BioSimilars

Implications for Medical Oncology

Session Objectives

- Tell you what I think
  - How biosimilars (BSims) will impact cost and quality of cancer care
- Explain myself
  - Equip you to reach your own conclusions
- Eliminate/establish uncertainty
  - Answer your questions (or tell you where/when to look)

AGENDA

- The State of BSims
  - In the world
  - In the US
  - Test case
- Defintions
  - Biologic
  - Biosimilar
  - Small molecule drugs
- Implementation
  - Coverage
  - Reimbursement
  - Pharmacovigilence
- Implications
  - Incentives
  - Costs of care
  - Access to medications
  - Practice operations

The State of BSims

May/June 2015

BSims in EU (and elsewhere)

- First BSim approved in 2007
- Currently 22 approved variants on Epoetin
- $45 per BSim
- ~30 percent savings
- Nomenclature remains an issue

Biologics Price Competition and Innovation Act

- New “pathway” created as part of ACA
  - Congress tells the truth
- The logic of BPCIA
  - The legacy of Hatch-Waxman
  - Two pathway’s
    - Similarity
    - Interchangeability
- Mechanisms of action
  - Industry as target
  - Incentives (patent protection versus exclusivity)

Case 15-1499

- March 6, FDA approves Zarxio
- Sandoz agrees not to market until May 11th
- Amgen files injunction to prevent market entry
- March 27, California court rules against Amgen
- Amgen appeals
- May 5, Federal Court sides with Amgen
  - At issue Is whether process for info exchange laid out in BPCIA is mandatory?
  - Does BS manufacturer need to give RP manufacturer 180 day notice?
- Case will shape the future of litigation in BioSims

Definitions

Biologics, Biosimilars, and Small Molecules

Biologics

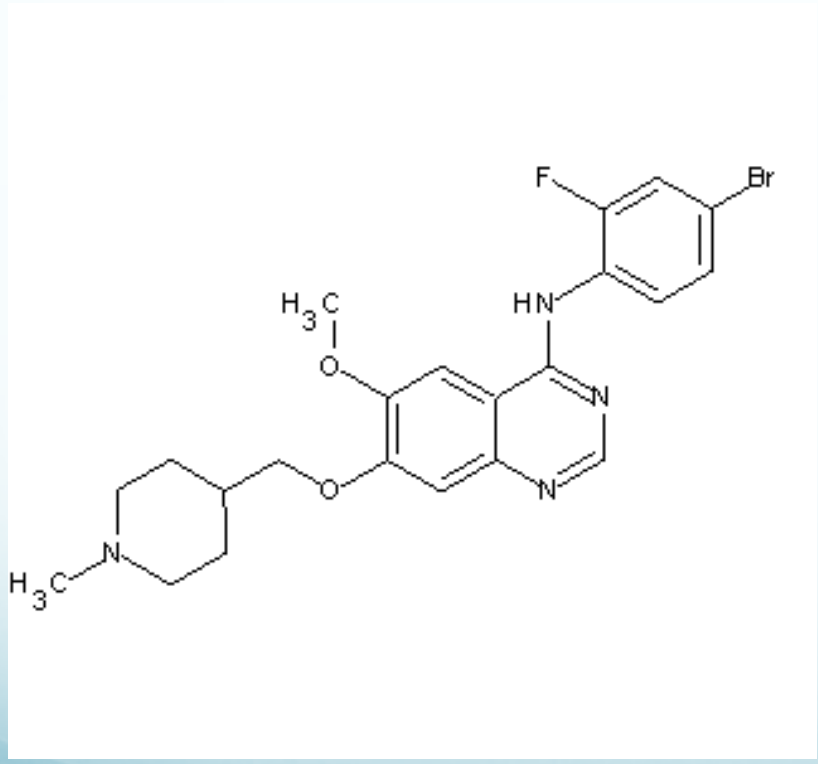
- Monoclonal antibodies
- Cytokines (Interferons, interleukins)
- Cancer treatment vaccines
- Bacillus Calmette-Guerin
- Oncolytic virus therapy
- Gene therapy
- Adoptive T-cell transfer therapy

