan [3,524] Lucentis [2,383]
2	**Pfizer** New York, New York [pfizer.com]	$45,011	$6,254.0	Lyrica [4,595] Prevnar 13 [3,974] Enbrel [3,774]
3	**Roche** Basel, Switzerland [roche.com]	$39,143	$8,293.5	Rituxan [7,503] Avastin [6,751] Herceptin [6,562]
4	**Sanofi** Paris, France [sanofi.com]	$37,701	$6,117.4	Lantus [7,592] Plavix [2,460] Lovenox [2,262]
5	**Merck & Co** Whitehouse Station, New Jersey [merck.com]	$37,519	$7,123.0	Januvia [4,004] Zetia [2,658] Remicade [2,271]
6	**GlaxoSmithKline** Brentford, England [gsk.com]	$33,055	$5,041.0	Seretide/Advair [8,251] Pediarix [1,349] Avodart [1,341]
7	**Johnson & Johnson** New Brunswick, New Jersey [jnj.com]	$26,475	$5,810.0	Remicade [5,334] Zytiga [1,698] Prezista [1,673]
8	**AstraZeneca** London, England [astrazeneca.com]	$24,523	$4,269.0	Crestor [5,622] Nexium [3,872] Symbicort [3,483]
9	**Eli Lilly** Indianapolis, Indiana [lilly.com]	$20,119	$5,316.2	Cymbalta [5,084] Alimta [2,703] Humalog [2,611]
10	**AbbVie** North Chicago, Illinois [abbvie.com]	$18,790	$2,831.0	Humira [10,659] AndroGel [1,035] Kaletra [962]

Sources: Company financial statements, SEC 10k reports, other *Pharm Exec* estimates, and contributions from the EvaluatePharma industry sales surveys.

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experienced across all geographies. Specialty pharmaceuticals comprised 19% of total global sales in 2008; in 2013, it reached 24%. More important, growth in the segment outpaced overall sales. Whereas, global sales of all pharmaceutical products in absolute terms rose from around $700 billion in 2008 to $880 billion in 2013—a 25% increase, according to IMS Health's MIDAS database—the specialty drug portion expanded at double the rate, at about 50% in absolute terms.

The conventional wisdom is to define specialty as products that treat smaller patient populations with higher treatment costs. In order to provide a consistent classification, IMS Health defines specialty products as medicines that treat specific, complex diseases with five or more of the following attributes:

» Use in treatment of chronic conditions.
» Initiated by a specialist.
» Requiring special handling and administration, including subcutaneous injection.
» Subject to unique distribution arrangements.
» High price points.
» Extensive patient care service, monitoring, or education.

In countries where individual patients bear a significant portion of the out-of-pocket costs of treatment, companies must deploy and fund novel approaches to increase disease awareness and identify patients at risk.

The trend in favor of specialty shows every sign of continuing. Specialty products now represent a larger portion of the biopharma R&D pipeline: we estimate that more than 50% of early- to late-stage pipeline compounds are specialty products. In addition, these products are selling outside the traditional geographic markets of the US, EU5, and Japan. There is an assumption that high prices limit the potential for these drugs in these non-traditional markets—in fact, sales are growing, though not always for the originators of the molecules.

As companies continue to invest in this space, a key area of interest is better understanding of the historical growth trends in specialty. Such context is critical to answering this question: which are the areas that Pharma 50 companies should concentrate their investments to expand and grow into the next decade?

Rank	Company headquarters [website]	2013 Rx Sales (USD in mln)	2013 R&D spend (USD in mln)	2013 Top-selling Drug [USD in mln]
11	**Amgen** Thousand Oaks, California [amgen.com]	$18,192	$3,941.0	Enbrel [4,551]
12	**Teva Pharmaceutical Industries** Petach Tikva, Israel [tevapharm.com]	$17,563	$1,422.0	Copaxone [4,328]
13	**Bayer** Leverkusen, Germany [bayer.com]	$15,594	$2,710.0	Kogenate [1,597]
14	**Novo Nordisk** Bagsvaerd, Denmark [novonordisk.com]	$14,886	$2,089.9	NovoRapid [3,001]
15	**Boehringer Ingelheim** Ingelheim, Germany [boehringer-ingelheim.com]	$14,468	$3,246.7	Spiriva [4,719]
16	**Takeda** Osaka, Japan [takeda.com]	$13,591	$3,351.6	Biopress [1,256]
17	**Bristol-Myers Squibb** New York, New York [bms.com]	$12,306	$3,715.0	Reyataz [1,551]
18	**Gilead Sciences** Foster City, California [gilead.com]	$10,804	$2,056.4	Atripla [3,648]
19	**Astellas Pharma** Tokyo, Japan [astellas.com]	$10,431	$2,132.3	Prograf [1,755]
20	**Daiichi Sankyo** Tokyo, Japan [daiichisankyo.com]	$10,268	$1,925.9	Benicar [2,116]

