The Specialty and Hospital environment

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INTELLIGENCE APPLIED.

Agenda

- **Key Global trends**
  - Continued rise of biologic and specialty medicines
  - The impact of the pipeline
  - Budgetary challenge and budgetary headroom
- The European Specialty and hospital environment
  - Key segments: Biologics, Oncology
- European specialty and hospital futures
  - Cell and gene therapy
- Conclusions

The prescription medicine world is an increasingly specialty focused environment

42% of the late stage pipeline of the top 20 companies focuses on specialty products

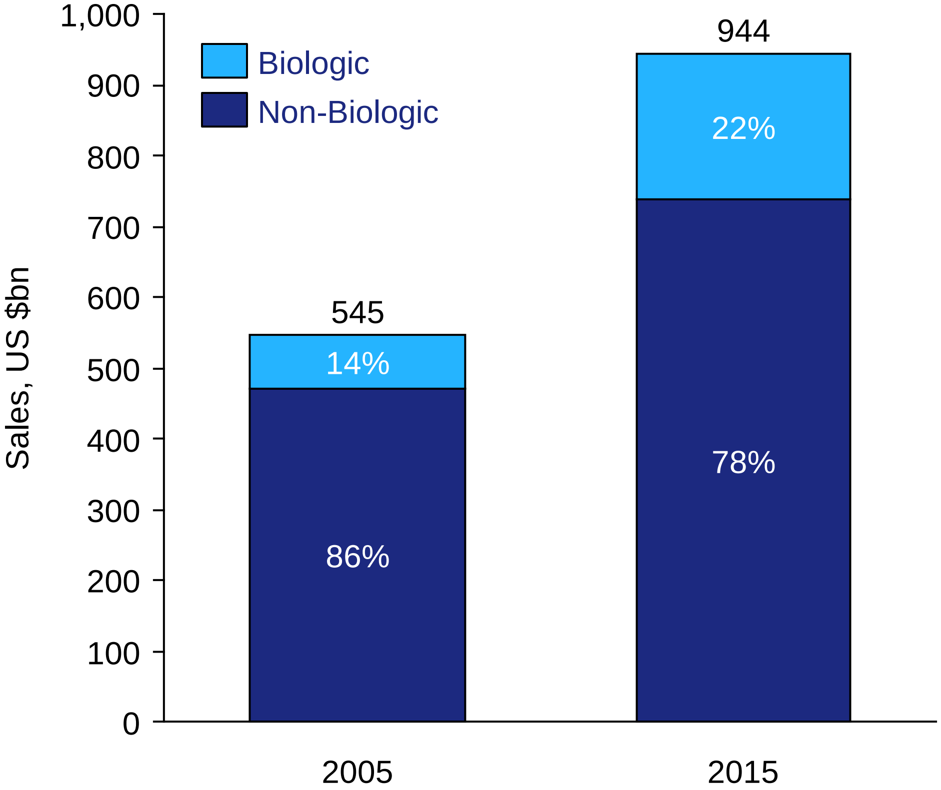
About **60%** growth in developed* markets will be lead by specialty areas

- Concentration of competition
  - Majority specialty
  - Focus on developed markets
- All competing for the same budget
  - Hospitals / Specialists
  - Budgets unlikely to grow in Europe
- Intense focus on the same specialists
  - Oncology
  - Specialty pool and their time does not grow
- Limited pool of patients
  - Determined by biomarkers
  - Orphan drugs

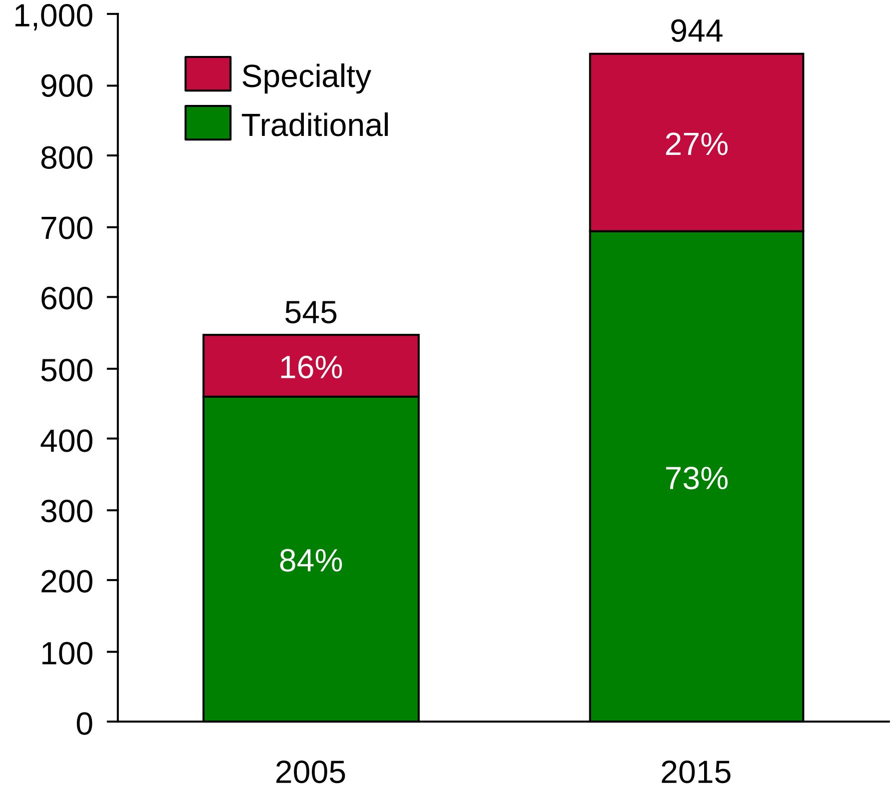
Source: IMS Market Prognosis and LifeCycle, Oct 2014, at ex-manufacturer price levels, not including rebates and discounts. Contains Audited+Unaudited data. Contribution to growth based on LCUS$.
Note: developed includes North America, Europe and Japan

Specialty and biologics drive global growth in Rx value

Global: Biologic sales (billion US$), list price, excludes rebates and discounts



Global: specialty (*) sales (billion US$), list price, excludes rebates and discounts



Source: IMS Health, MIDAS, MAT Q2 2015; (*) IMS definition: Specialty products defined as medicines that treat specific, complex chronic diseases with four or more of the following attributes: Initiated only by a specialist, require special handling and administration; unique distribution; High cost; warrants intensive patient care; might require reimbursement assistance