BSims

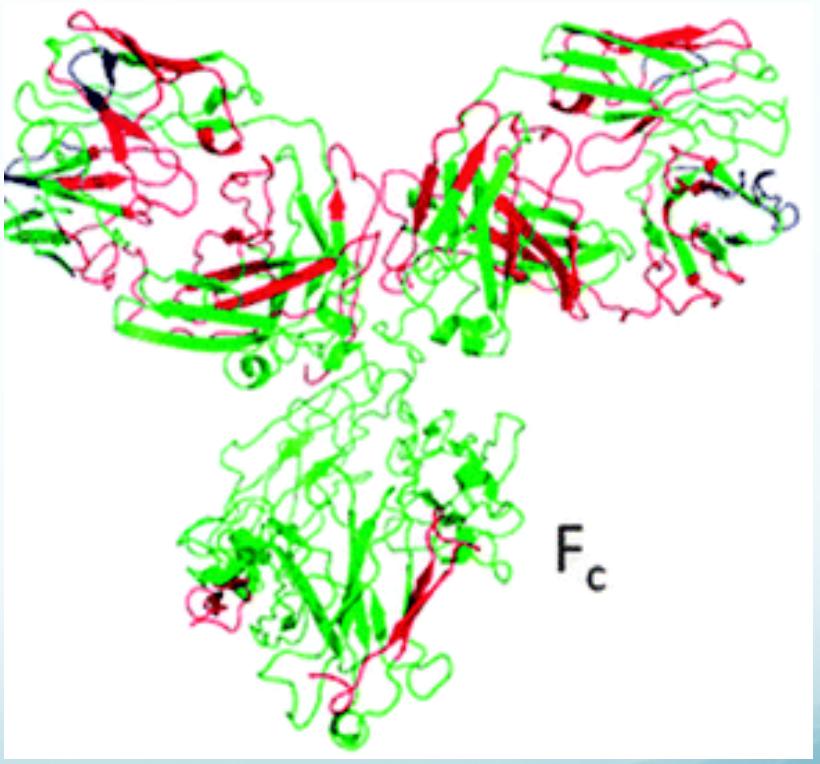
"*A biological product that is highly similar to a U.S. licensed reference biological product notwithstanding minor differences in clinically inactive components, and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product.*"

Size Counts: Small and Large Molecules

Vandetanib (475 g/mol)



Bevacizumab (149K g/mol)