Sources: Company financial statements, SEC 10k reports, other *Pharm Exec* estimates, and contributions from the EvaluatePharma industry sales surveys.

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Our analysis finds three answers to the question. First, building a truly global business requires developing assets in the specialty segment, if only because sales and volumes of these drugs are increasing in almost every geography. Market demand is turning more towards specialty products, and for the top integrated players represented in the Pharma 50, being able to meet this demand is an acute strategic imperative. Second, the market channel structure within the specialty field is changing, as more products are being sold in the retail sector rather than in hospital or specialty clinics. This opens significant new possibilities in terms of a broader audience reach, with a strong "willingness to pay" component. Finally, we are seeing therapeutic class concentration, with a potential impact on the future competition: the top seven therapeutic areas in specialty now seem to account for about 75% of all sales of specialty products.

In the EU5, there seems to be a higher proportion of specialty product usage than in the US, and a rise in both hospital and retail sales. This is being driven by adoption of newer therapies under the single-payer structure of these markets.

An important caveat in interpreting all figures in this article is that IMS sales data is based on the ex-manufacturer invoice price, exclusive of rebates, discounts, and patient access schemes. In some geographies (e.g., oncology in Europe), this could mean that the entire increase in sales does not translate directly back to the manufacturer because discounts to the price may be in place. Nevertheless, we are confident that the trends identified are representative of what is actually occurring in the market.

Geographic growth

As companies expand outside the mature US, EU5, and Japan triad, they

Rank	Company headquarters [website]	2013 Rx Sales (USD in mln)	2013 R&D spend (USD in mln)	2013 Top-selling Drug [USD in mln]
21	**Otsuka Holdings** **Tokyo, Japan** [otsuka.com]	$8,655	$2,032.6	**Abilify** [5,510]
22	**Baxter International** **Deerfield, Illinois** [baxter.com]	$8,265	$1,070.0	**Gammagard Liquid** [2,118]
23	**Merck KGaA** **Darmstadt, Germany** [merckgroup.com]	$7,913	$1,594.0	**Rebif** [2,477]
24	**Actavis** **Zug, Switzerland** [actavis.com]	$7,206	$581.1	**Methylphenidate ER** [610]
25	**Mylan** **Canonsburg, Pennsylvania** [mylan.com]	$6,772	$456.2	**EpiPen** [829]
26	**Celgene** **Summit, New Jersey** [celgene.com]	$6,359	$1,650.4	**Revlimid** [4,280]
27	**Biogen Idec** **Weston, Massachusetts** [biogenidec.com]	$5,429	$1,444.1	**Avonex** [3,005]
28	**Allergan** **Irvine, California** [allergan.com]	$5,398	$1,034.7	**Botox** [1,982]
29	**Les Laboratoires Servier** **Neuilly-sur-Seine, France** [servier.com]	$5,058	$1,264.4	**Coversyl** [912]
30	**Abbott Laboratories** **Abbott Park, Illinois** [abbott.com]	$4,974	$239.0	**Biaxin** [416]

Sources: Company financial statements, SEC 10k reports, other *Pharm Exec* estimates, and contributions from the EvaluatePharma industry sales surveys.

How the listings were compiled: *Pharm Exec* would like to thank EvaluatePharma for assisting in the development of this year's Pharma 50 listing. In the case of privately held companies and in some other instances, the numbers reflect a best estimate, based on a consensus methodology that includes forecasts from brokers covering these companies. All figures represent the fiscal year that ended in 2013. For most American and European companies, that means the year ending December 31, 2013. For many Japanese companies, we used the fiscal year ending March 31, 2013. Historic averages were used in the conversion of companies'native currency to USD.

