



Office of Biotechnology Products

Site Visit Cellular, Tissue, and Gene Therapies Advisory Committee Meeting July 26, 2016

Steven Kozlowski, Director, OBP
Edward Max, Assoc. Dir. Research, OBP



**Office of Biotechnology Products:
Therapeutic Proteins**

Rituxan

Monoclonal Antibodies

Enzymes

Fabrazyme

ReoPro

**mAb Fragments
Fab, sFv, diabodies**

Cytokines

Avonex

Adcetris

**mAb Conjugates
Radionuclide, drug, toxin**

Growth Factors

Epo

Enbrel

Fc-Fusion Proteins

Toxins

Botox

Office of Biotechnology Products (OBP)

Steven Kozlowski, MD, *Director*

Jeffrey Baker, *Deputy Director*

Edward Max, MD, PhD, *Assoc Dir Research*

DBRR I

Kathleen Clouse, PhD
Director

DBRR II

DBRR III

DBRR IV

Gibbes Johnson, PhD
Director

**Lab of Molecular and
Developmental Immunology**

Lab of Immunology

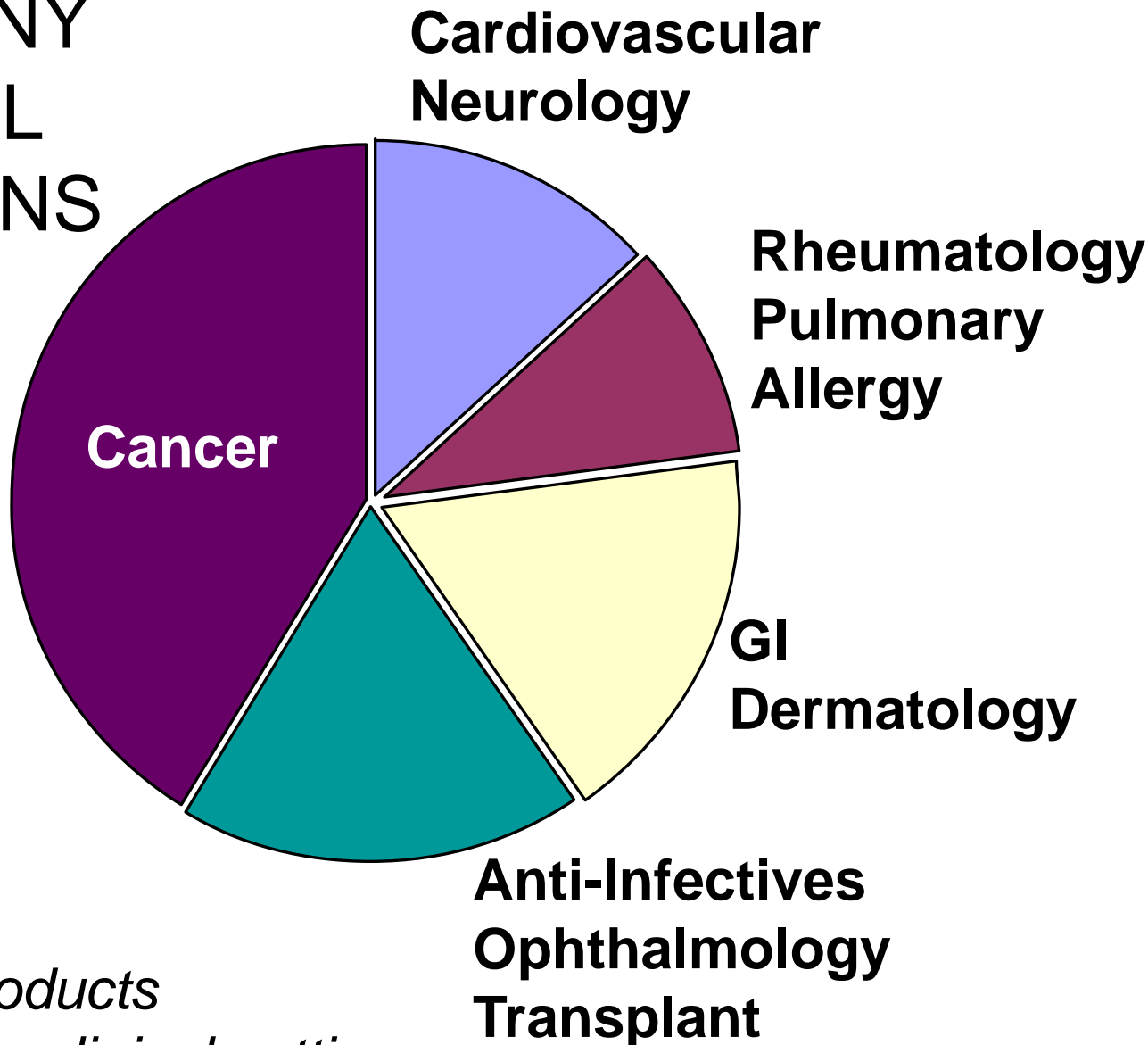
Lab of Molecular Oncology
Wendy Weinberg, PhD, *Chief*

