Drug Portfolio Analysis – Targeted Anticancer Therapies

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Agenda

- Drug Development
  - Approval Process Overview
  - Small molecule vs. targeted monoclonals
  - Pathways – Targets & Resulting Cancers
  - Successful Pipeline Search Tips
  - Case Studies: EGFR & Multiple Myeloma
- Conclusions

Fewer FDA Approvals

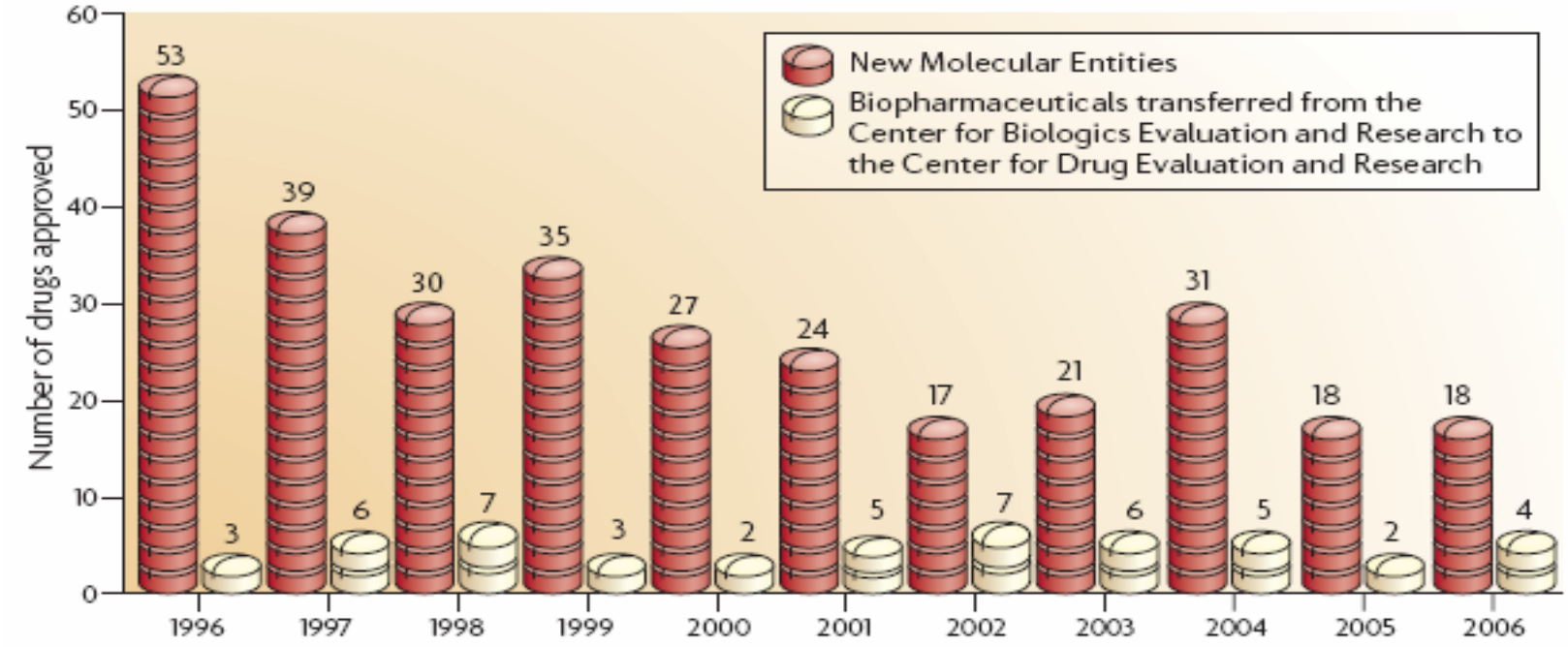
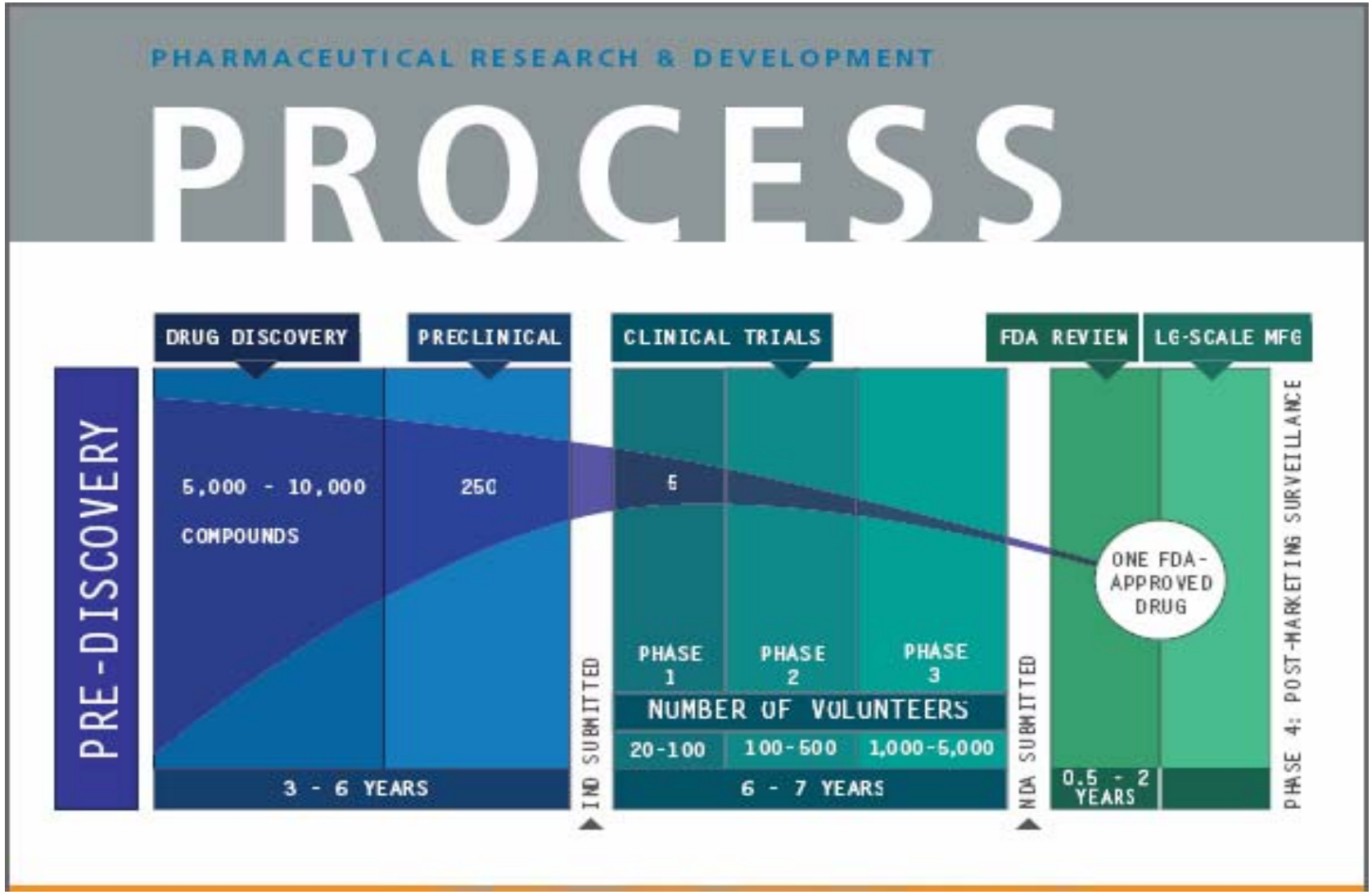


Figure 1 | **FDA drug approvals.** New molecular entities (NMEs) and biologic license applications approved by the US FDA by year. The number of NMEs approved in 2006 stayed the same as in 2005, with a slight increase in the number of approved biologics.