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have adapted their traditional commercial models to the customized needs of alternate geographies. For specialty products, this has posed a difficult challenge as treatments may require complex handling or levels of patient care that are hard to secure in areas with poor infrastructure and sporadic practice patterns. In addition, in countries where individual patients bear a significant portion of the out-of-pocket costs of treatment, companies must deploy and fund novel approaches to increase disease awareness and identify patients at risk. It is a necessary pre-condition to gain patient acceptance and position the local market for sales of higher priced therapies. It suggests higher fixed costs to developing the business there.

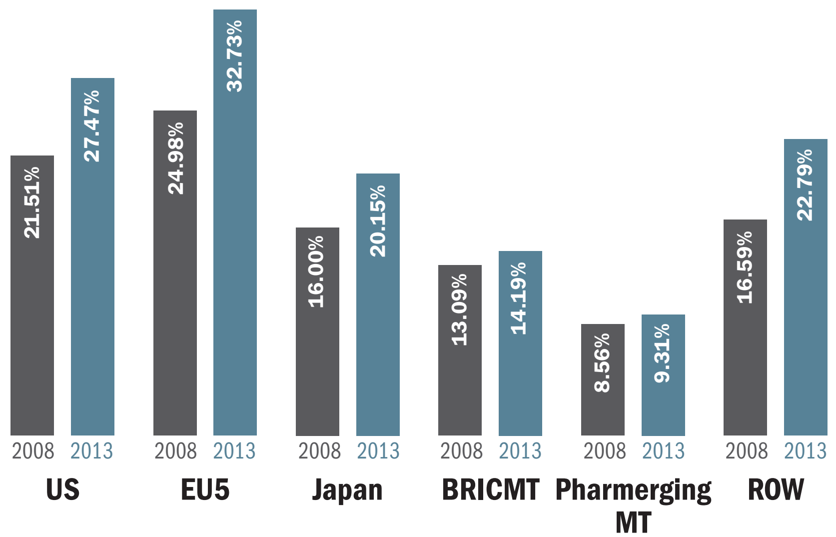

Figure 1: Specialty market percent of total sales by geography (Data: IMS)

Despite these challenges, the past few years have seen a significant increase in specialty sales and volumes across all geographies (see Figure 1). Using our proprietary information, we find that even with absolute growth in all the markets, the proportion of the specialty segment still increased. The increase was most prominent in the US, EU5, and Japan, with the proportion rising by at least five percentage points in each region. For example in the US, 27.5% of sales were in spe-

Rank	Company headquarters [website]	2013 Rx Sales (USD in mln)	2013 R&D spend (USD in mln)	2013 Top-selling Drug [USD in mln]
31	**CSL** **Melbourne, Australia** [csl.com.au]	$4,875	$427.1	**Privigen** [2,089]
32	**Shire** **Dublin, Ireland** [shire.com]	$4,847	$890.2	**Vyvanse** [1,228]
33	**Eisai** **Tokyo, Japan** [eisai.com]	$4,821	$1,318.0	**Aricept** [797]
34	**Valeant Pharmaceuticals International** **Mississauga, Ontario** [valeant.com]	$4,196	$156.8	**Solodyn** [214]
35	**UCB** **Brussels, Belgium** [ucb.com]	$3,802	$1,137.1	**Keppra** [946]
36	**Chugai Pharmaceutical** **Tokyo, Japan** [chugai-pharm.co.jp]	$3,648	$765.4	**Neutrogin/Granocyte** [234]
37	**Fresenius** **Bad Homburg, Germany** [fresenius-kabi.com]	$3,604	$336.1	**Heparin Sodium** [73]
38	**Mitsubishi Tanabe Pharma** **Osaka, Japan** [mt-pharma.co.jp]	$3,505	$703.8	**H1N1 HA flu vaccine** [152]
39	**Forest Laboratories** **New York, New York** [frx.com]	$3,380	$771.7	**Namenda** [1,537]
40	**Menarini** **Florence, Italy** [menarini.com]	$3,324	N/A	**Lobivon/Nebilet/Nebilox** **[301]**

Sources: Company financial statements, SEC 10k reports, other *Pharm Exec* estimates, and contributions from the EvaluatePharma industry sales surveys.