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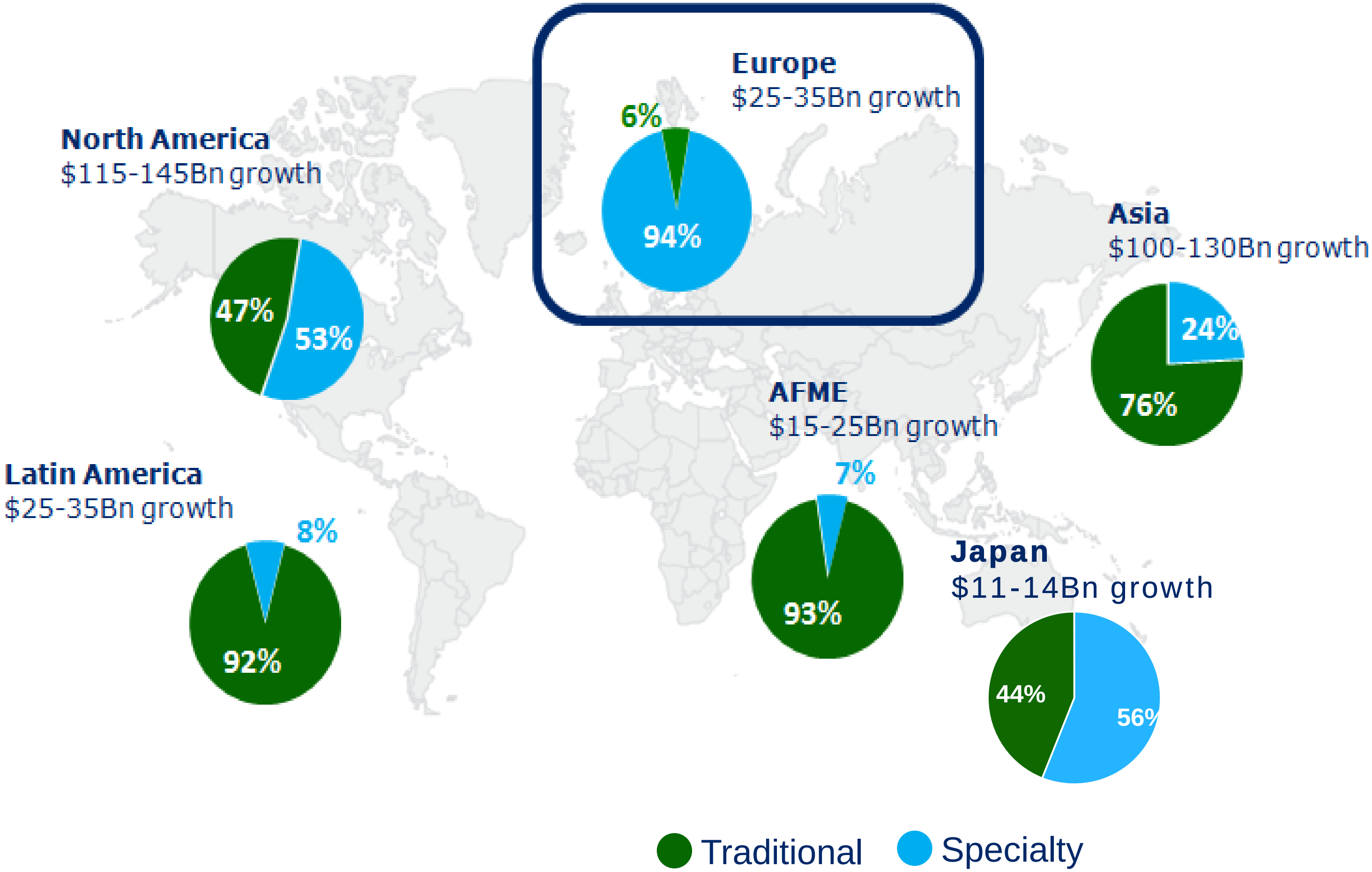
And European Rx value growth is particularly driven by specialty medicines

Share of absolute growth 2013-2018 by region, specialty and traditional



Key Takeaway:

While all developed markets will be driven by majority specialist growth, Europe is an extreme outlier in percentage terms because austerity forces payers to reserve funds for specialty NCEs (US still leads in absolute terms

Adaption from global use of medicine, 2018

Source: IMS Market Prognosis, Oct 2014, at ex-manufacturer price levels, not including rebates and discounts. Contains Audited+Unaudited data. Contribution to growth based on LCUS$. $US used for Argentina and Venezuela due to hyperinflation