Source: Nature Drug Discovery *Nature Reviews Drug Discovery* **6**, 99–101 (2007);

Differences Between Small Molecules & "Targeted" Monoclonal Antibodies –

- Small Molecules (Traditional Pharmaceutical Drugs)
  - Oral or Intravenous
  - Target multiple pathways
  - Cheaper to manufacture
  - Short half-life
  - Enter cytoplasm therefore target any molecule or pathway regardless of location
- Monoclonal Antibodies (Biotech drugs)
  - Intravenous only
  - Target specific protein
  - Expensive to manufacturer
  - Inconvenient to administer but longer half-life
  - Confined to proteins in extra cellular matrix



Source: 2007 PhRMA's Innovation.org

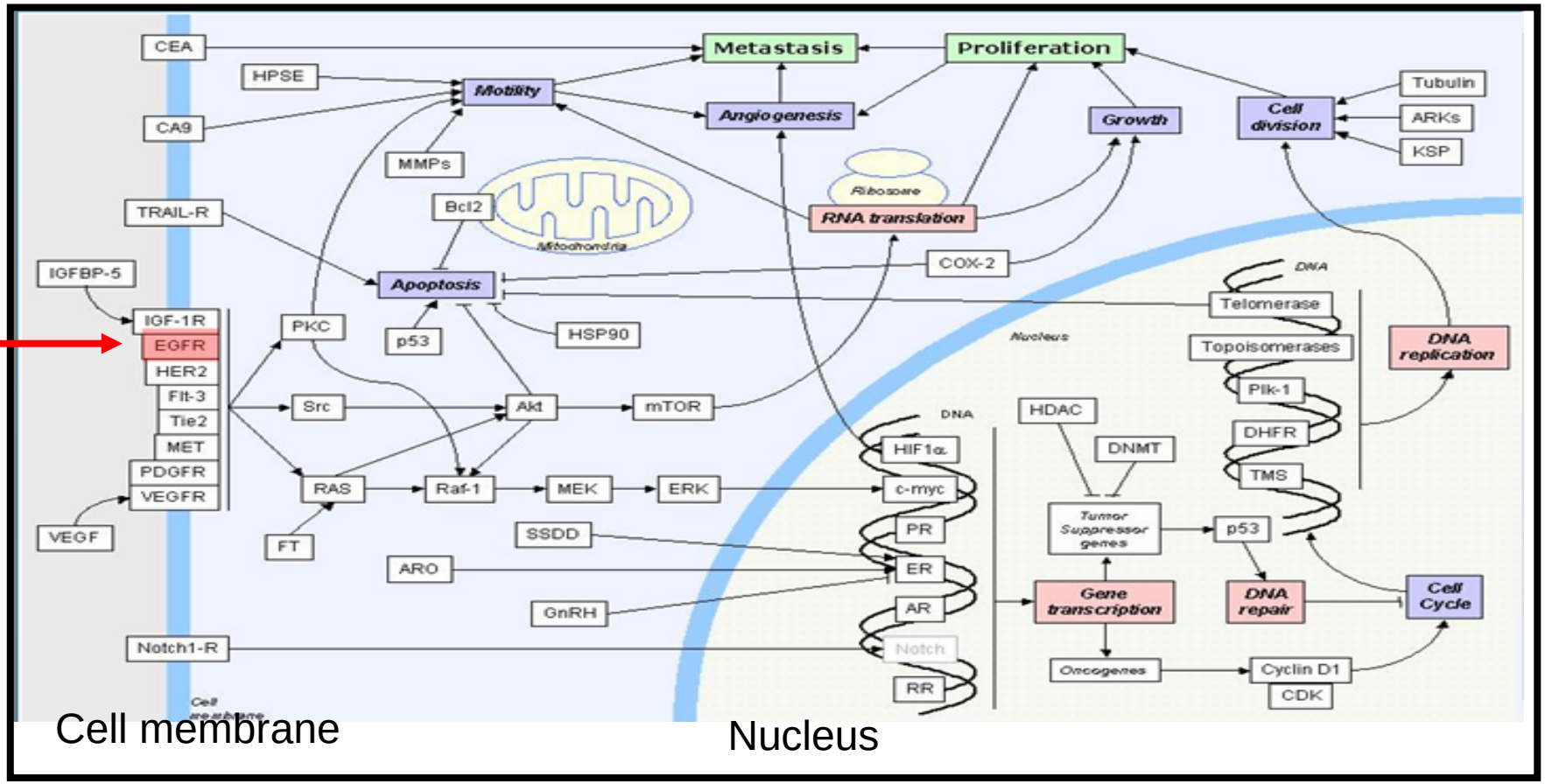
Changes in the Investigational Drug Research Process

- Increase in the number & size of clinical trials per New Drug Application
  - 1985 – 1988: Average # = 36 (**3,200** patients tested/NDA)
  - 2000 – 2005: Average # = 70 (**4,500-5,000** patients/NDA)

- Clinical testing phase gradually lengthening
  - 1985 – 1988 → 5.5 years
  - 1990 – 1999 → 6.5 years
  - 2002 – 2004 → 7 years

(Source: PhRMA 2007 Innovation.org)

