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Antibodies: Evolution & Revolution
David Fuller, Chief Medical Officer
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The Current Global Climate



- Increasing Regulation
- Increasing Hurdles
 - What is a significant benefit? And at what price?
- Increasing Costs
 - Decreasing big pharma productivity
- Increasing Gap: Innovation vs. Generics

- Increasing and healthy antibody market!
 - An antibody revolution

A brief history of mAbs



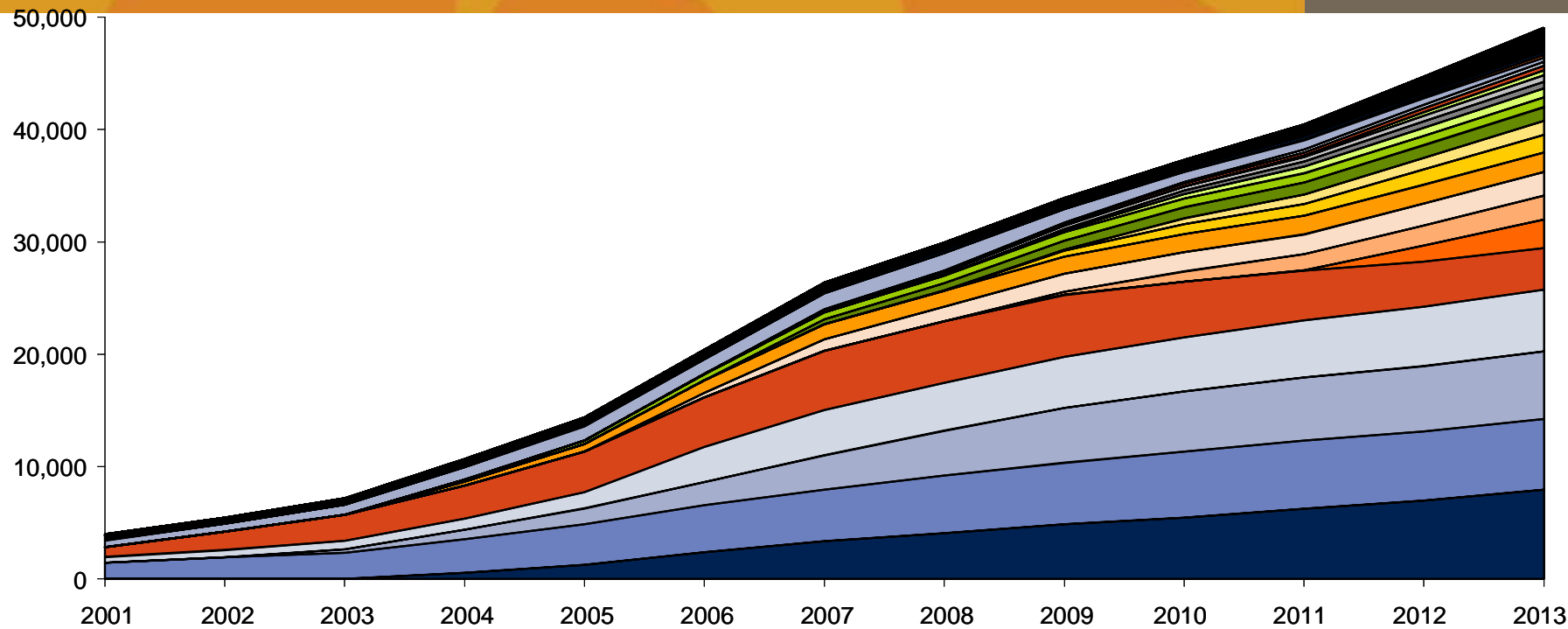
1974 - Kohler & Milstein publish

1986 – First antibody product: OKT3

2000 – mAb sales > \$1 billion

2007 – mAb sales > \$ 25 billion

mAbs – Today & Tomorrow (Sales)