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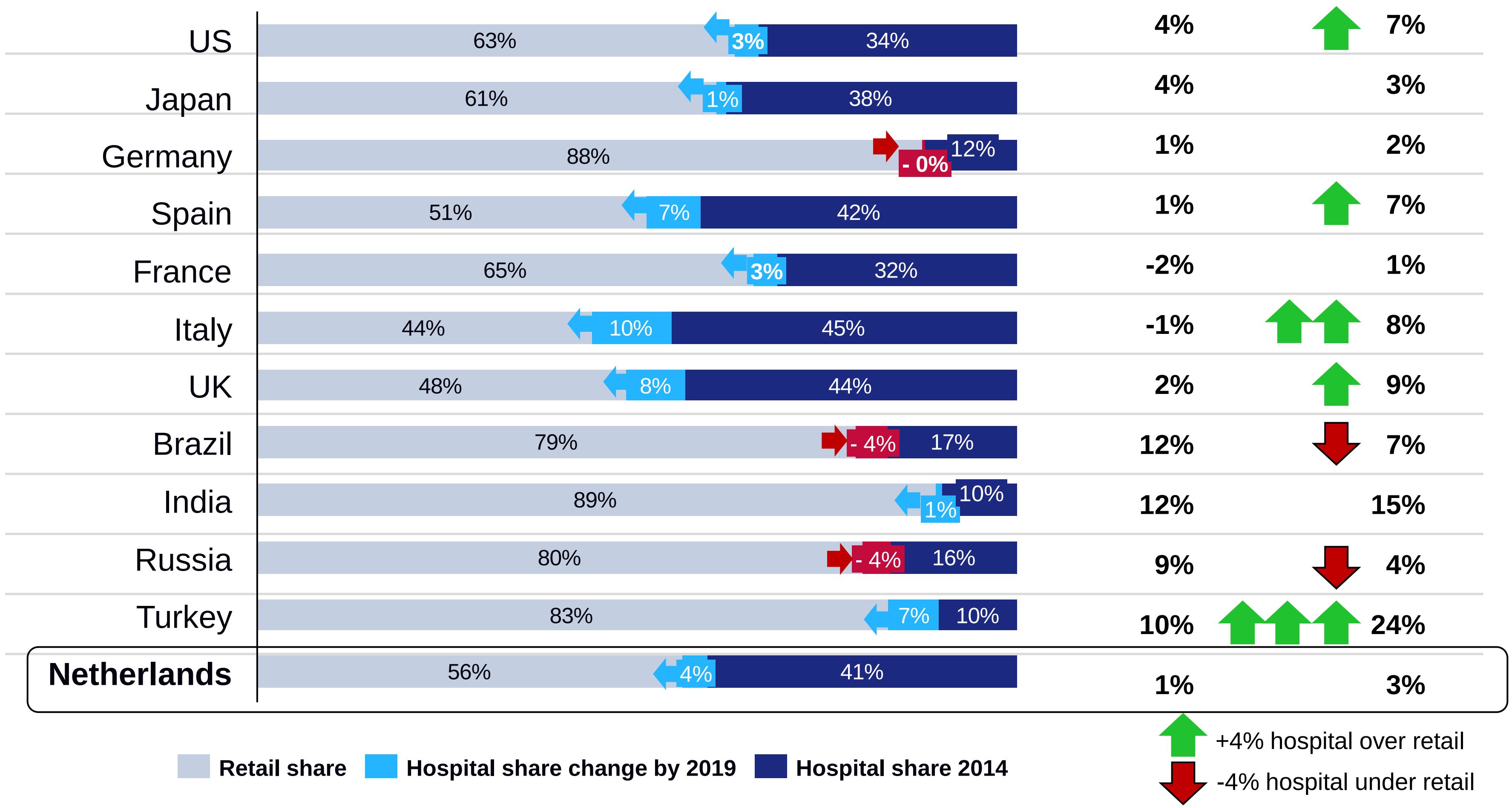
There is a long term shift to hospital in many markets

2014 to 2019 value share of retail vs. hospital (Total pharma markets)

5 year CAGR (2015-19)



Source: IMS Health market prognosis Sept 2015; Audited segments only, Italy DPC excluded; Russia DLO excluded; Brazil & Mexico hospital = non-retail; US retail includes drug and food store only; US hospital includes hospital and clinic sectors only

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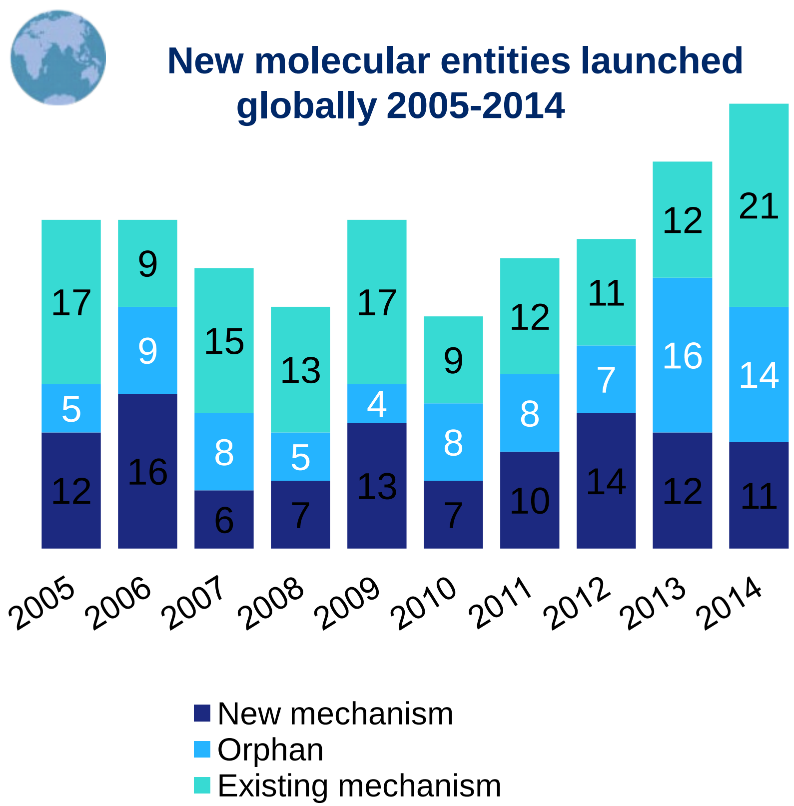
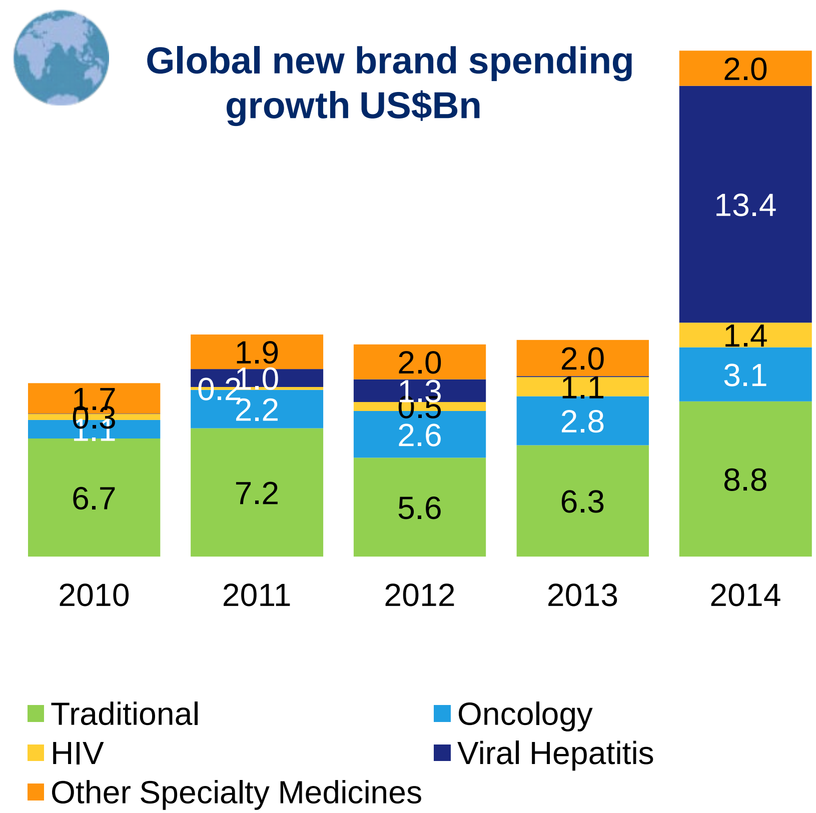
The surge in recent innovation is drawing heavily on healthcare budgets

Significant advances in therapy can have profound effect





Source: IMS Institute for Healthcare Informatics, *The Role of Generic Medicines in Sustaining Healthcare Systems: A European Perspective,* June 2015.