Cancer Pathways: Cellular Targets



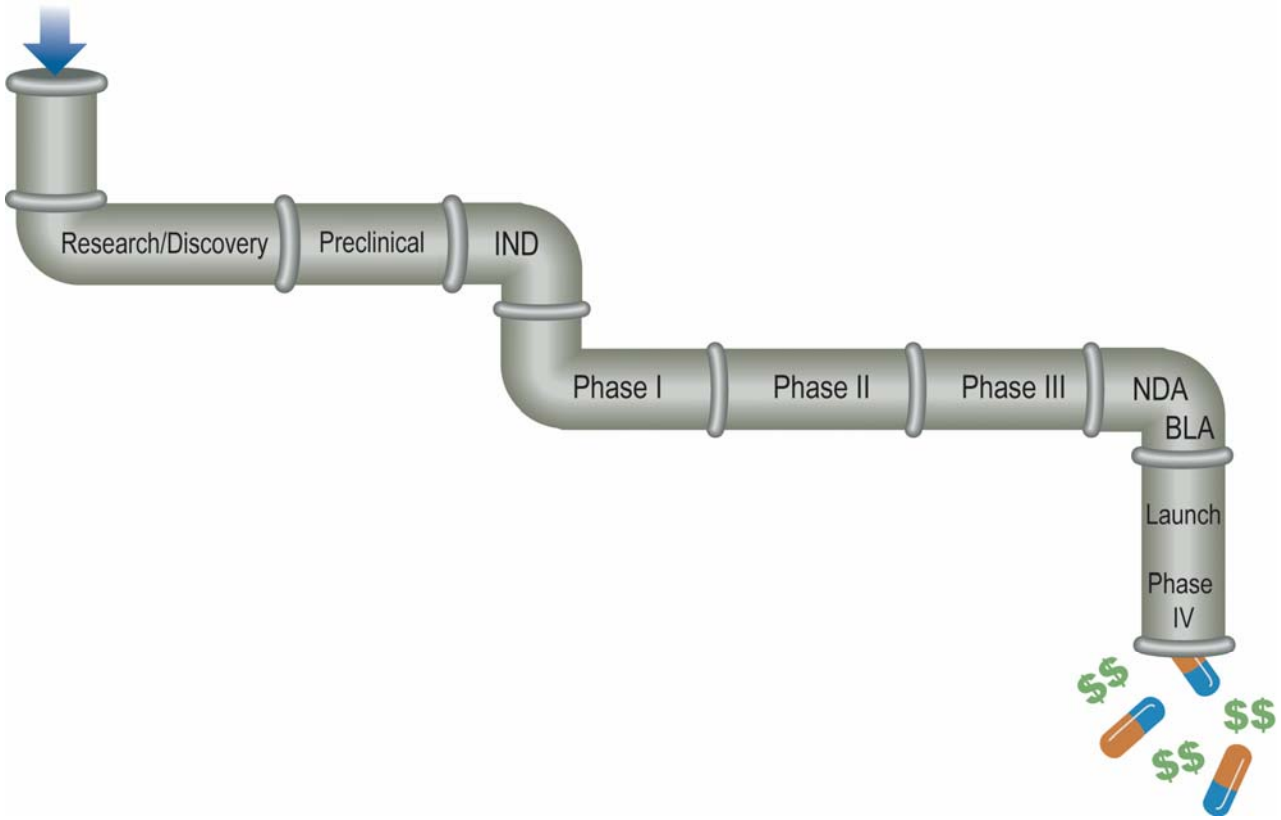
Source: Prous Integrity Target Landscapes

Pathway Mutations & Resulting Tumors

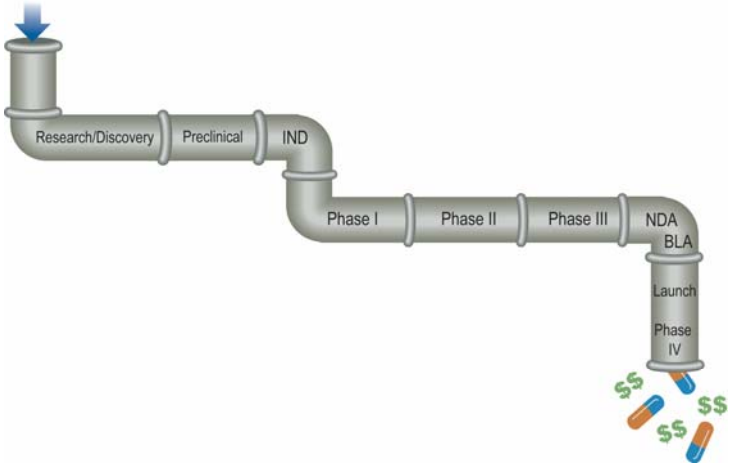
Mechanism	Site of Mutation (= Target)	Resulting Cancer
Growth factors / growth factor receptors	PDGF **Epidermal growth factor Receptor (EGFR) (Case #1)** Vascular Endotheial Growth Factor (VEGF) HER-2 RET growth factor receptor	Brain & breast cancer Brain, breast, lung, colorectal, **multiple myeloma (Case #2)** Breast, colorectal & lung cancer Breast & ovarian Thyroid
Cytoplasmic relays in stimulatory signaling pathways	K-ras N-ras	Lung, ovarian, colon, pancreas Leukemia's
Transcription factors that activate growth promoting genes	C-myc N-myc L-myc	Leukemia, breast, stomach Brain Lung
Cytoplasmic proteins	APC DPC4 NF-1 & NF-2	Colon & stomach Pancreatic Brain, nerves & leukemia
Nuclear proteins	RB, p53, WT1, BRCA1 & BRCA2	Retinoblastoma, bone, bladder, lung, breast & Wilms tumors

Planning is critical.