- | | | | | | |
|---------------|--------------|--------------|----------------------|---------------------|-------------------------|
| ■ Avastin | ■ Rituxan | ■ Humira | ■ Herceptin | ■ Remicade | ■ bapineuzumab |
| ■ denosumab | ■ Lucentis | ■ Erbitux | ■ Numax | ■ golimumab | ■ Tysabri |
| ■ Xolair | ■ Actemra | ■ Cimzia | ■ Vectibix | ■ ocrelizumab | ■ Soliris |
| ■ ustekinumab | ■ Synagis | ■ pertuzumab | ■ Raptiva | ■ ReoPro | ■ mepolizumab |
| ■ lumiliximab | ■ ipilimumab | ■ Humax CD20 | ■ galiximab | ■ Humax CD20 (I&I) | ■ MAB Campath |
| ■ Aurograb | ■ Mylotarg | ■ Simulect | ■ canakinumab | ■ MAB Campath (CNS) | ■ Rencarex |
| ■ Removab | ■ Mycograb | ■ teplizumab | ■ epratuzumab | ■ Zevalin | ■ Humax CD4 |
| ■ ABT-874 | ■ Bexxar | ■ Zenapax | ■ Humax-EGFR | ■ belimumab | ■ inotuzumab ozogamicin |
| ■ Theraloc | ■ reslizumab | ■ abagovomab | ■ Proxinium/Vicinium | | |

Reasons for continued mAb Success

- ✓ Novel target space
- ✓ Unmet need
- ✓ Specificity
- ✓ Potent
- ✓ “Natural”
- ✓ Flexibility - formats
- ✓ Production improvements
- ✓ Biogeneric protection
- ✓ Changing patient lives
 - e.g Rheumatoid & Crohn’s

Growth drivers

Level of Unmet Need

Access to Novel ‘Target Space’