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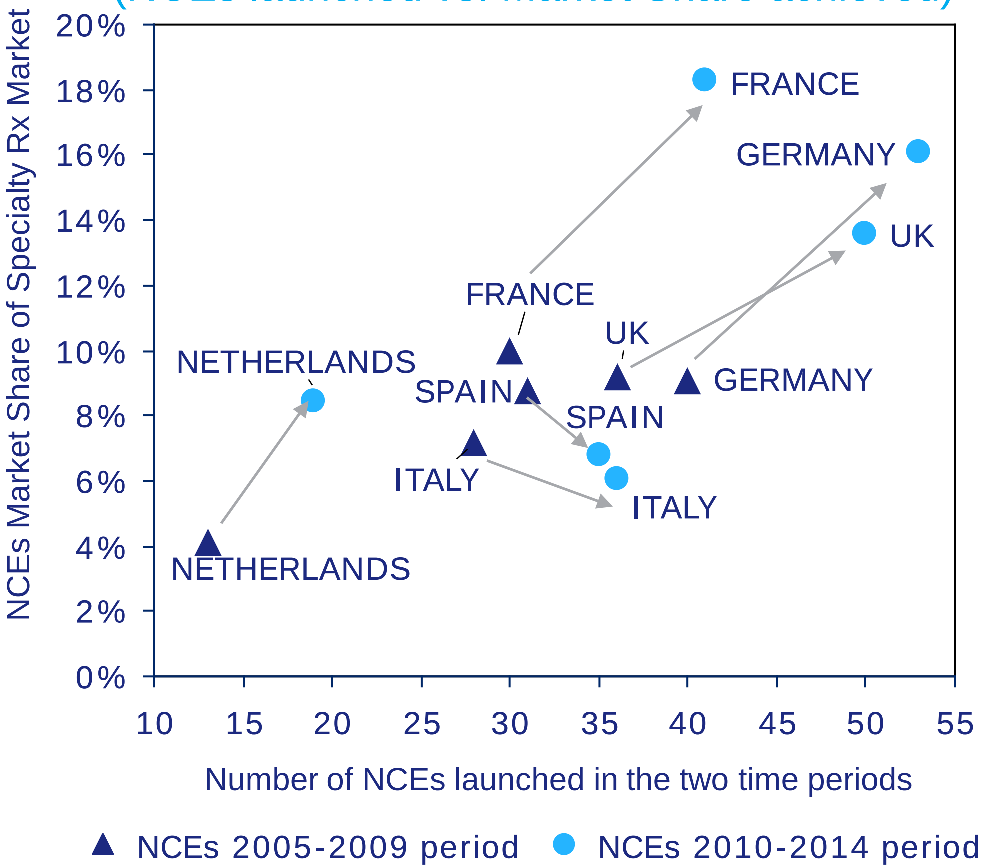
Specialty launch numbers rise, as does specialty share, except Italy/Spain

Country Innovation profile – Specialty (generally hospital, often biologic/injectable, serious diseases, eg autoimmune, cancer)
(NCEs launched vs. Market Share achieved)



The specialty market of NCE across the EU5 is evolving

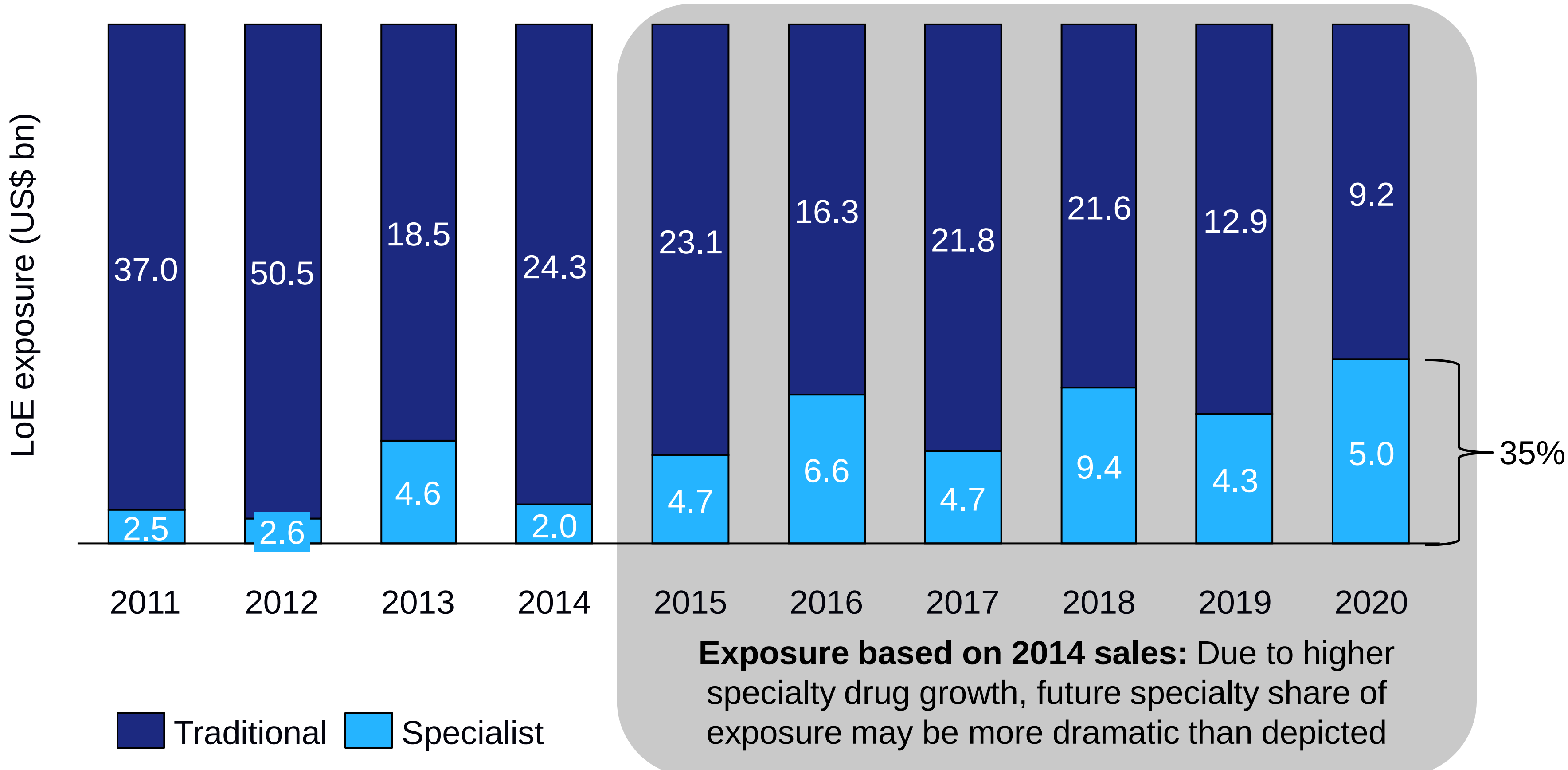
- The number of NCE launches between 2005-2009 versus 2010-2014 has increased in every country (average of NCE launches has passed from 33 to 43)
- NCE launches increased significantly in France, Germany and UK.
- NCE launches take also increased over time in the EU5 with the exception of Italy and Spain, which also suffer from share per NCE deterioration
- Germany is the leading country for specialty NCE launches whereas France leads the market in take with 18.3%. France also leads in terms of share per NCE