Pipeline – Focus by stage

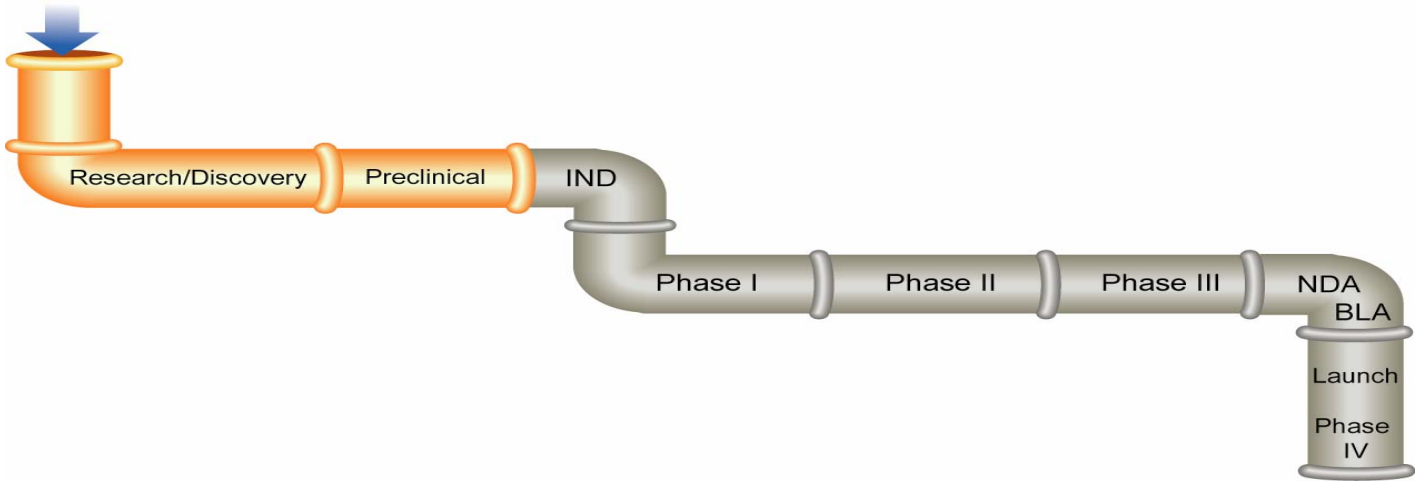


Where to look & what to look for will depend on phase of development -



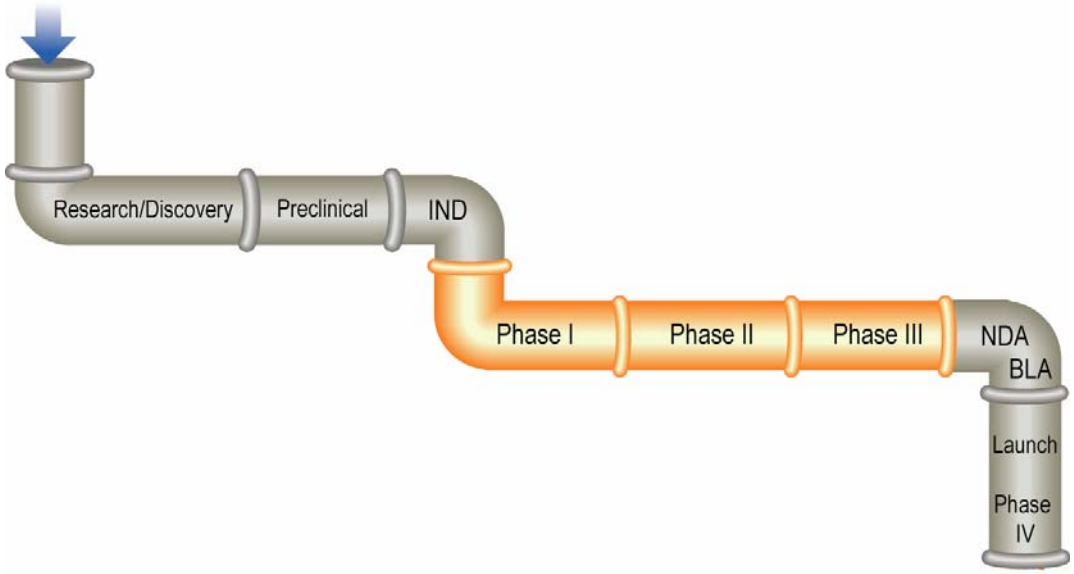
Pre-clinical	Phase I	Phase II	Phase III	Submission	Launch
■ Scientific & conference literature ■ Patent literature ■ Epidemiology & Health Statistics ■ Pipeline databases ■ Business news	■ Drug pipeline databases ■ Scientific & clinical literature ■ Clinical trials databases ■ Wall Street Analysts ■ HCUP data	■ Drug pipeline databases ■ Scientific, conference and clinical literature ■ Business news ■ Wall Street analysts	■ Drug pipeline databases ■ Business news ■ Scientific / clinical trials databases ■ Wall Street analysts ■ Deals databases	■ Drug pipeline databases ■ Press releases re: NDA submissions ■ FDA	■ Wall Street analysts & VC firms ■ CEO interviews ■ Wall Street Transcripts ■ Press releases ■ PDR/ GenRX ■ Redbook ■ IMS Audits

Drug Development – Early Research



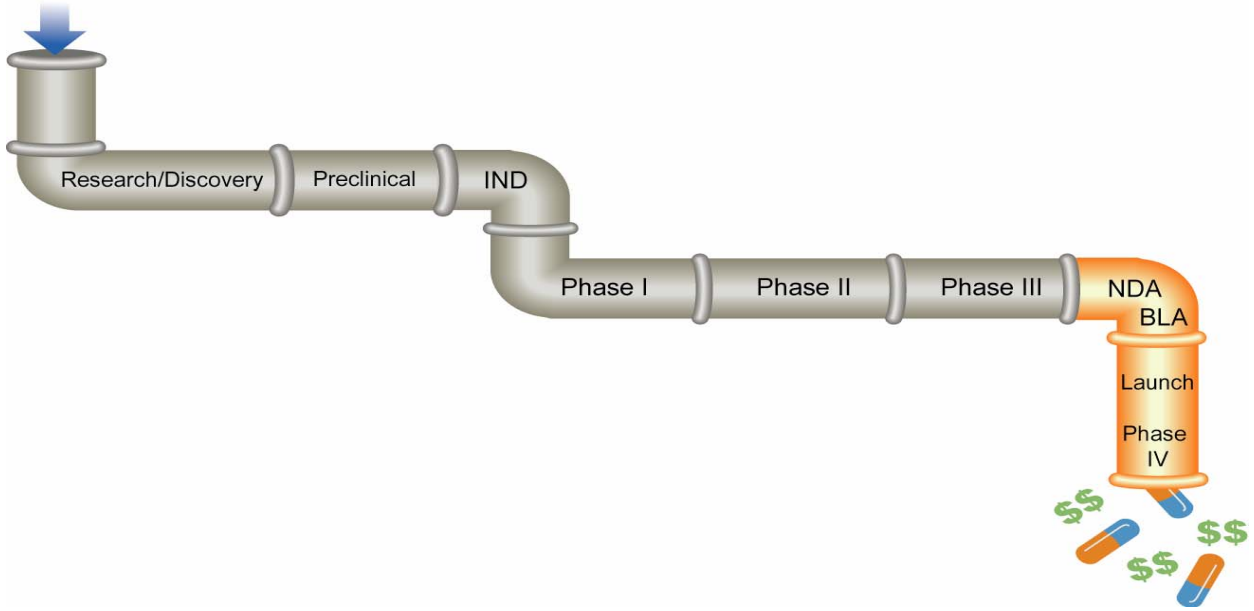
Nomenclature	Sources
■ Chemical names ■ Laboratory Codes ■ CAS registry numbers ■ Target gene / receptor	■Conference proceedings ■Patents ■Drug pipeline databases ■Scientific literature

Drug Pipeline Development – Clinical



Nomenclature	Sources
■ *USAN (U.S. adopted names)* ■ *INN (International non-proprietary names)* ■ Lab codes, CAS RN's and chemical names ■ Target gene / receptor ■ *Indication*	■ Scientific literature ■ Meetings & conference proceedings ■ Big 5 Drug pipeline databases ■ Clinical trial databases ■ Wall Street broker reports