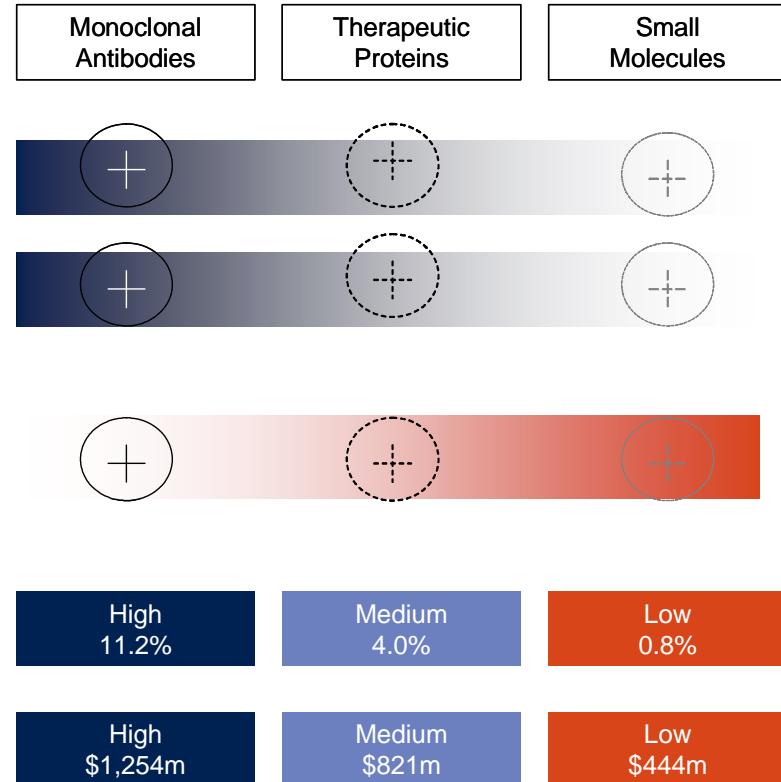
Growth resistors

Generic/Biosimilar Exposure

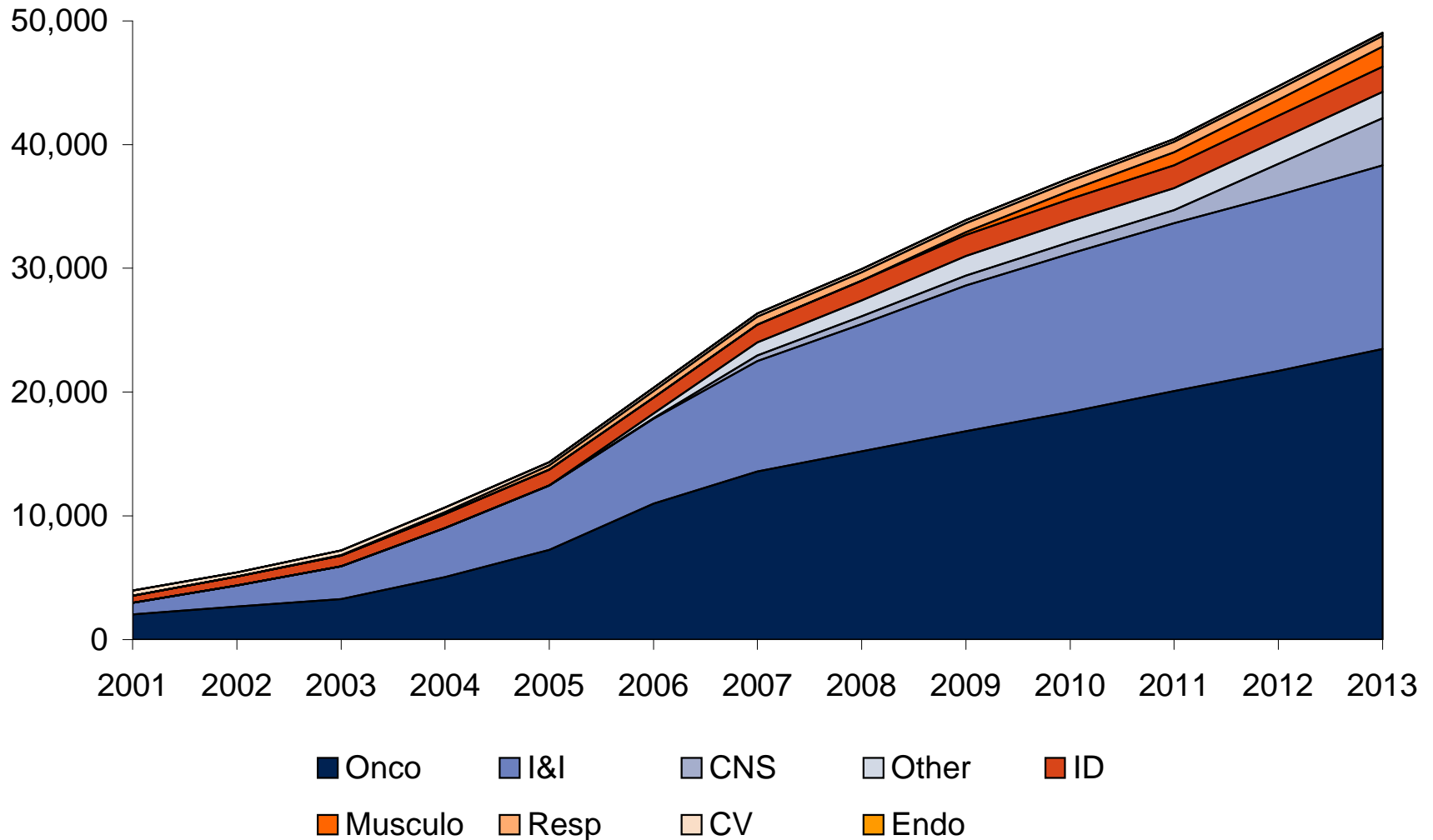
