Global Industrial Perspective of Novel Biologicals Development

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What Kind of Biotechnological Therapeutic Products Have Been Licensed/Approved? From Which Expression Systems? For What Therapeutic Areas? Who Developed These Products?

Biopharmaceutical Industry 2006 – Marketed Products

- 101 therapeutic biopharmaceutical products are approved/licensed in the US (PhRMA 2006)
  - 3 cellular therapies
  - 39 rDNA products expressed in microbes
  - 33 rDNA products expressed in cell culture
  - 26 monoclonal antibody products expressed in cell culture
- US sales expected to exceed $ 11 billion and to represent about 48% of worldwide sales for 2006

Licensed/Approved J&J/BIO Products

REMICADE®
INFLIXIMAB

Pr EPREX*
epoetin alfa
To Live Life

REOPRO®
abciximab

NATRECOR®
nesiritide

Some Recent Worldwide Biopharmaceutical Approvals

- Exubera (Pfizer) – inhaled rDNA insulin
- Omnitrope (Sandoz) – hGH (approved as biosimilar in EU; as new drug under 505 (b)(2) in US)
- Valtropin (BioPartners) - hGH (approved as biosimilar in EU)
- Myozyme (Genzyme) – alglucosidase alfa
- Elaprase (Shire) – idursulfase

Some Recent Worldwide Biopharmaceutical Approvals

- Lucentis (Genentech) – ranibizumab[anti-integrin]
- Tysabri (Biogen Idec) – natalizumab[anti-integrin] (reintroduction)
- Vectibix (Amgen) – panitumumab [anti-EGF-R]
- Actemra (Chugai) – tocilizumab [anti-IL6-R]
- Orencia (BMS) – abatacept [CTLA4-Ig]

Who Developed the Current Approved Biopharmaceutical Products ?

- 93 of 98 therapeutic protein products have known development history
  - 39 were developed by largest 7 biotech firms
  - 11 were developed by small biotech firms without help
  - 43 were developed by large pharma firms
    - 22 of the 43 came from 3 firms, each with 50+ years of natural protein product experience (Lilly, Novo Nordisk, Serono) who largely replaced their natural protein products with rDNA derived ones
- Large biotech firms are arguably the strongest competitors, with many large pharma firms also active

What Therapeutic Areas Have Approved Biotechnology Products in 2006?

- 25 years ago, natural biological products were concentrated in the therapeutic areas of endocrinology, anti-infectives, and coagulation
  - It is therefore, not surprising that these therapeutic areas have the most branded protein products (53 of 98)
  - However, correcting for multiple brands for a few targets, only 21 therapeutic targets of 56 are in these therapeutic areas
- The march of science and medicine has also enabled biotechnology products for therapeutic targets in oncology and immunology/inflammation
  - 23 of 56 therapeutic targets are in these two new fields

What Therapeutic Areas Have Approved Biotechnology Products in 2006?

Therapeutic Area	Brands	Products	Targets	3 or More Brands on Same Therapeutic Target
Oncology	21	21	18	Anti-CD20 Mabs (3)
Immunology/Inflammation	9	9	5	Anti-TNFalpha (3)
Endocrinology	27	19	10	hGH (8), insulin (9)
Coagulation	12	10	6	Thrombolytics (4), FVIII (4)
Anti-infective	11	11	5	IFNalpha (5), IFNbeta (3)
Other	12	12	12	

Biopharmaceutical Industry 2004 - Products in Development

- 324 biopharmaceuticals in nonclinical or clinical development
- Of these, 121 are novel therapeutics in the clinic
  - 11 cellular therapies (1 in late development)
  - 28 are microbially-expressed rDNA (11 late)
  - 21 are mammalian-expressed rDNA (8 late)
  - 61 are monoclonal antibodies (11 late)
- Over half the therapeutic molecules presently in the clinic are monoclonal antibodies, and two – thirds are cell culture products

Biopharmaceutical Industry 2006 - Products in Development

- 418 biopharmaceuticals in nonclinical or clinical development
- Of these, 216 (+95 more than 2004) are novel therapeutic biological products in the clinic
  - 23 cellular therapies (1 in late development)
  - 30 are microbially-expressed rDNA (5 late)
  - 33 are mammalian-expressed rDNA (7 late)
  - 130 (+69 more) are monoclonal antibodies (9 late)
- Two – thirds of the therapeutic biological molecules presently in the clinic are monoclonal antibodies, and 85% are cell culture products

Who Was Developing Therapeutic Biopharmaceutical Products in 2004 ?