Source: IMS Health, MIDAS, Year 2014, Rx only. IMS analysis

Specialty generics will be a larger part of future small molecule cost saving opportunities

The opportunities for new primary care generics remain, but new specialty small molecule generics will become an increasingly large share of opportunity.

Small molecule LoE exposure 2011-2020

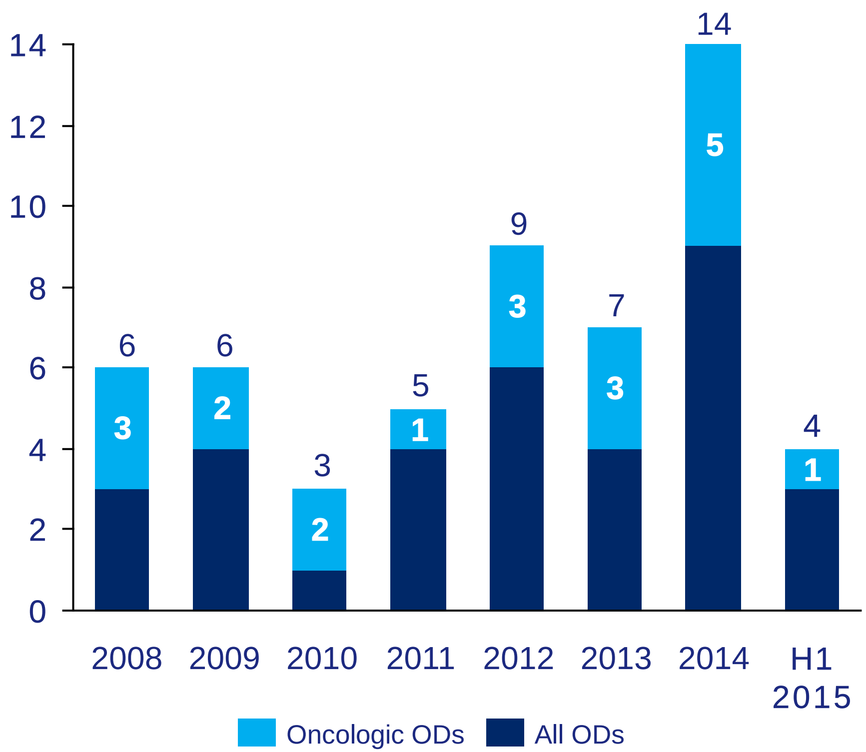


Source: IMS MIDAS MAT Q4 2014; Market seg countries only; small molecules only; LoE exposure given as previous year sales in US$, for 2015-2020, 2014 sales have been used

Orphan drug (OD) approvals surge in Europe, making ~1/3 of all NCE's launched in 2014

Vigorous patient advocacy, medical breakthroughs, legislative incentives, venture capital investment and industry collaboration, are dramatically changing the landscape of rare disease research

Number of ODs in Europe with European market authorization (MA) and orphan designation



- **Oncology** represents the largest category of products, including blockbusters such as Revlimid and many other high earning products such as Tasigna, Sprycel and Nexavar
- ~15% are **Alimentary Tract and Metabolism** products, which include many of the most expensive ODs such as the enzyme replacement therapies
- **Cystic Fibrosis** treatments account for 6% of all approved ODs (Cayston, TOBI Podhaler, Bronchitol, Kalydeco)