Market Performance

Forecast sales %CAGR 2007-12

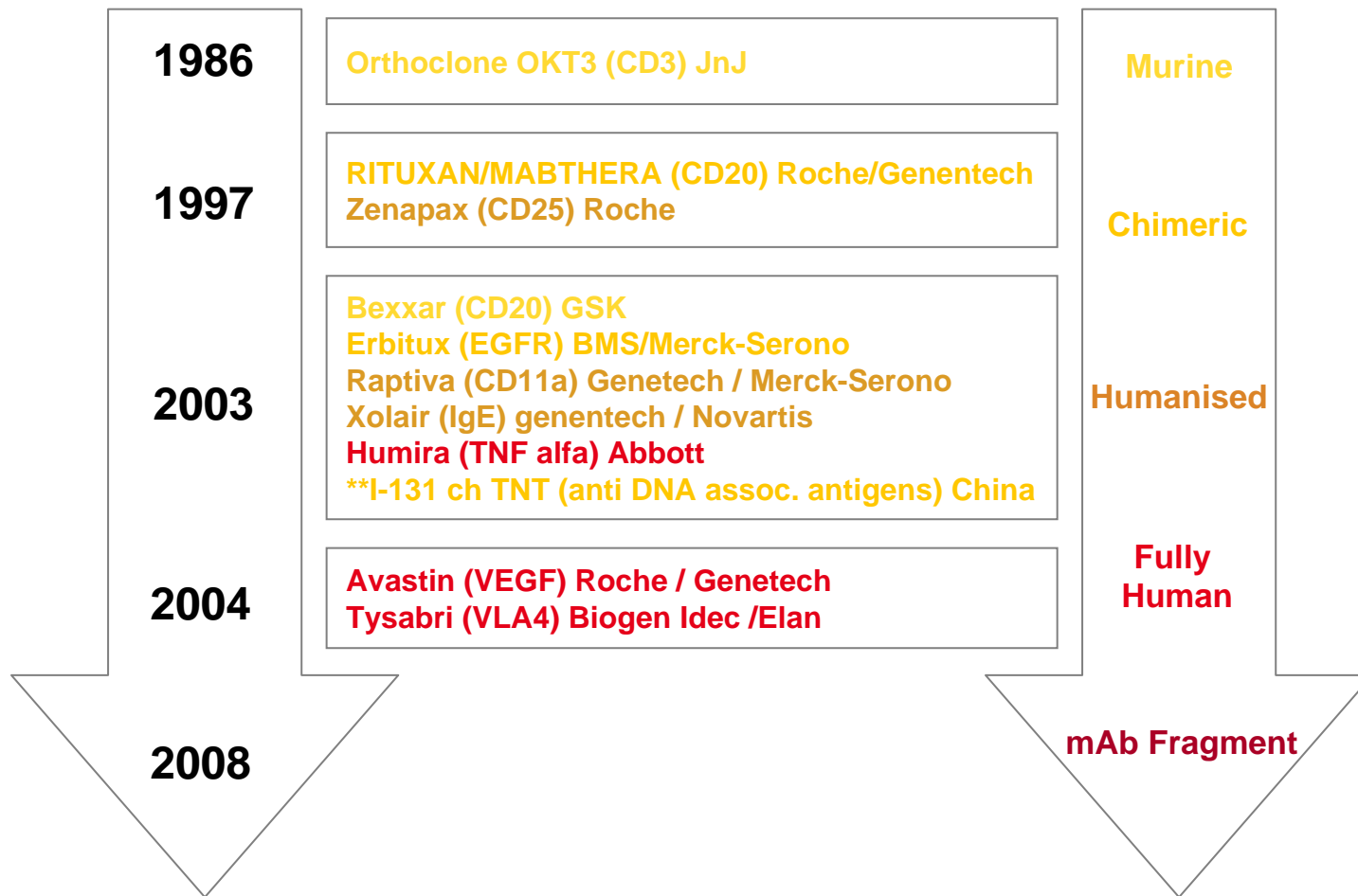
Av. 2007 Revenue per product (\$m)