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cialty products in 2013 while the remaining 72.5% were primary care, OTC, and all other prescription products. This proportion increased from 21.5% in 2008, and was driven by new launches and broader adoption of existing treatments.

The geographies on the X-axis represent the market tiering approach employed by IMS Health. For example, what we call the "Pharmerging" markets are split into three tiers. Tier 1 is China, Tier 2 is India, Russia, and Brazil, and Tier 3 includes the remaining 17 Pharmerging countries that have greater than $25,000 per capita income, expressed on a purchase price parity basis, and have five-year pharmaceutical market aggregate growth of greater than $1 billion. Tier 3 countries include Algeria, Argentina, Colombia, Egypt, Indonesia, Mexico, Nigeria, Pakistan, Poland, Romania, Russian Federation, Saudi Arabia, South Africa, Thailand, Turkey, Venezuela, and Vietnam.

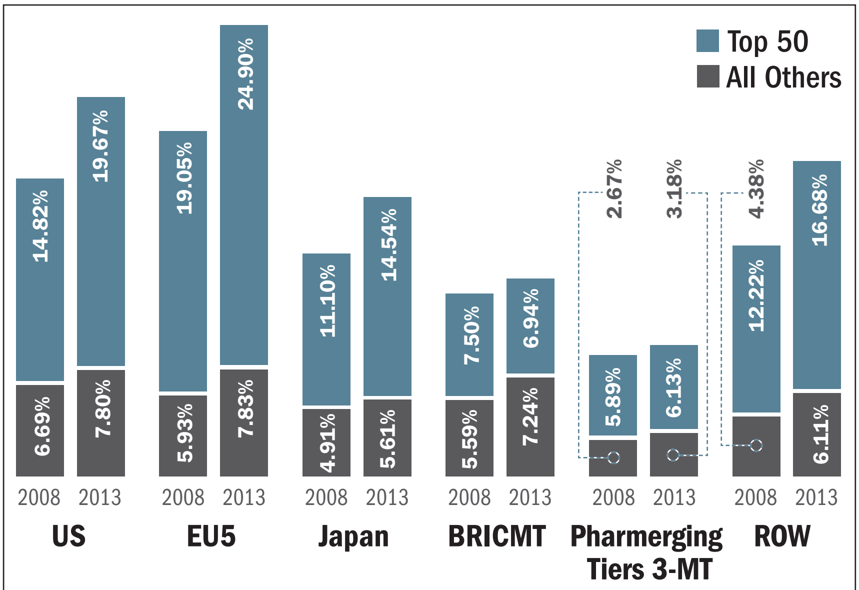

Figure 2: Specialty market percent of total sales by geography and by Pharma 50 (Data: IMS)

For this article, we diverged from the tier model and put Mexico and Turkey with the remaining BRIC countries to reflect the priorities of most pharmaceutical companies, and because these countries are more advanced in their adoption of specialty medicines. In addition, we have included non-retail sales for Brazil

Rank	Company headquarters [website]	2013 Rx Sales (USD in mln)	2013 R&D spend (USD in mln)	2013 Top-selling Drug [USD in mln]
41	**Dainippon Sumitomo Pharma** **Osaka, Japan** [ds-pharma.com]	$3,286	$689.1	**Lunesta** [517]
42	**Grifols** **Barcelona, Spain** [grifols.com]	$3,245	$163.5	**Gamunex IGIV** [1,105]
43	**Hospira** **Lake Forest, Illinois** [hospira.com]	$2,759	$301.7	**Precedex** [288]
44	**Aspen Pharmacare** **Durban, South Africa** [aspenpharma.com]	$2,710	$1.6	**N/A**
45	**Lundbeck** **Copenhagen, Denmark** [lundbeck.com]	$2,431	$511.6	**Cipralex** [1,057]
46	**STADA Arzneimittel** **Bad Vilbel, Germany** [stada.de]	$2,407	$74.2	**Apokyn** [58]
47	**Kyowa Hakko Kirin** **Tokyo, Japan** [kyowa-kirin-pharma.com]	$2,334	$435.7	**Nesp** [559]
48	**Sun Pharmaceutical Industries** **Mumbai, India** [sunpharma.com]	$2,311	$175.3	**Levulan Kerastick Topical** [61]
49	**Purdue Pharma** **Stamford, Connecticut** [purduepharma.com]	$2,217	$456.1	**OxyContin** [1,900]
50	**Ranbaxy Laboratories** **Haryana, India** [ranbaxy.com]	$2,199	$108.0	**Atorvastatin** [210]