Pipeline Development – NDA/Launch/Post Marketing

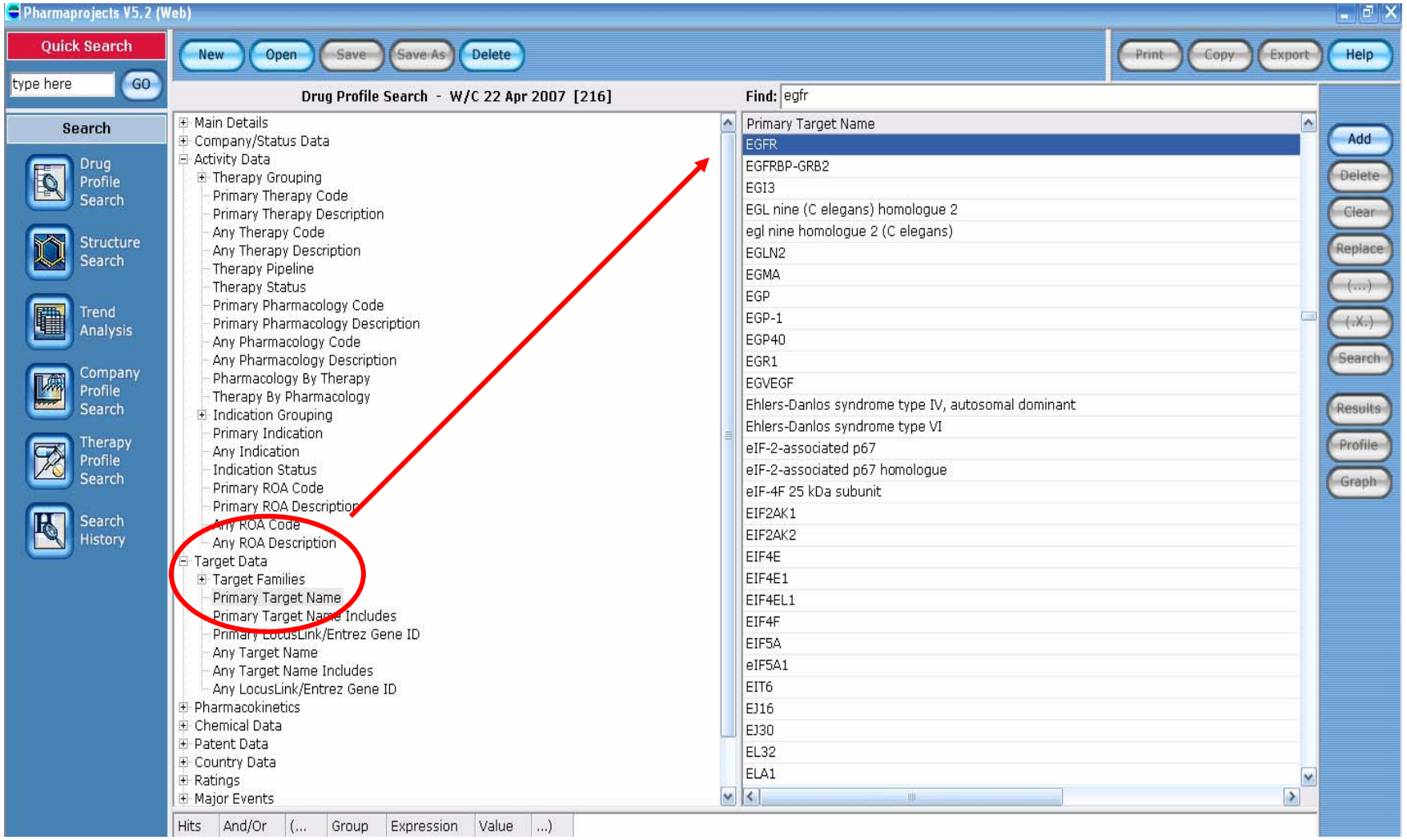


Nomenclature	Sources
■ USAN/USP (established name) ■ Proprietary names / Chemical names ■ *Generic names* ■ *Brand names* ■ Indication	■ Patent literature ■ Business literature ■ Clinical literature ■ Sales audits & analyst reports ■ FDA & internet regulatory sites

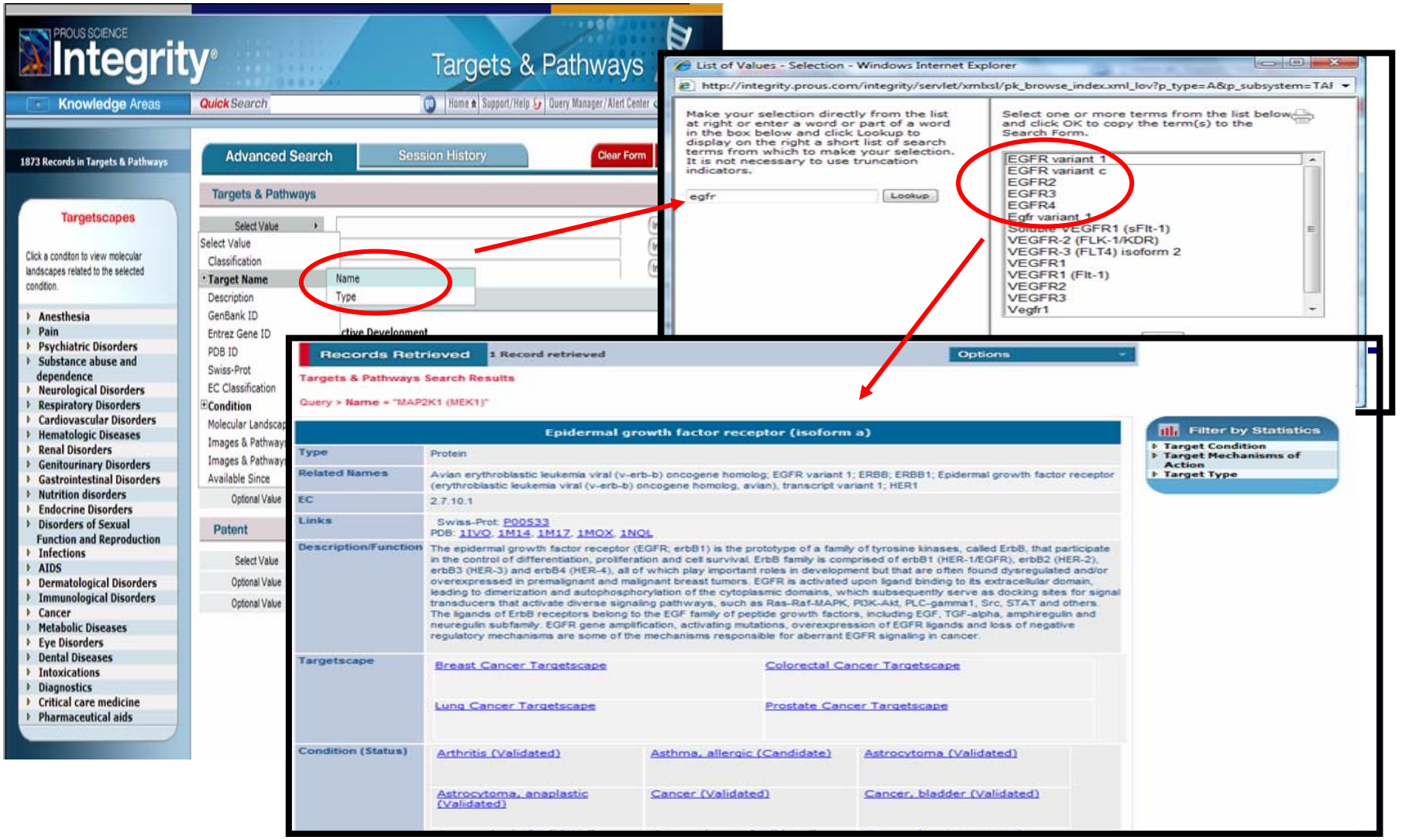
Big 5 Drug Databases

- ADIS - R&D Insight – Wolters Kluwer
- IMS R&D Focus – IMS Health (IMS Global Services)
- Investigational Drugs Database (IDDB) – Thomson Scientific
- Pharmaprojects – Informa Healthcare
- Prous Integrity – Thomson Scientific