Source: European Medicines Agency July 2015

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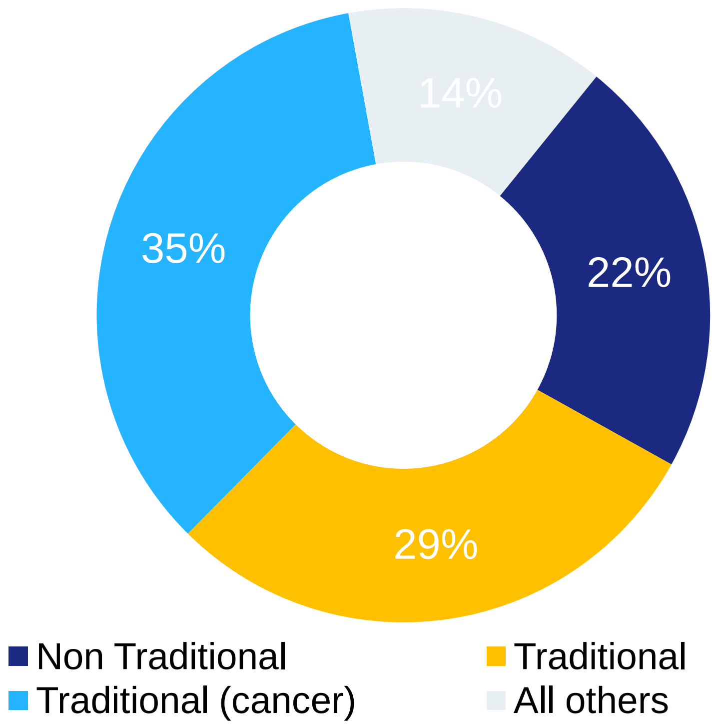
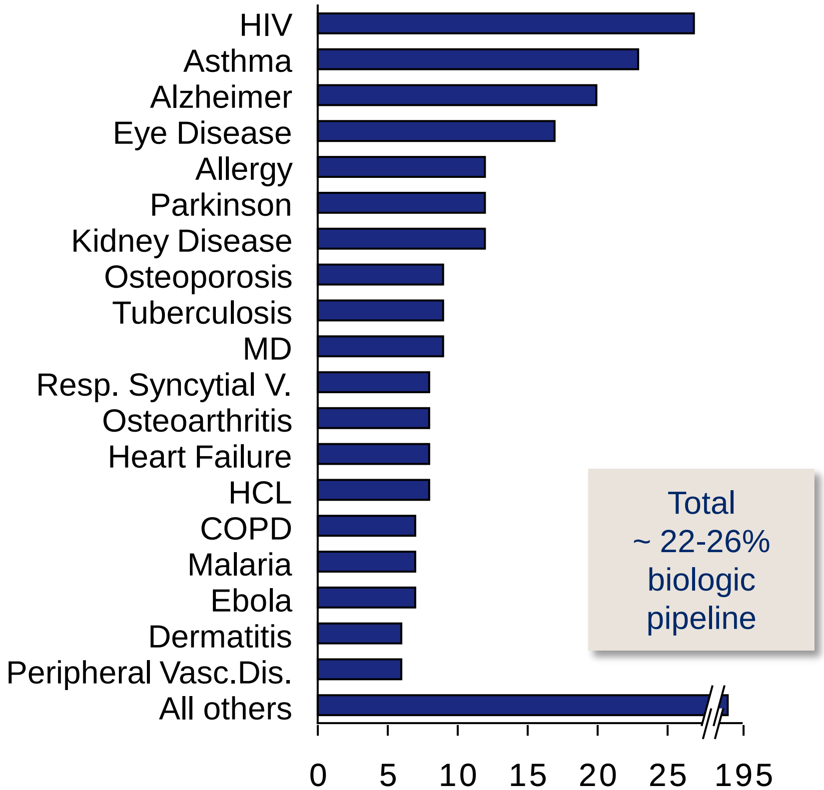
A growing share of biologics in development will be in areas largely new to biologics

Indications in development*
(Traditional vs. non traditional biologic area)



(Indications with 3 or less compounds in development, non cancer)

Top Indications in non traditional biologic areas



HCL: Hypercholesterolemia
MD: Muscular Dystrophy

Source: IMS Health R&D cycle Jan 2015. The number of indications in the Pipeline is defined as the number of compounds currently at a life cycle stage between Clinical and Registration. Indications based on highest phase for associated molecule.

Biosimilars continue to make steady progress...

ROW

Market trends

Omnitrope sole subsidised somatropin from Jan 2015 in NZ

Granix close to 20% penetration USA

Novartis launches Zarxio in US at 15-percent discount to Neupogen

Regulatory

FDA approves first biosimilar Zarxio

Australia to recommend pharmacy-level substitution of biosimilars

Enbrel BS approval south Korea

2015

2015 Jan Mar Jun Jul Aug Sep Dec

Europe

Market trends

Hospira launches first BS mAbs Inflectra in major European markets

Biosimilar 15% share of Spanish infliximab market (June only)

Biosimilar 90% share of Danish infliximab market (July only)

Celltrion files rituximab with EMA

Regulatory

Samsung submits Enbrel Biosimilar application to EMA

Samsung submits infliximab biosimilar to EMA (March)

Finland stands behind interchangeability of biosimilars

Lilly/BI launch Lantus BS in UK (15% list price discount)

Source: Secondary research. List not exhaustive. (*) at ex-manufacturer price levels, not including rebates and discounts.

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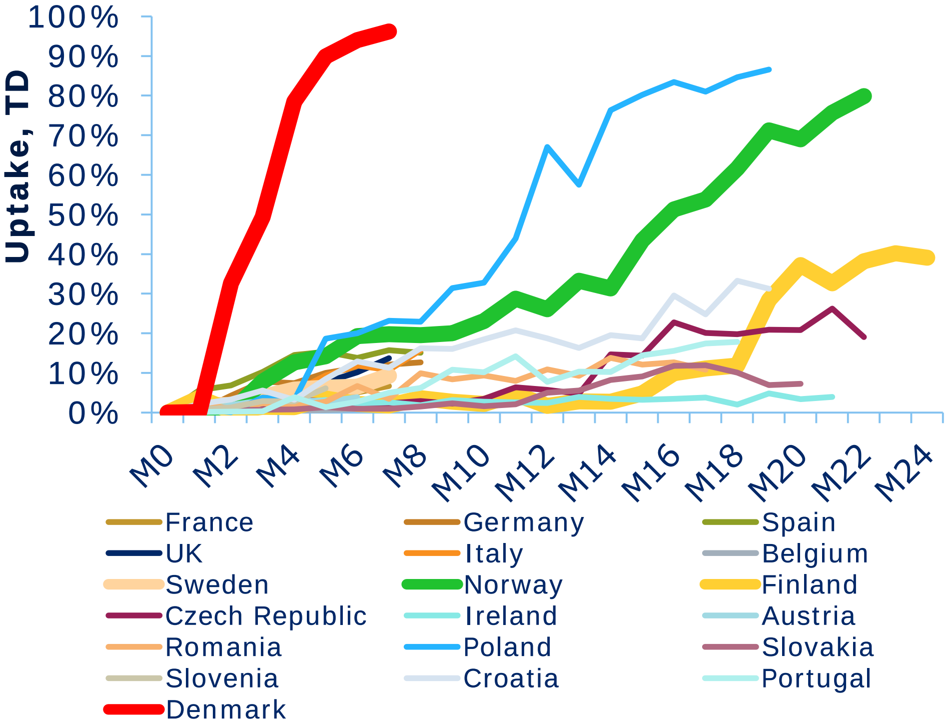
Infliximab biosimilar has shown strong uptake in tender markets, more moderate in others