Sources: Company financial statements, SEC 10k reports, other *Pharm Exec* estimates, and contributions from the EvaluatePharma industry sales surveys.

and Mexico. All other remaining countries outside the BRIC and the other 17 Pharmerging countries are grouped together as ROW. This group includes the smaller European countries as well as Canada and Australia.

If we look specifically at the companies in the Pharma 50 list, we see that the increase in specialty pharmaceutical sales for US, EU5, and Japan is primarily driven by these top companies in global sales of Rx products (see Figure 2 on page 30). In these markets, there is already a high level of specialty products usage, aided by a well-established infrastructure of specialist facilities and physicians to treat and prescribe these medicines.

There is also a strong increase in their usage likely due to the large investments companies have placed in securing access for specialty medicines in these markets, an increased aging population in these countries, and societal willingness and ability to pay for treatments for complex—often rare— diseases.

The increasing spend on specialty drugs for the Pharmerging markets, including BRICMT and Tier 3, is relatively smaller than the other markets, likely reflecting a higher cost of therapy relative to income, higher levels of cost borne directly by patients, and a relatively younger patient population that carries a greater need for products focused on primary care.

Although companies have been placing significant emphasis on expanding their specialty franchise into these areas, they still face challenges around drug awareness, availability, and affordability. This has slowed the transition to specialty and led to smaller changes in the product mix than in the US, EU5, and Japan. The significant increase in specialty products within ROW also reflects the investments being made by Pharma 50 companies in smaller markets outside of the G7 that have established infrastructure for these types of products (e.g., in Scandinavia, East Europe, Australia, and Canada).

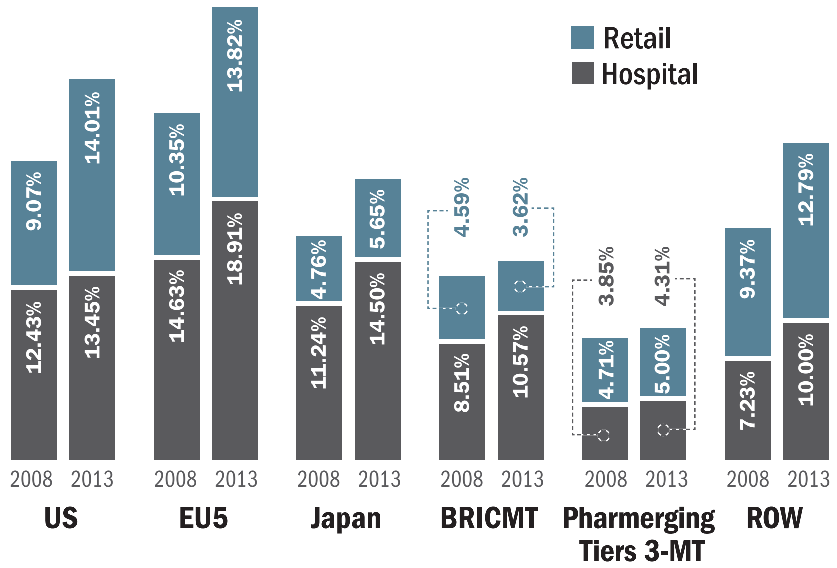

Figure 3: Specialty market percent of total sales by channel (Data: IMS)

Channel growth

The sale of specialty products historically has been through hospital or specialized care settings that can provide the infrastructure required for the administration of biologically complex products. With advances in technology and new classes of drugs, we have seen a trend towards increased sales through the retail sector. Existing products also have been recast in formulations that are more amenable to use in the retail sector. Examples of these innovations include oral administration rather than injection for rheumatoid arthritis, multiple sclerosis, hepatitis C virus, cancer, and a number of orphan-drug diseases; more robust formulations that have less need for special storage requirements, like self-injectable pen devices; or subcutaneous formulations, like Roche's Rituxan, which can be administered by health professionals outside of a hospital or home care setting.