Therapeutic Areas: Historical & Forecast



Evolution



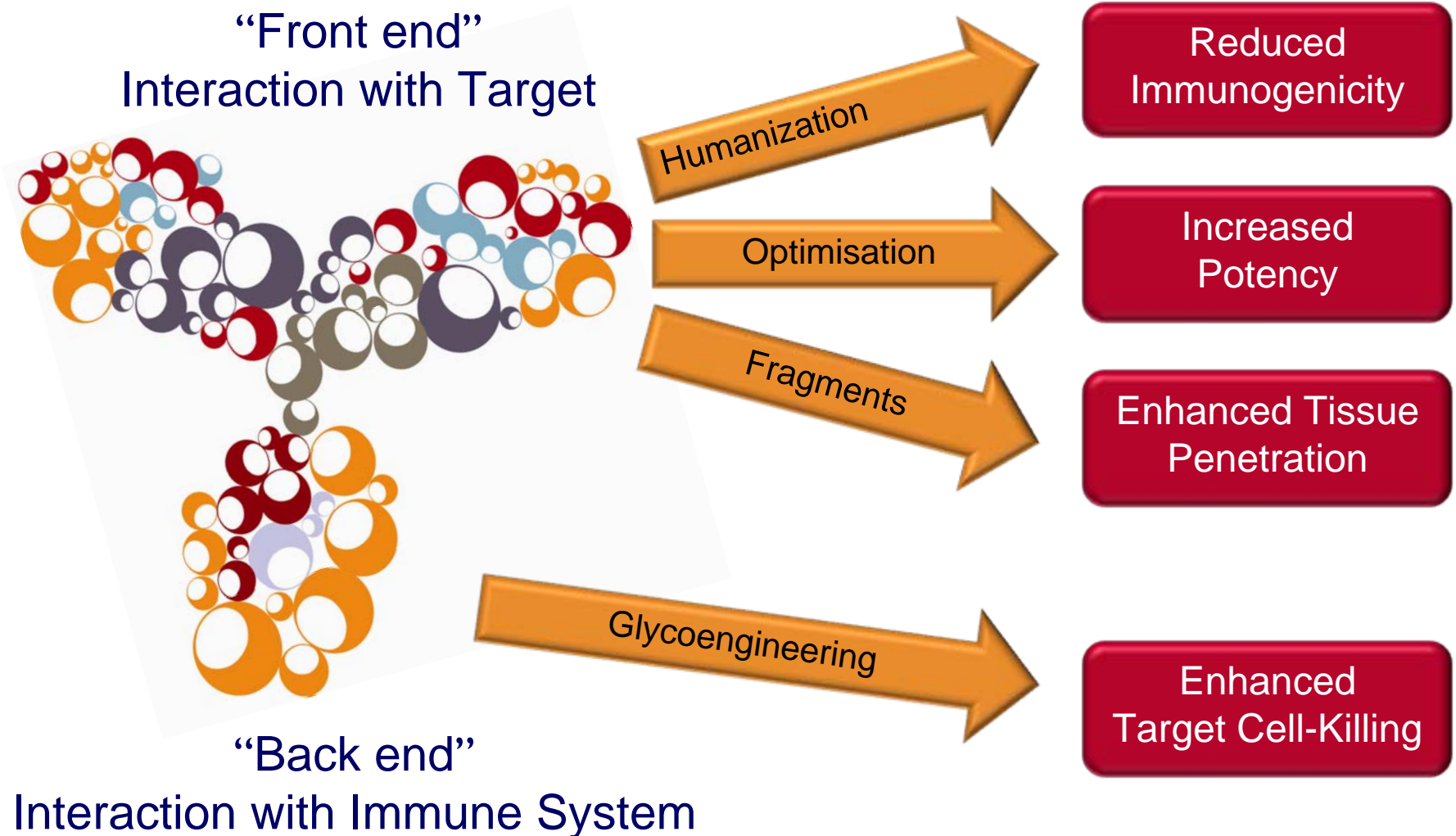
BMS = Bristol Myers-Squibb GSK = GlaxoSmithKline JnJ = Johnson and Johnson
*Panorex was withdrawn from the Market **Launched in China

Continuing Evolution



- More innovation: formats / fragments / payloads
- Growth: earlier treatment & new therapy areas
- Improved safety
- Risk (shifting risk management) e.g. Cimzia
- Improved efficacy - improved cost:benefit
- Production, Cost reduction
- Rationalisation (Industry)
- Bio-generics / Biosimilars (> 10 years)

Innovation: Engineering Antibodies



Format Flexibility



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**Remicade
Humira
CNTO 148**

Full size mAb

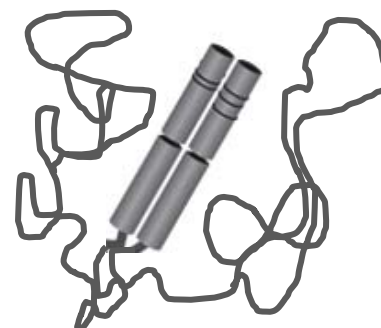
MW **150** kDa



Enbrel

Fusion protein

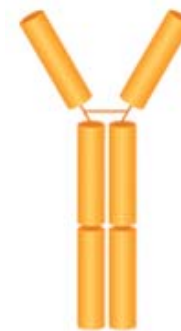
MW **150** kDa



Cimzia

Pegylated

MW 90 kDa
Effective
MW **>300** kDa



ART621

dAb fusion

MW **75** kDa

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- July 2008: Genentech (NYSE:DNA) gained \$12.06 (15%) to \$93.88 on Monday after Roche (SWX:ROG) proposed to acquire the 44.1% of Genentech it does not already own for \$89 per share in cash, or **\$43.7 billion**....
- Roche's three biggest selling drugs were all in-licensed from Genentech:
 - **Rituximab** for NHL and RA with \$2.8 billion sales
 - **Herceptin** for breast cancer with \$2.4 billion sales
 - **Avastin** for various cancers with \$2.3 billion sales

- July 2008: Immunomedics (NASDAQ:IMMU) will grant Nycomed an exclusive, worldwide license to develop and commercialize subcutaneous veltuzumab for non-cancer indications. Nycomed plans to develop veltuzumab for rheumatoid arthritis (RA) as the primary indication. Immunomedics will receive **\$40 million up front** and be eligible for **\$580 million in milestones**, plus escalating, **double-digit royalties**.

Questions / Discussion



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