Nordic countries top for uptake (and published discounts), EU5 slow growth

Infliximab Monthly uptake
- European markets



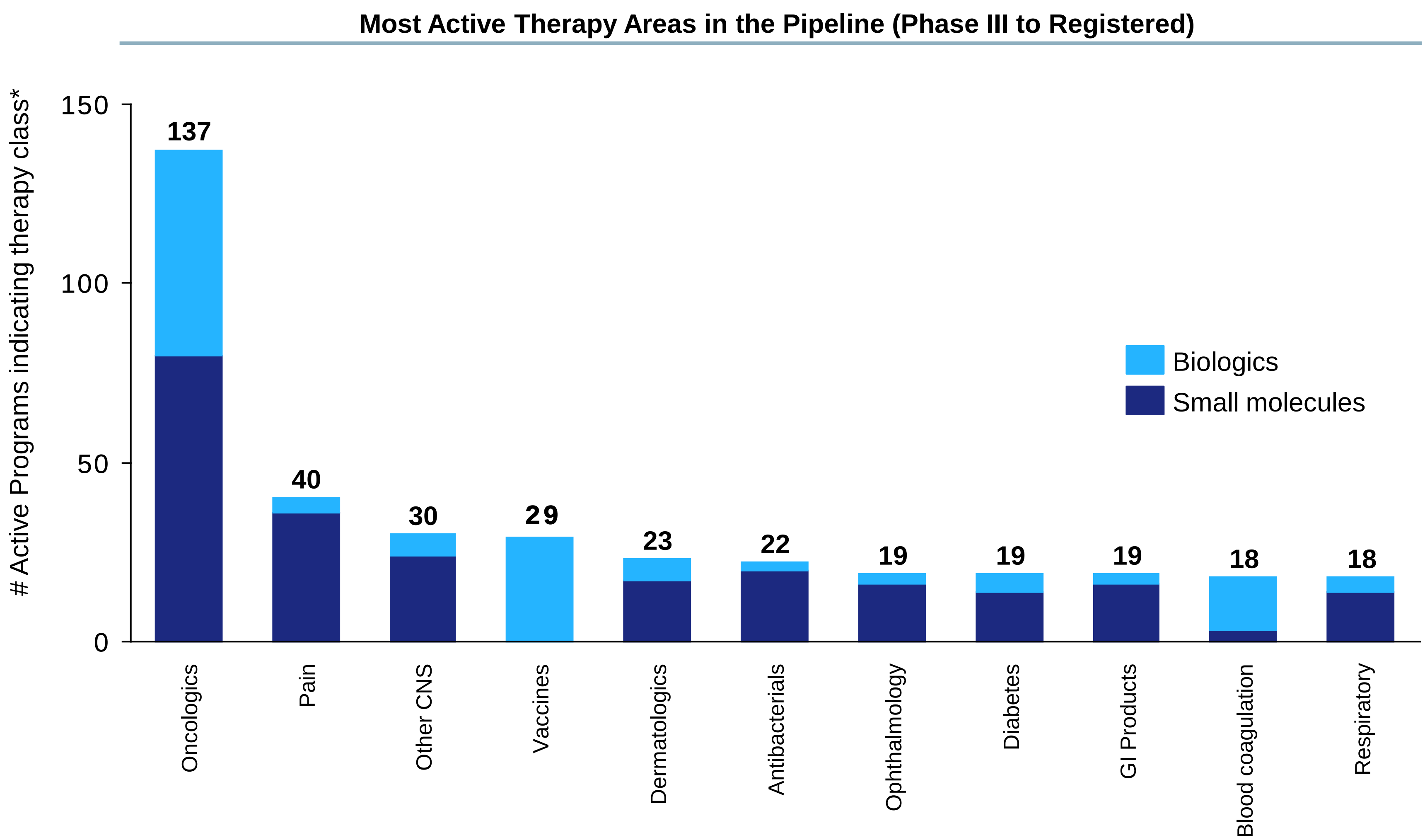
Infliximab September uptake*

Country	September volume penetration of biosimilar
Denmark	96%
Poland	87%
Norway	80%
Finland	39%
Croatia	31%
Hungary	21%
Czech R.	19%
Portugal	18%
Italy	16%
Spain	15%
UK	14%
Germany	13%
Romania	11%
Sweden	9%
Slovakia	7%
France	7%
Ireland	4%

*Positive initial data from Nor-switch study for biosimilar infliximab announced at 2015 EULAR. Physicians expect these types of studies to encourage real-world switching, with nearly a third of rheumatologists expecting switch data to drive 'significant' usage of biosimilars in existing TNF-inhibitor patients***

Source: IMS MIDAS monthly Sep 2015. Denmark data from MIDAS Monthly Restricted database. Penetration calculated in treatment days (TD); *Bulgaria, Latvia excluded because only biosimilar manufacturers present in market; **FirstWord physician poll, June 2015

In terms of innovation oncology continues to dominate the late stage pipeline



* Some programs in pipeline are multi-indicational and are assigned to multiple ATC classes.
Source: IMS R&D Focus, Nov 2014

Immuno oncology will disrupt budget management

Innovation

Immunotherapy/ Targeted Agents

- Emergence of PD-1s and PD-L1s
- Durable treatment responses
- Personalized medicine and genomics
- Defining treatments based on mutations / pathways over tumor types

Combination Regimens

- Synergistic effects of combining targeted therapies and/or chemotherapies
- Exploration of previously thought “failed” or “mediocre” agents
- Blocking and / or stimulating multiple pathways

Sustainable access and value

Rationing

- Maximum value for $/spent
- Limited access to high cost novel interventions in oncology
- Regional availability
- Delisting of onco drugs from reimbursement list

Payment by Use

- Payment by Use allows multiple (net) price points to be set for one product
- Identification of use that is not consistent with the population
- Opens the door to a variety of innovative schemes

Value in Cancer Care

- What constitutes good “value” in oncology
- Adapting physician behaviors
- Innovative payment models
- Individual vs. Societal value
- Cost-benefit analyses and drug scorecards

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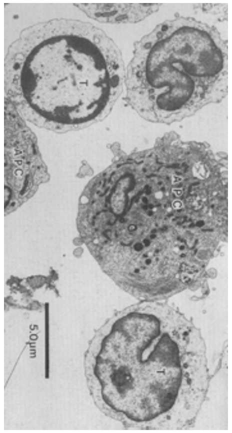
Cell and gene therapy have the potential to revolutionise hospital treatments and outcomes