The growth of this retail market is most pronounced in the US (see Figure 3). In 2008, if we break down the 21.5% of specialty from Figure 1, we see that 12.4% of total pharma products in terms of value were specialty products administered through the hospital setting and about 9.1% through the retail setting. By 2013, the hospital setting remained relatively stable at 13% whereas the retail setting increased to 14%.

For the US, this large movement of value through retail channels sets up newer challenges for pharmacy benefit managers who are now saddled with larger payouts for products which they were not necessarily having to reimburse before. This means that specialty products are now on the radar screen for payers, suggesting that increased sensitivity to cost among the reimbursement community will have an as yet unquantifiable impact on future rates of sales growth, in a segment where price has rarely been a contentious issue.

In the EU5, there seems to be a higher proportion of specialty product usage than in the US, and a rise in both hospital and retail sales. This is being driven by adoption of newer therapies under the single-payer structure of these markets, and the proportional increase is amplified by the declines in spending on traditional medicines related to patent expiries, widespread take up of generics, and pricing and reimbursement controls. This comparison to the US may be impacted by the fact that sales are based on the ex-manufacturer invoice price,

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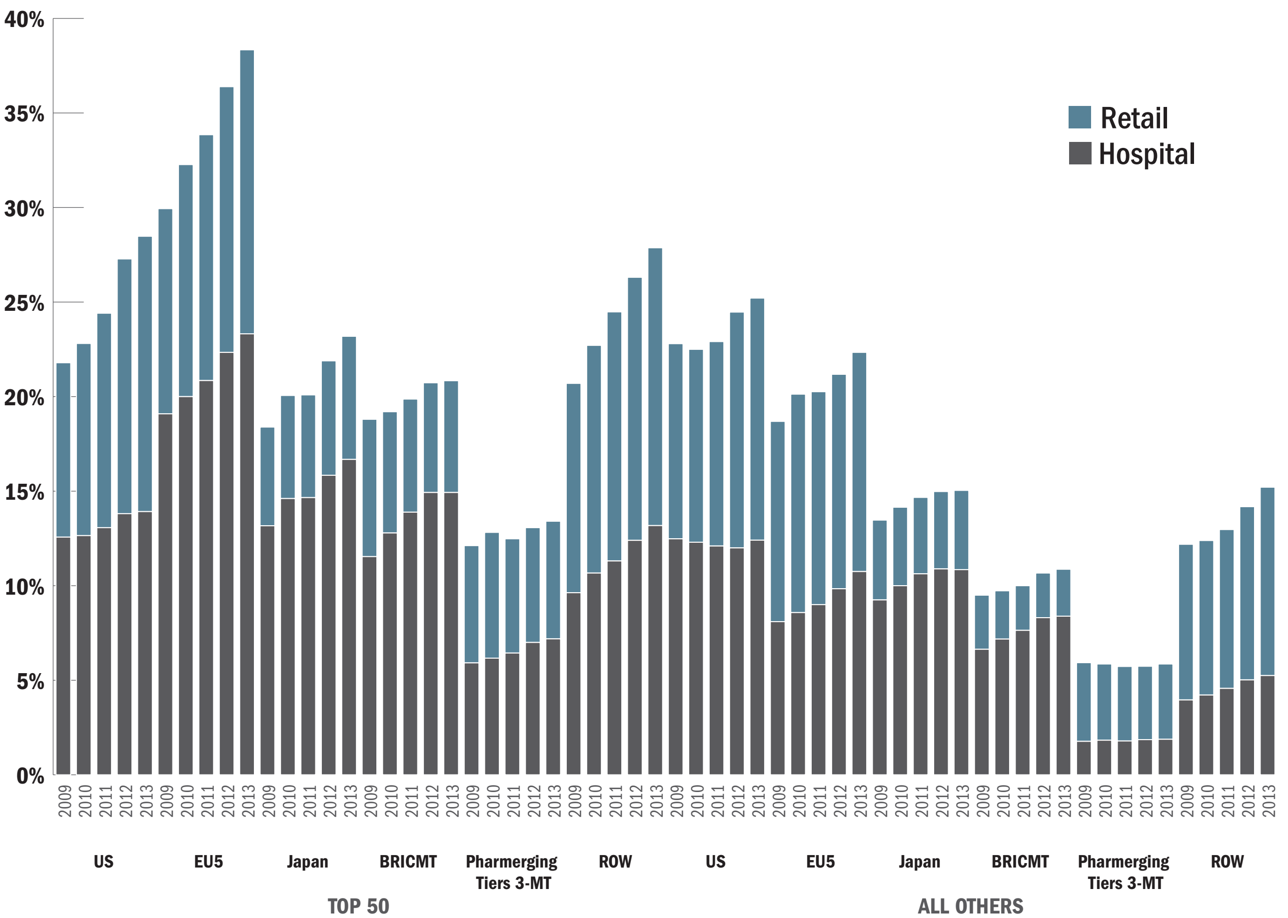