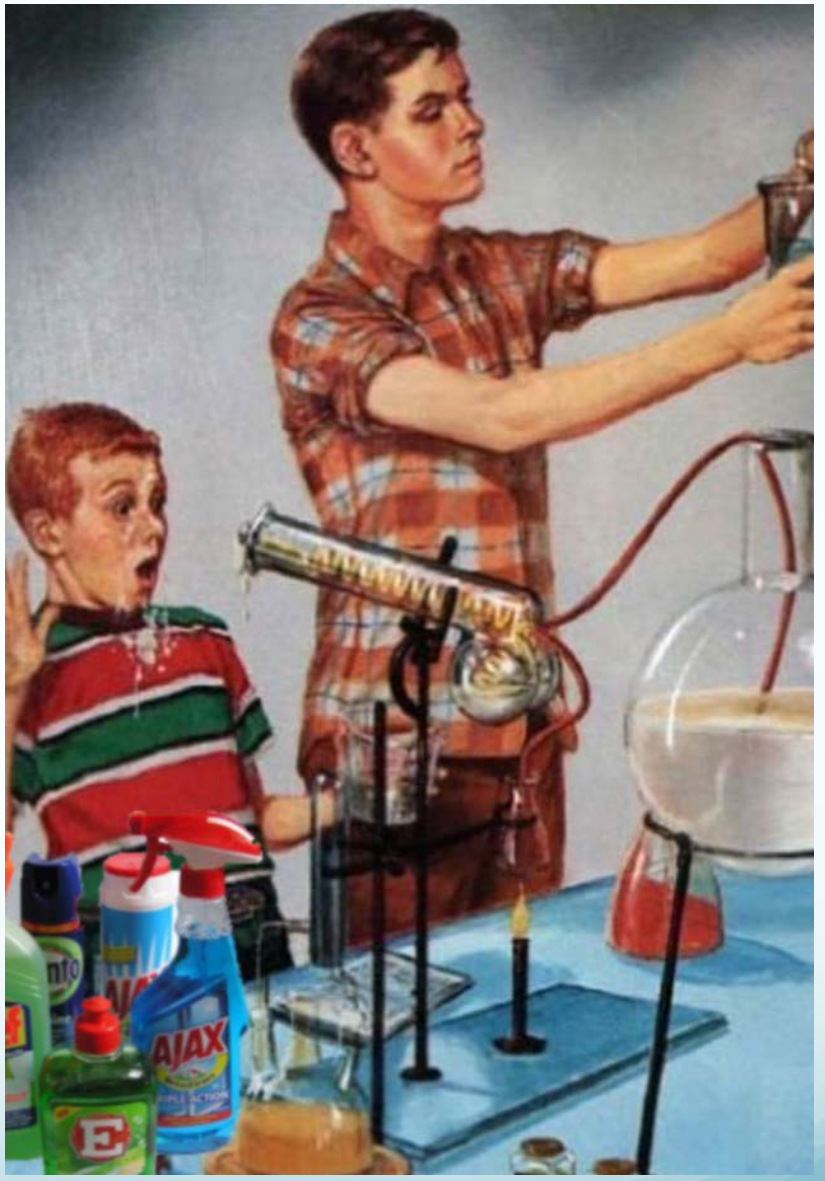
Making Vandetanib

Ingredients

- Carbon (22 units)
- Hydrogen (24 units)
- Bromine (1 unit)
- Floride (1 Unit)
- Nitrogen (4 Units)
- Oxygen (2 Units)

In a large vat:

- *Mix ingredients*
- *Stir until smooth*
- *Heat and serve* |



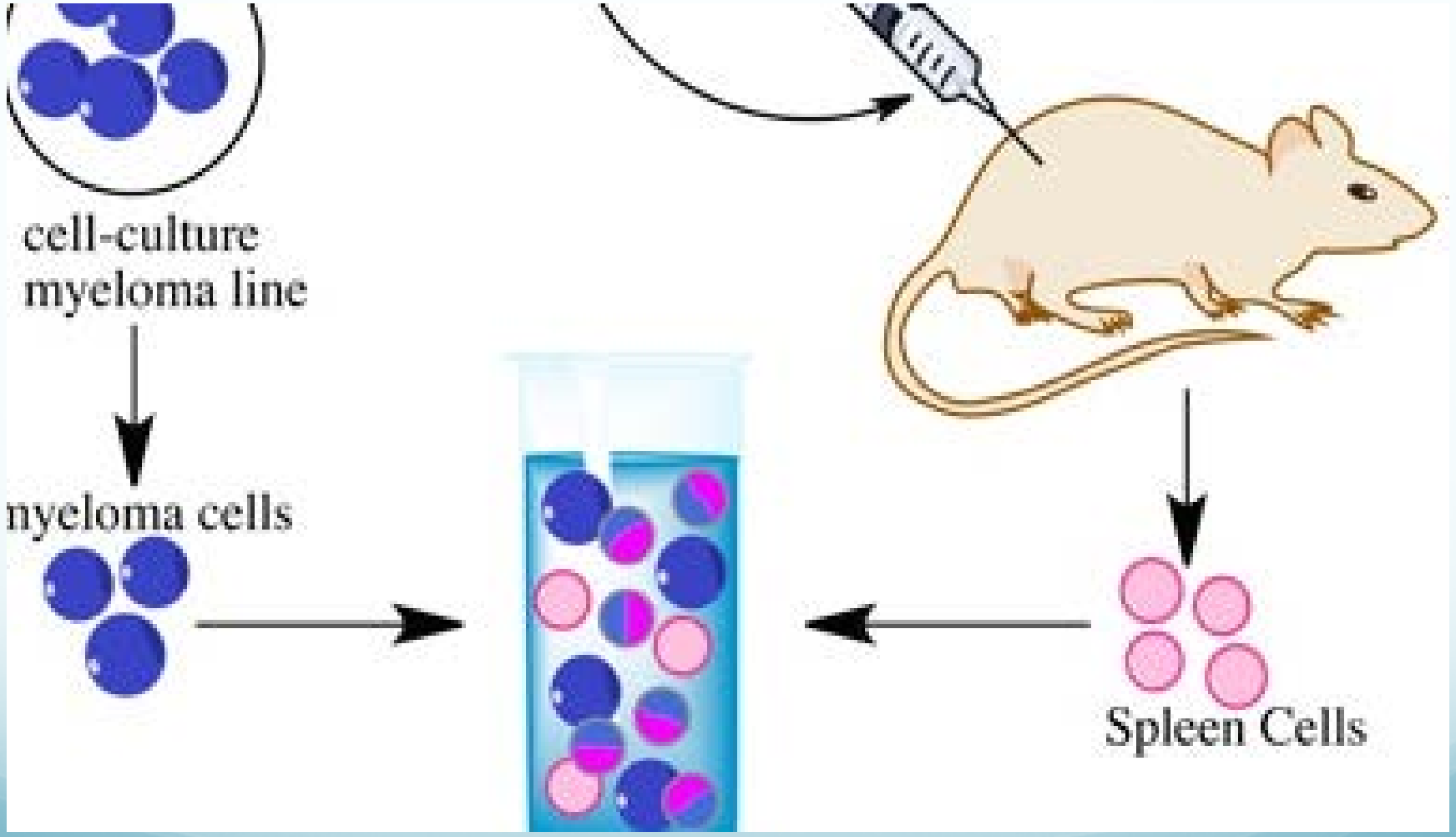
Making Bevacizumab

Ingredients

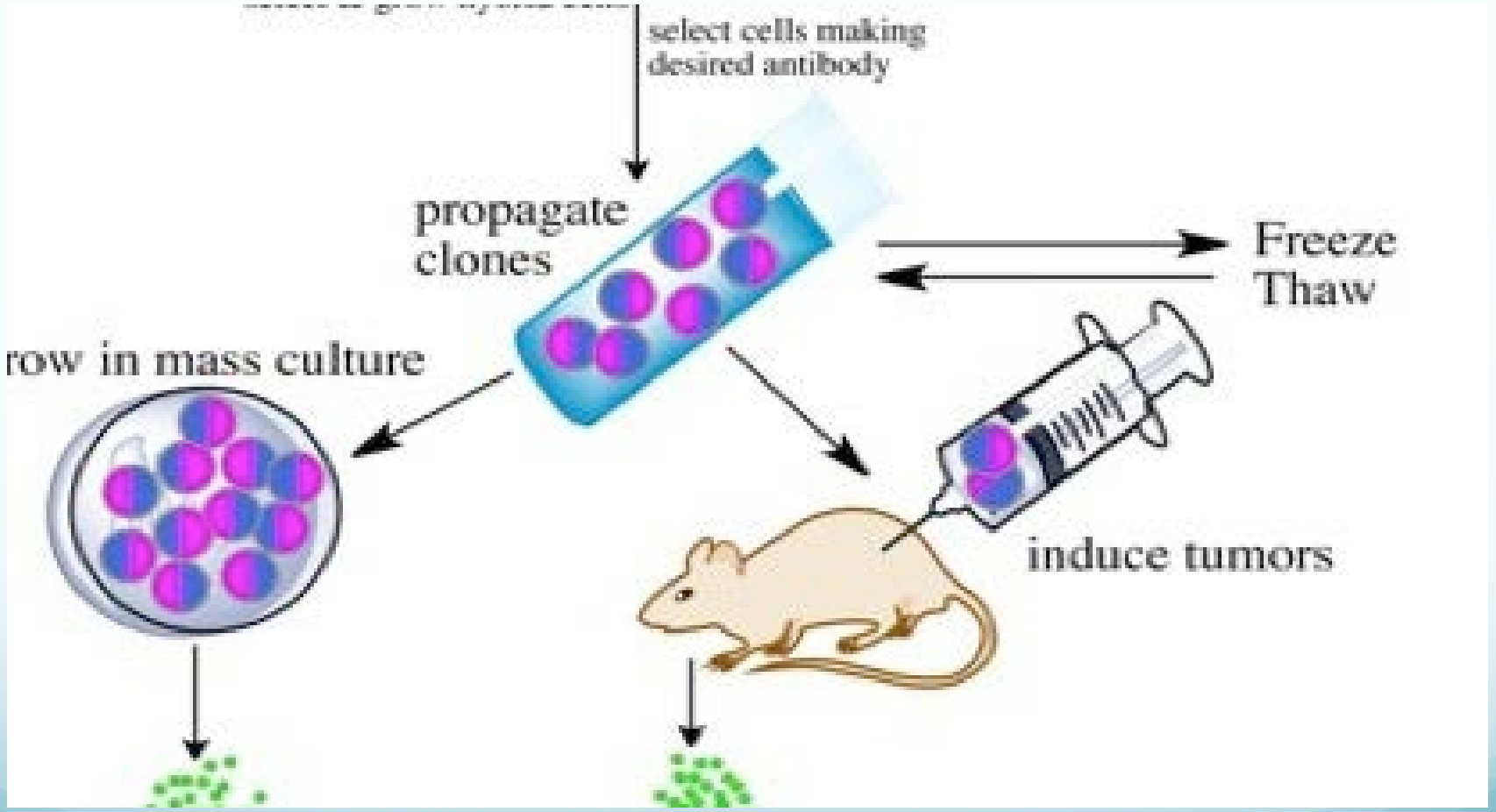
- Carbon (6,638 Units)
- Hydrogen (10,160 Units)
- Oxygen (2,108 Units)
- Nitrogen (1,720 Units)
- Sulfur (44 Units)