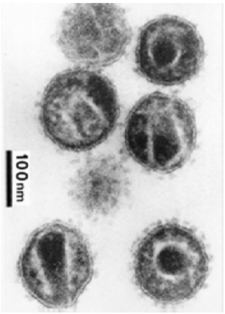
Cell therapies

Treatments in which intact, living human cells are injected in to a patient with the intention of therapeutic benefit



Gene therapies

Treatments which introduce functional genes in to cells in place of missing or defective ones in order to correct genetic disorders. The most common way this is done by utilising a viral vector

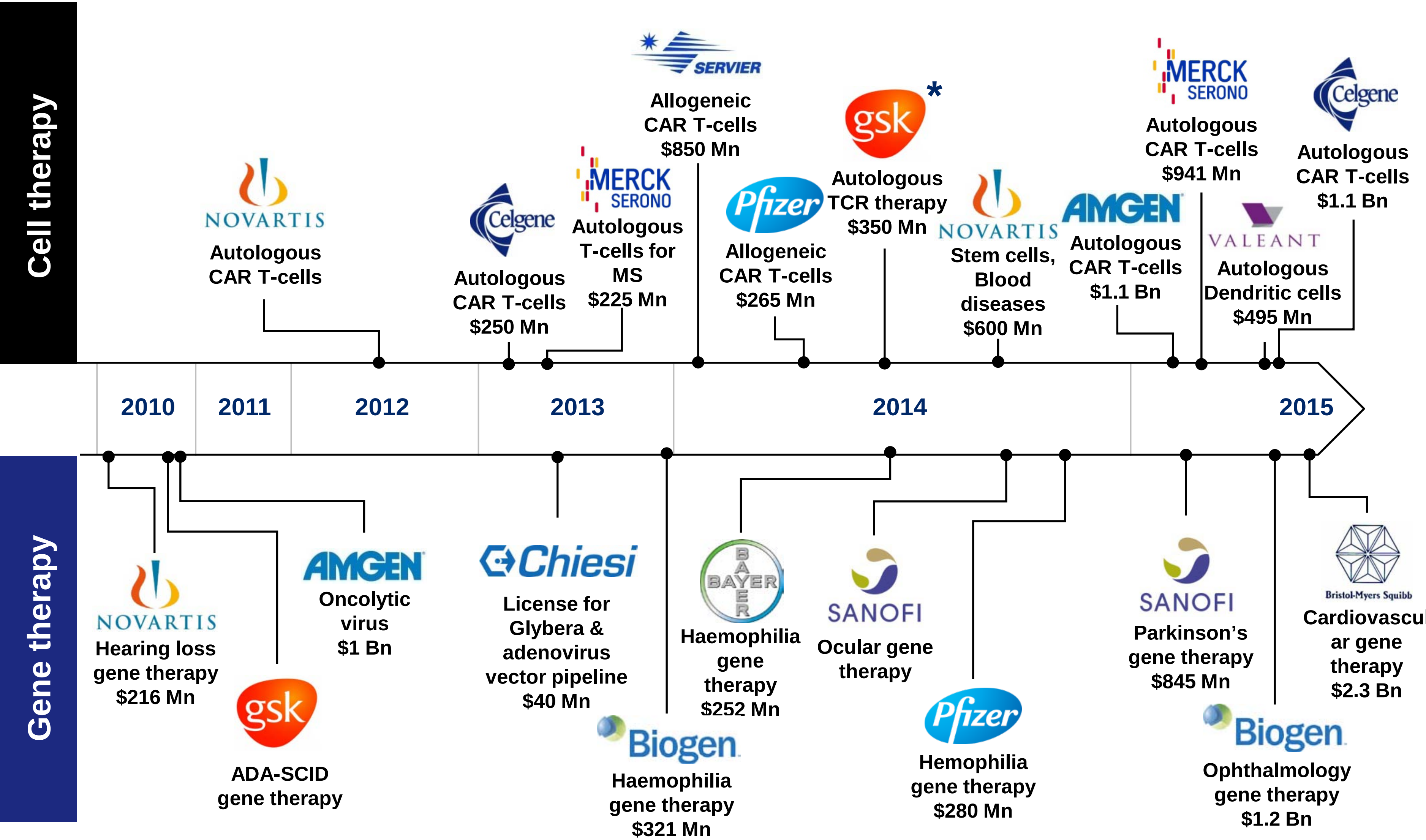


Unique qualities

- **Highly specific**
- **Personalised**
- **Potentially curative**
- **Scientifically designed**

- **Complex**
- **Novel – untested**
- **Immunogenic**
- **Oncogenic**

Major companies are now actively engaged



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Source: IMS Health Thought Leadership analysis March 2015; IMS Health Pharma Deals; deal values given are including milestones; * Novartis has opt-in rights for GSK's current and future oncology R&D pipeline;

Transition to specialty will see a paradigm shift in companies' commercial models

We see a transition from scale, reach and prescriber focus, to precision, selective geographies and patient-centricity joining prescriber segmentation

Past Paradigm

Competitive advantage driven by

Promotional *Scale, bandwidth*

Geographic *Reach*

Effective prescriber segmentation – *targeting of prescribers*

Future Paradigm

Competitive advantage driven by

Promotional *Precision, broad bandwidth*

Geographic *Focus – Selective approach*

That, plus effective patient segmentation – *supporting healthcare systems in identification of patients*

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Six key challenges for the next five years

Geography	•Specialty products drive developed market growth, but not pharmerging-specialty competition geographic ally concentrated •Growth gap between pharmerging and developed narrower now than in a decade
Portfolio	•Specialty is driving protected value growth and global top 20 are key drivers •Global top 20 will be overwhelmingly specialist focused by 2020 •Biologic products enter traditionally non biologic therapy areas
Payer	•European payer environment hardening even more because overall budgets are flat but increasing demands on specialist/hospital budget •Choices will be made between drugs and increasingly between therapy areas
Partnership	•Majority of IP now originated from sub-top 20 companies, even if they don't commercialise •As new launches become ever more specialist, smaller companies can increasingly launch their own products
Biosimilars	•After almost a decade of biosimilar experience, penetration in Europe remains highly diverse •First mAb biosimilar is now rolling out across major Europe; potential to squeeze original biologics in autoimmune
New competitors	•Gilead, Actavis, Biogen, Celgene, Shire all companies that are or could be top 20 with a non traditional approach to pharma •What can be learned from their generally lean structures and rapid decision-making?

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