Figure 4: Specialty market percent of total sales by channel and by Pharma 50 past 5 years (Data: IMS)

since discounting is more prevalent in the EU. For Japan, the retail sector has not increased significantly, presenting an opposite picture to the US. This is largely because complex therapies continue to be administered in hospitals.

We would expect that retail sales for specialty in the BRICMT and Tier 3 countries would not increase significantly given the traditional infrastructure difficulties of selling these products outside of the hospital setting; in fact, the share of specialty medicines in retail in BRICMT has actually declined over the past five years.

When looking at the Pharma 50 companies sales in specialty over the past year by channel, we can see the accelerated pace of growth in this market (See Figure 4). In almost every geography, there has been an increasing surge in specialty products driven mostly by the Pharma 50 companies. This effect is most pronounced in the EU5 and US. It is also notable that the EU5 share of sales that is specialty exceeds that of the US, as does the growth rate for top 50 companies, but this comparison may also be impacted by the use of ex-manufacturer invoice price. Also interesting is the increasing gap between Japan and the BRICMT markets in their specialty share of overall spending, as Japan has encouraged greater usage of specialty products, especially in cancer and autoimmune diseases.

Therapeutic area growth

When looking at the top therapeutic areas in the specialty market, we see that the top 7 out of 22 categories usually account for anywhere from 70% to 80% of the value depending on the geography (See Figure 5 on facing page). From 2008-2013, these therapy areas have stayed a relatively stable percent of value within the geographies, except for the US, where they increased from 72% to 76% of total US sales of specialty products.

The leading specialty categories are oncology, autoimmune (including treatments for rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, psoriatic arthritis), HIV, multiple sclerosis, erythropoietins, hematopoietic growth factors (e.g., Neupogen or Neulasta), and hepatitis C treatments. This group of products represents the most commonly used, and often most expensive specialty medicines. They also represent a strong level of recent innovation. For example, the US and EU5 have seen