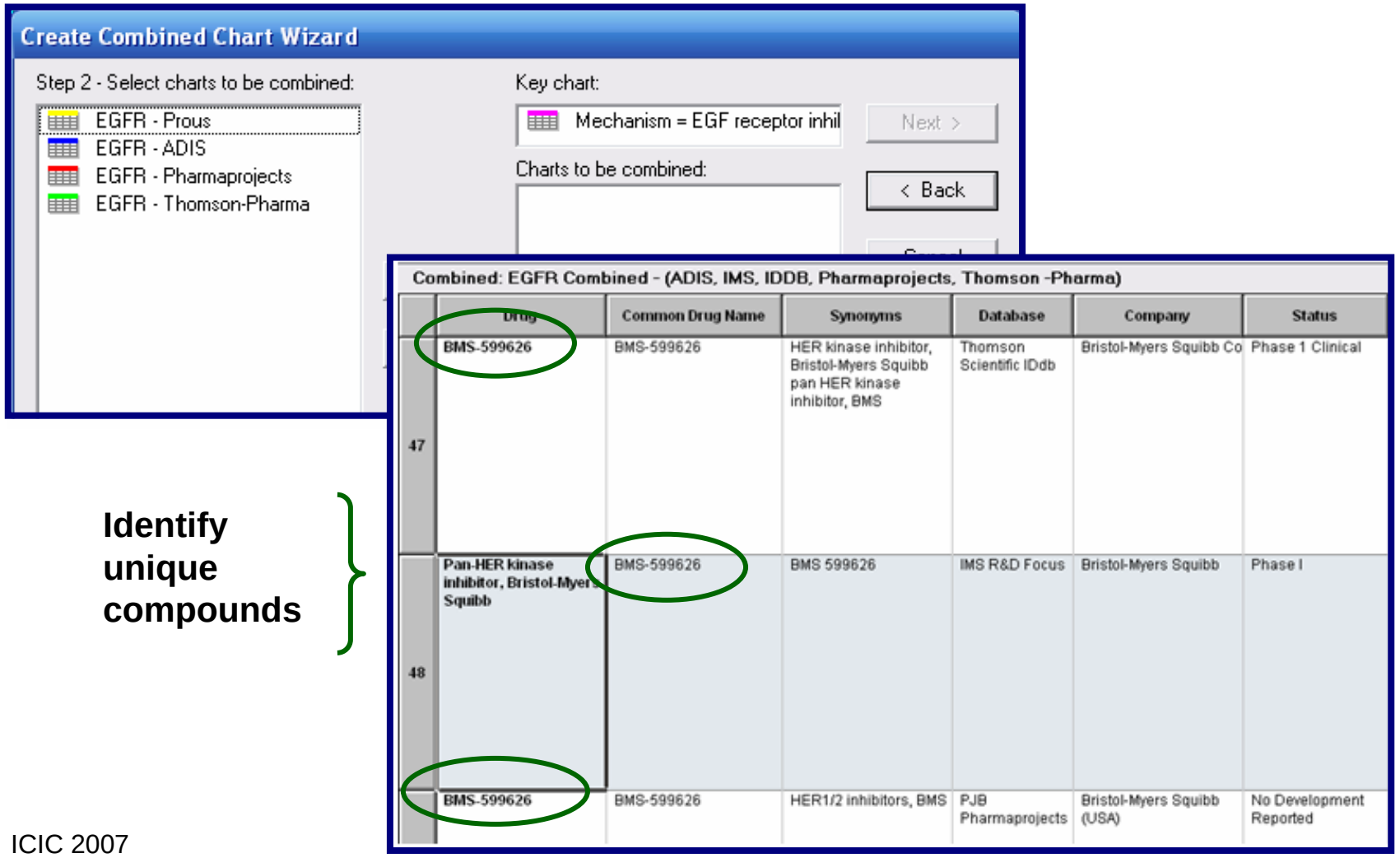
Pharmaprojects - Search



Prous Integrity – EGFR Target Search

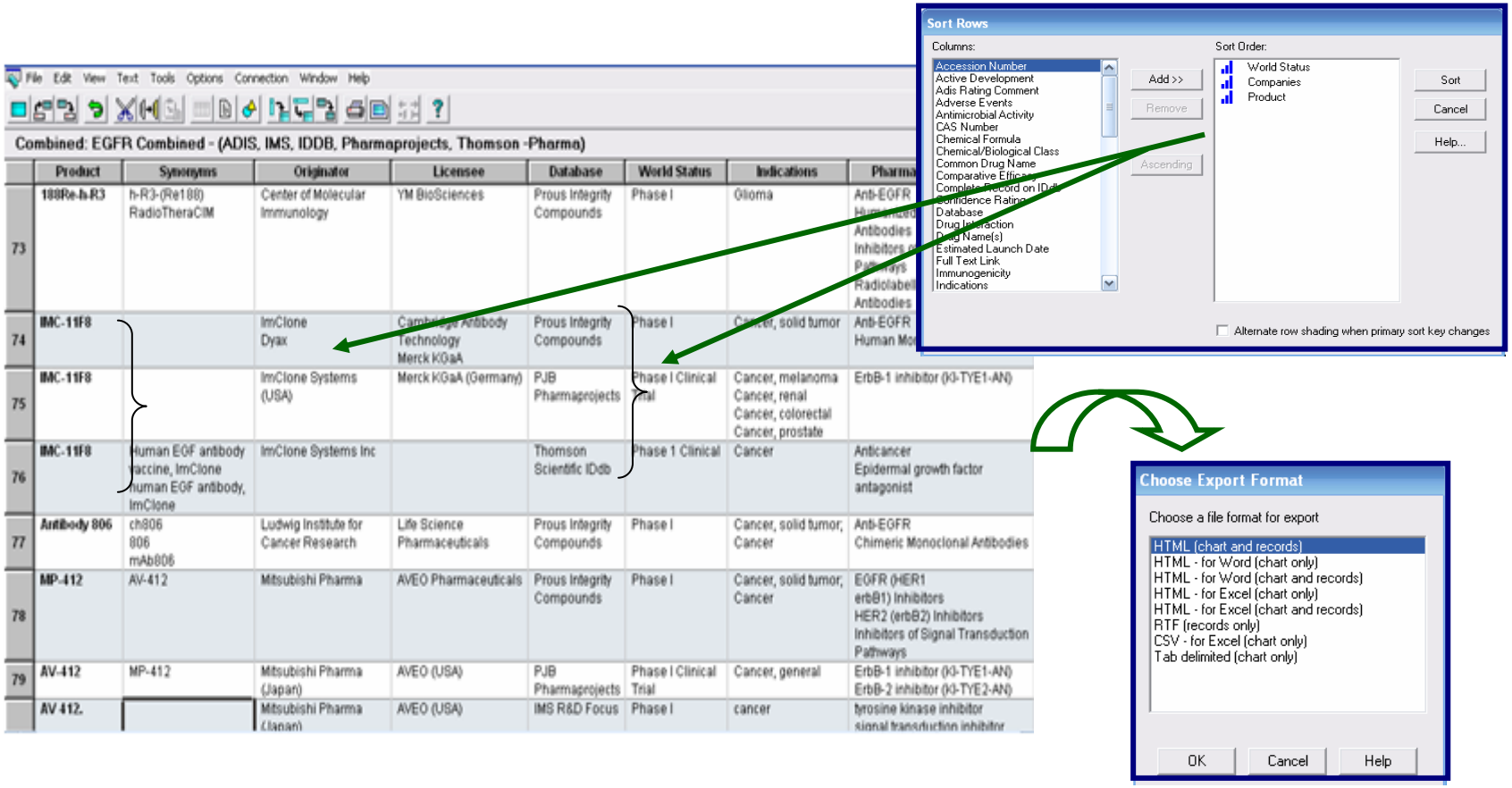


BizInt Smart Charts – Data Integration



Identify unique compounds

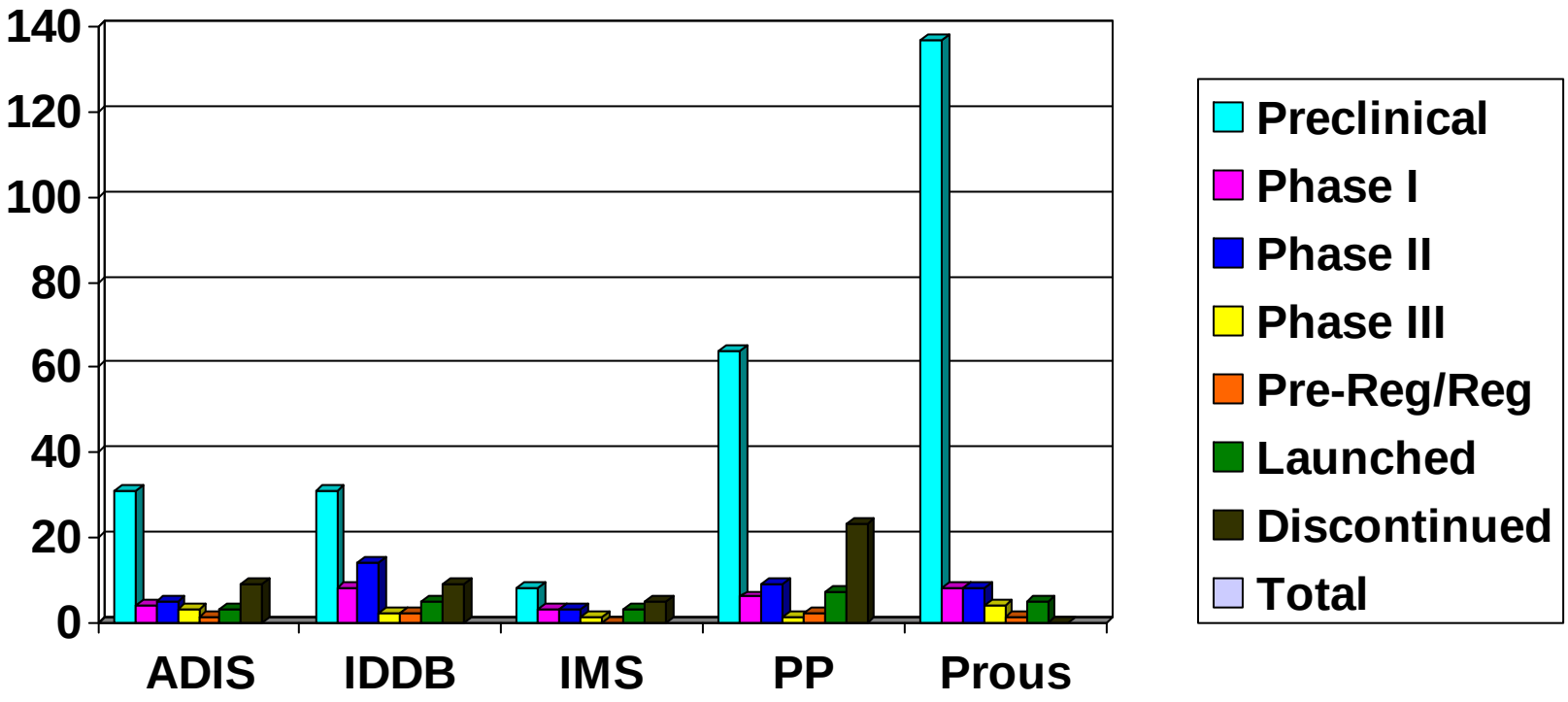