- Large biotech firms are developing 35 entities (5 microbial, 7 cell culture, 23 Mab)
- Small biotech firms are developing 49 entities (15 microbial, 8 cell culture, 26 Mab) – but if promising, many are likely to be inlicensed by large biotech or large pharma for PhIII
- Large pharma are developing 18 entities (9 microbial, 4 cell culture, 5 Mab)
- US National Cancer Institute is developing 8 entities (mostly Mabs)

Who Was Developing Therapeutic Biopharmaceutical Products in 2006 ?

- Large biotech firms are developing 35 entities (4 microbial, 5 cell culture, 26 Mab)
- Small biotech firms are developing 123 entities (19 microbial, 23 cell culture, 81 Mab) – but if promising, many are likely to be inlicensed by large biotech or large pharma for PhIII
- Large pharma are developing 18 entities (3 microbial, 4 cell culture, 21 Mab)
- US National Cancer Institute is developing 8 entities (mostly Mabs)

Who Was Developing Therapeutic Biopharmaceutical Products in 2006 ?

- 95 more biotech products are in development in 2006 compared to 2004 (216 vs 121)
- Biggest increases are in Mabs (130 vs 61)
  - Most of the increase in activity is in small biotech companies (81 vs 26)
  - Some increase in big pharma (21 vs 5)
  - Little change in big biotech firms (26 vs 23)
- Most of the increase is in early stage development which is within the capability of small firms
- Late stage products decreased from 31 to 22

What Therapeutic Areas Have Products in Clinical Development Aimed at Novel Targets?

- Oncology – 50 in 2004, 67 in 2006
- Immunology/Inflammation – 25 in 2004, 35 in 2006
- Endocrinology – 2 in 2004, 17 in 2006
- Coagulation – 1 in 2004, 2 in 2006
- Anti- infective – 2 in 2004, 17 in 2006
- Other – 14 in 2004, 35 in 2006
- Clearly, oncology and immunology/inflammation are likely to see most of the new product growth in the next decade!

Possible Conclusions from the Last Two PhRMA Biotechnology Surveys

- The biopharmaceutical industry is still growing
  - About 5 new products per year are approved in the US
  - Substantial increase in products in early development
  - Substantial shift of emphasis toward Mabs
  - Substantial shift of emphasis toward oncology and immunology applications
- Recent trends toward developing Mabs in oncology and immunology likely will continue for the next decade (assuming that successful products continue to be found in clinical studies)

Other Important Trends in Biotechnology

- Globalization of biotechnology
  - Widespread adoption of technology to discover, develop, and manufacture in developing world
- Pressure to control costs of health care
  - Increasing interest in biosimilar products by governments and other payors
  - Continued interest in reducing development & manufacturing costs by developers
  - Interest in reducing time of development

What Does Global Development Need to Continue Biotech Product Growth?

- Global technical requirements for product development and market authorization
  - ICH guidances need to become the ceiling, not the floor
  - No need for regional guidances with extra requirements
- Global technical requirements for process changes and their regulatory acceptance
  - Consider for potential future ICH topic
- Scientific improvements which reduce the time and cost of clinical trials

Summary

- Biotechnology continues to provide tools for development of exciting new therapeutic products which may benefit millions of additional patients
- Regulatory and industrial scientists must continue to collaborate to find faster ways to develop therapeutic biotechnology products, and more efficient ways to make global process improvements after approval