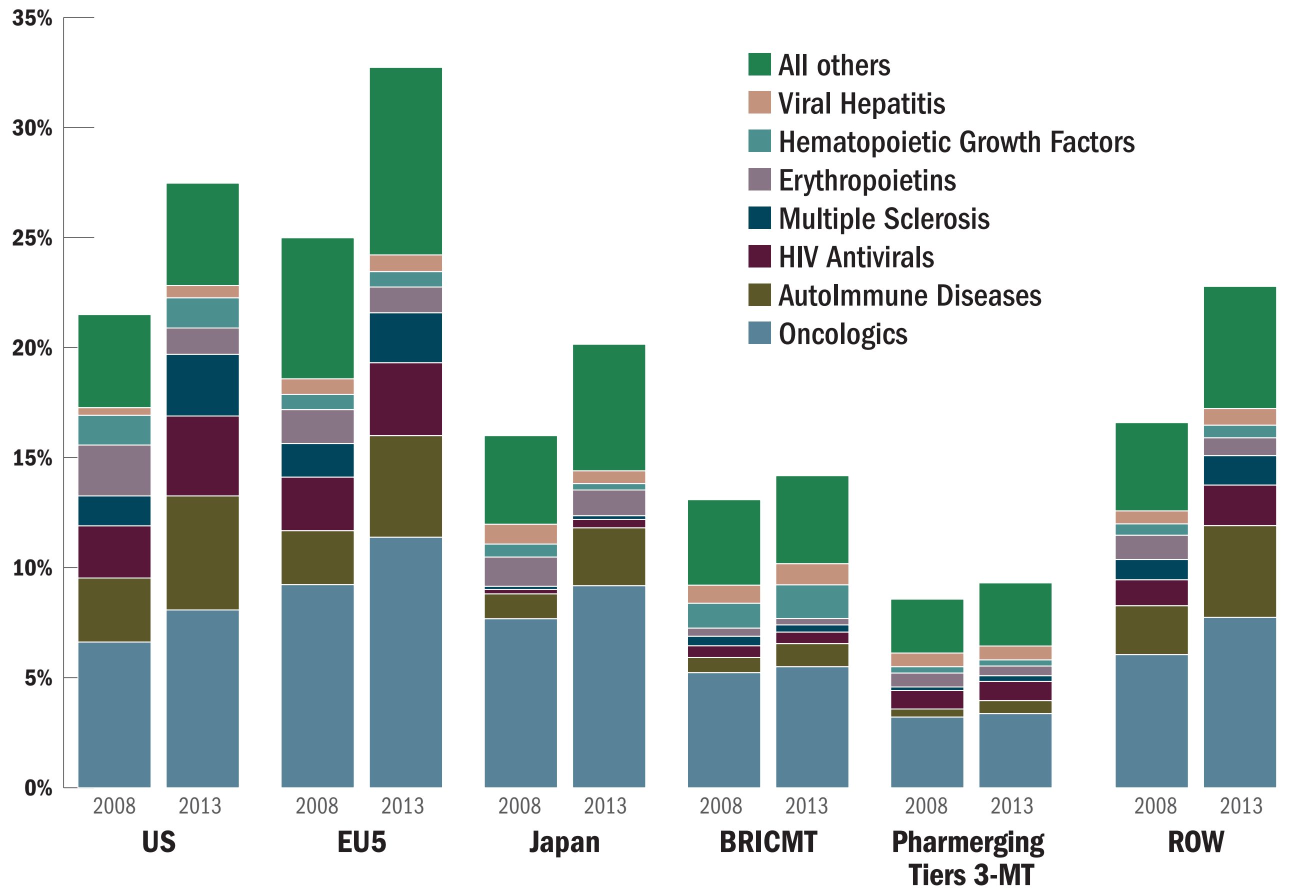

Figure 5: Specialty market percent of total sales by therapeutic area (Data: IMS)

growth in oncology, autoimmune, MS, HIV, and hepatitis C categories, driven by the availability of newer medicines. Of course, the wide range in share of sales for the different therapy areas across geographies highlights differing priorities for medicine spending, along with differing disease prevalence and affordability for high-cost medicines.

Conclusion

The value and volume of specialty products is increasing substantially across all geographies, and this is being driven by the increased development of specialty medicines across a range of diseases. This is a positive indicator that innovation in medicines is continuing to expand the societal and economic benefits from investments in medical progress. It may be that as diseases addressed by these products receive higher recognition by societies and governments, the costs will be more easily shared across geographies and among newer stakeholders.

It is also critical to note that growth of the specialty market can be linked to rising global incomes. For Pharmerging markets, this will continue to be true in the future. The rise and empowerment of the middle class, increased initiatives by pharmaceutical companies in partnering for the expedited delivery of healthcare, and greater private insurance to augment government healthcare funding will all contribute to patients gaining greater access to medicines.

The growing specialty market is a ripe opportunity for companies that are well-established in the field and have considerable marketing presence. A key factor for success of these companies will be to develop innovative solutions that distribute costs of these therapies between manufacturers, payers, and patients in order to achieve broader access in and between geographies and across patient populations. The challenges are many, however, and are not limited to protecting IP in emerging markets or addressing payer resistance to prices for innovative products in the G7 countries. This is especially true when access decisions and pricing negotiations in one country have a trickle-across effect on others. PE

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