BizInt Smart Charts – Sort & Export



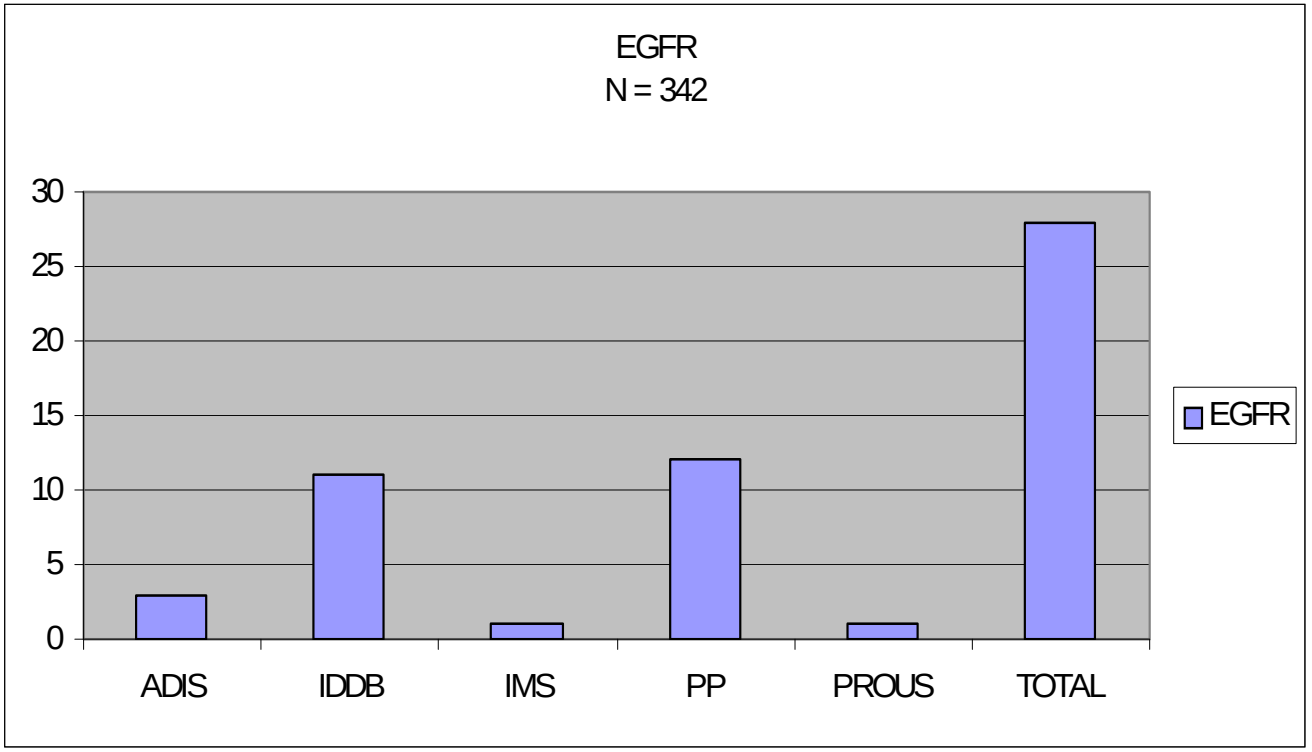
2 Case Study Comparisons

- Big 5 Drug Development databases – 2 case studies
  - Epidermal Growth Factor Receptor (EGFR) antagonists (target search)
  - Multiple Myeloma (indication search)