Then

Making mAbs, part 1



Making mAbs, part 2



Step-by-Step

- Inject antigen into mouse
  - Wait
- Extract spleen
- Culture myeloma cells
- Fuse spleen cells w myeloma cells
- Grow hybrid cells
- Select cells making desired antibody
- Clone selected cell(s)
- Grow in culture

Summary of Differences*

Small Molecule Drugs

- Small (low molecular weight)
- Chemical (organic synthesis)
- Small number of critical steps
- Well-characterized
- Known structure
- Homogeneity
- Low risk of immune response

Biologics

- Big
- Made from living stuff
- Many steps
- Not well-characterized
- Structure not always know
- Heterogeniety
- Risk of immune response

Testing & Oversight

- Process—not product—oriented
- Uncertainty a certainty
- Ever vigilant

Implementing BPCIA

Coverage

- Part B
  - No difference from SM drugs
  - Implications for RP coverage
- Part D

- For formulary requirements (they are the same), Can't add one & remove the other.
- P & T review same as for branded products
- For "transition fills" treated as differentproducts.
- BSims subject to the higher maximum copayments for LIS eligible individuals.
- Not subject to requirement of Part D Coverage Gap Discount Program

Medicaid

- BSims fall under the definition of a single source drug and will be subject to applicable Medicaid Drug Rebates.
- CMS requires that Medicaid prescribers specifically prescribe the biosimilar. CMS recommends that states consider:
  - Adding biosimilars to state supplemental rebate programs.
  - Using DUR and state P&T Committees to educate physicians and pharmacists on appropriate prescribing and dispensing, and
  - Educating prescribers and pharmacists on biosimilars through e-prescribing messaging and point of sale (POS) edits.

CMS, generally

- CMS *will not* treat a BSim as different from RP when it comes to meeting drug access requirements and LIS discounts, but
- *will* treat BSim different drug from RP when it comes to other reimbursement issues, transition fill, and P&T approval.

Reimbursement (PFS)

ASP-based

- Before ASP established:
  - 106 percent of BS's WAC
- After ASP established
  - BS's ASP +
  - 6 percent of RP's ASP

e.g. Zarxio wil be reimbursed by adding its ASP to 6% of ASP for Neupogen

Reimbursement (OPPS)

Identity

- Coding for BSims
  - Product 1, 2, …..?
- EU
  - INN recommendations
- Industry
  - Forum
- FDA
- Current state

So What?

Expectations in the short term

Implications for Cancer Care

- Incentive structure
  - Industry
  - Plans
  - Providers
- Costs of care
  - How much, how soon
- Patient access
  - To what?
- Running your practice

Summary

- Too many barriers for quick uptake
- Not many implications (as long as safe)
- Other forces more likely to define impact