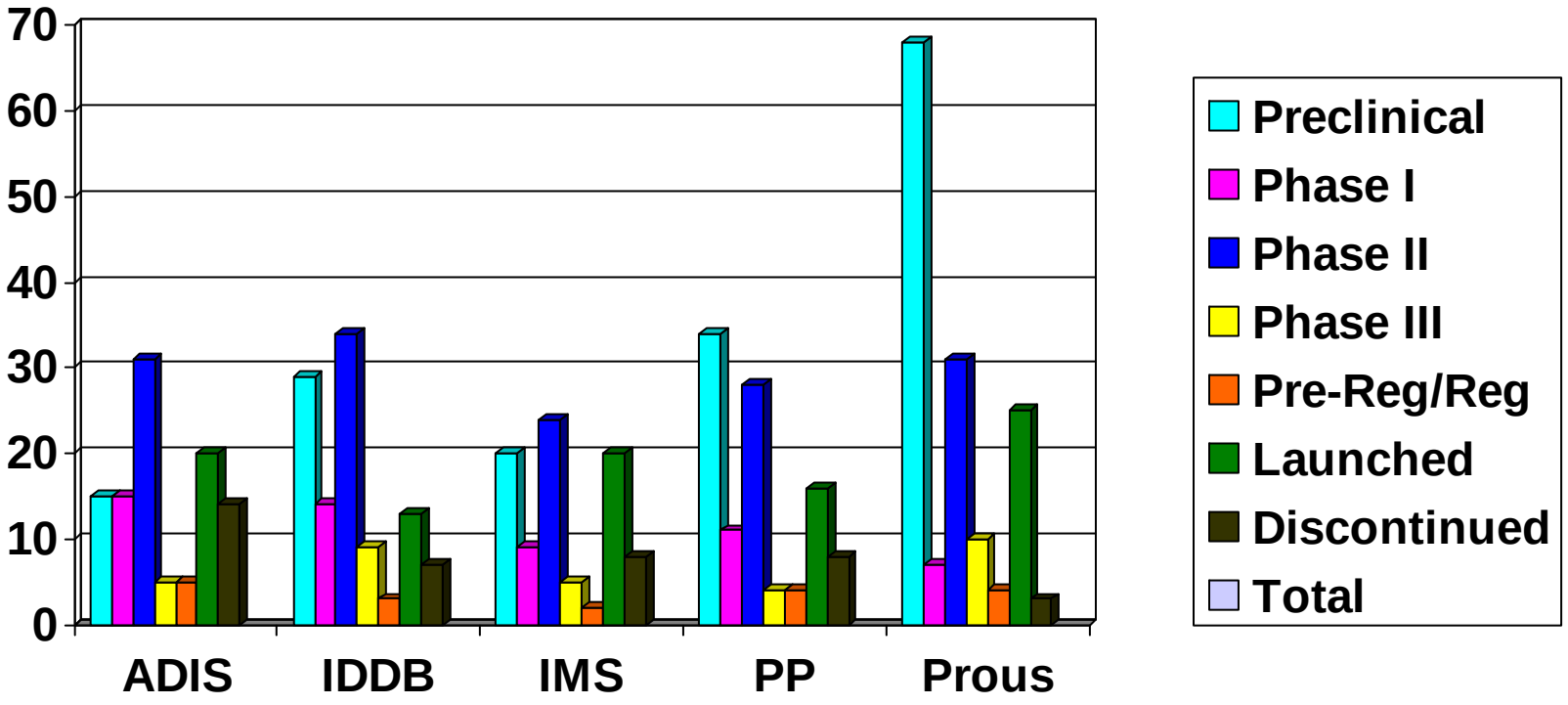
Target: EGFR


140
120
100
80
60
40
20
0
ADIS
IDDB
IMS
PP
Prous
Preclinical
Phase I
Phase II
Phase III
Pre-Reg/Reg
Launched
Discontinued
Total

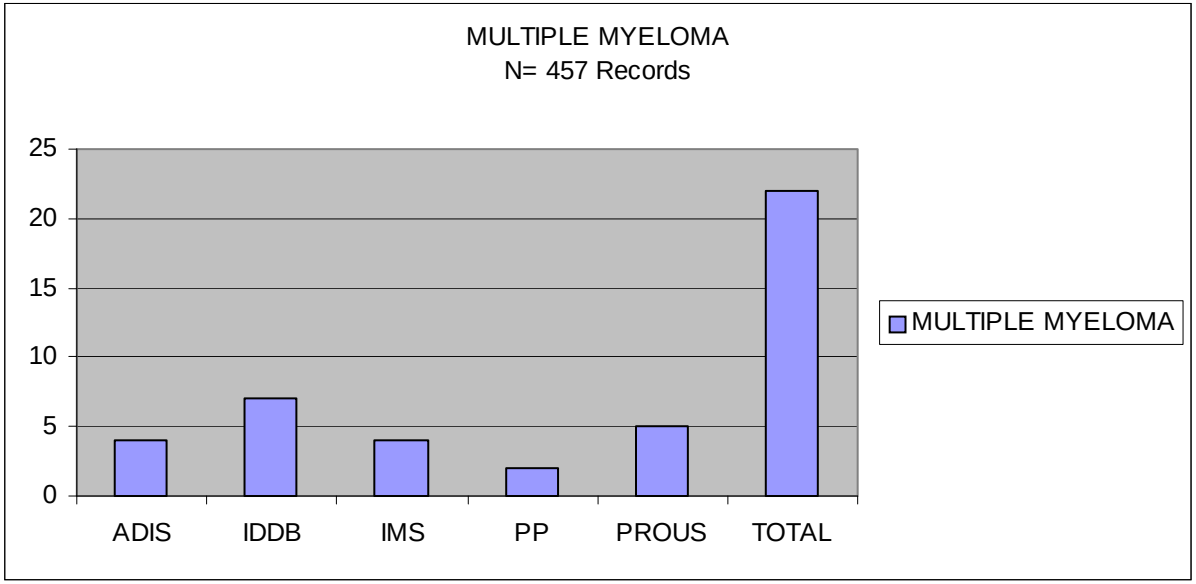
EGFR: Unique Content



Indication: Multiple Myeloma



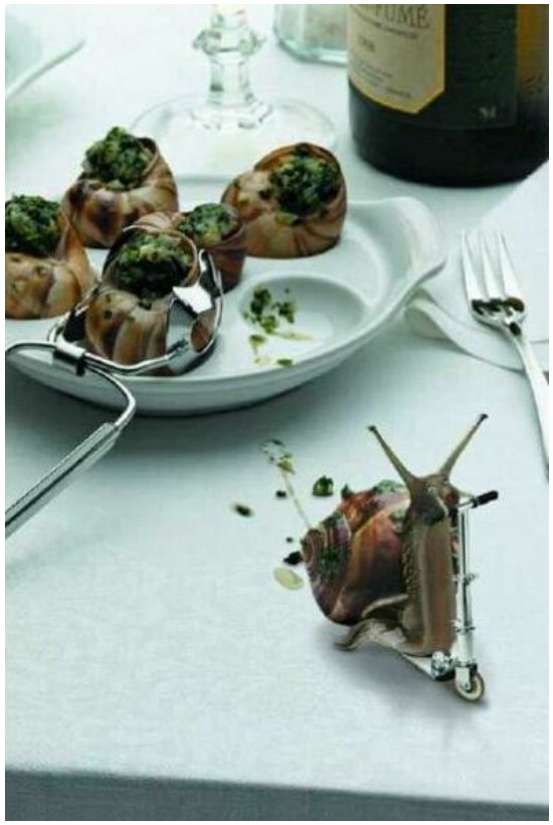
Multiple Myeloma: Unique Content



Drug Pipeline Databases

- Leverage work of numerous databases
- Differences exist in coverage & content
- Differences exist due to editorial rules at each company
- Data from one source not complete picture
- Staff at companies differ in experience
- Update schedules differ between databases
- Unique content exists in some of the databases

Conclusion -



- There are several avenues to success when collecting information.

Acknowledgements

- Adam Schaeffer – ADIS R&D Insight
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- John Willmore – BizInt Solutions, Inc.

Questions?

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