Lab of Biological Chemistry
Serge Beaucage, PhD, *Chief*

Wen Jin Wu, PhD
PI

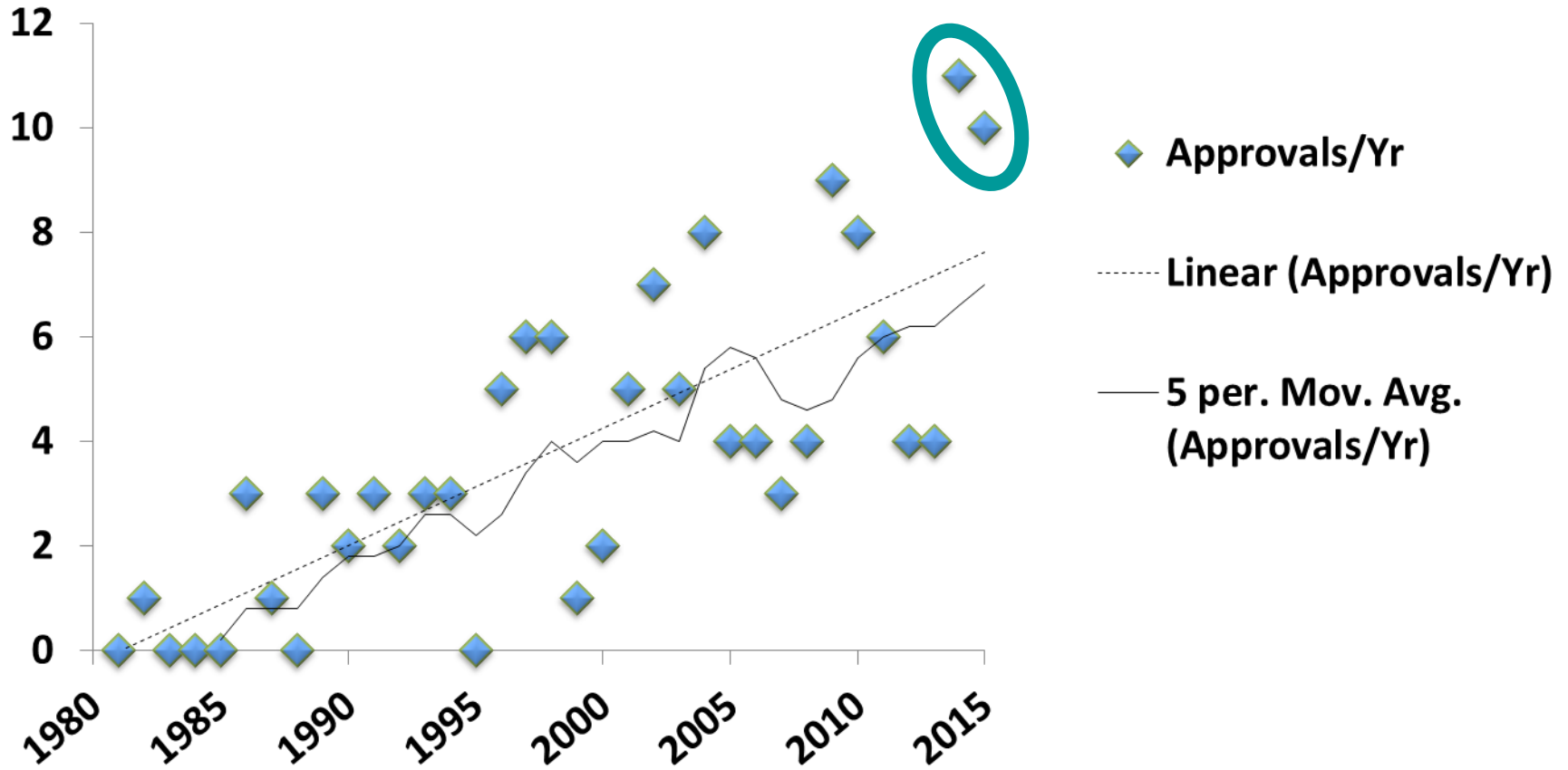
Baolin Zhang, PhD
PI

OBP PRODUCTS HAVE MANY CLINICAL INDICATIONS



*Non-cancer
indications
expanding;
Biotechnology products
being used in new clinical settings*

OBP Product Approvals/Year



2014-2015 Approvals

Trade Name	NP name	Indication Summary	Target or protein	Class
Zarxio	filgrastim-sndz	Neutropenia	GCSF	Cytokine
Plegridy	peginterferon beta-1a	Multiple Sclerosis	IFN bet	Cytokine
Strensiq	asfotase alfa	Hypophosphatasia		Enzyme
Kanuma	sebelipase	Wollmans Disease LAL Deficiency		Enzyme
Vimizim	Elosulfase alfa	Morquio A MPS IV a		Enzyme
Blincyto	blinatumomab	Ph- B cell ALL		Bispecific ab
Entyvio	vedolizumab	Inflammatory b		Mab
Darzalex	daratumumab	Multiple		Mab
Praxbind	idarucizumab	D	abigatran	Mab
Unituxin	dinutuximab		GD2	Mab
Cosentyx	secukinumab		IL-17	Mab
Nucala	memorizumab	asthma	IL-5	Mab
Sylvant	reslizumab	ase	IL6	Mab
Praluent	evolocumab	some clinical CVD	PCSK9 (proprotein conve	Mab
Repatha	alirocumab	PH or some clinical CVD	PCSK9 (proprotein conve	Mab
Opdivo	nivolumab	Metastatic myeloma & squamous NSCLC	PD-1	Mab
Keytruda	pembrolizumab	Non-small cell lung cancer	PD-L1	Mab
Cyramza	ramucirumab	Cancer (lung, gastric, colorectal)	VEGF-R2	Mab
Tanzeum	albiglutide	Type 2 Diabetes	GLP-1 agonist	Met. Hormone
Trulicity	dulaglutide	Type 2 Diabetes	GLP-1 agonist	Met. Hormone
Myalept	Metreleptin	Generalized lipodystrophy	leptin	Met. Hormone

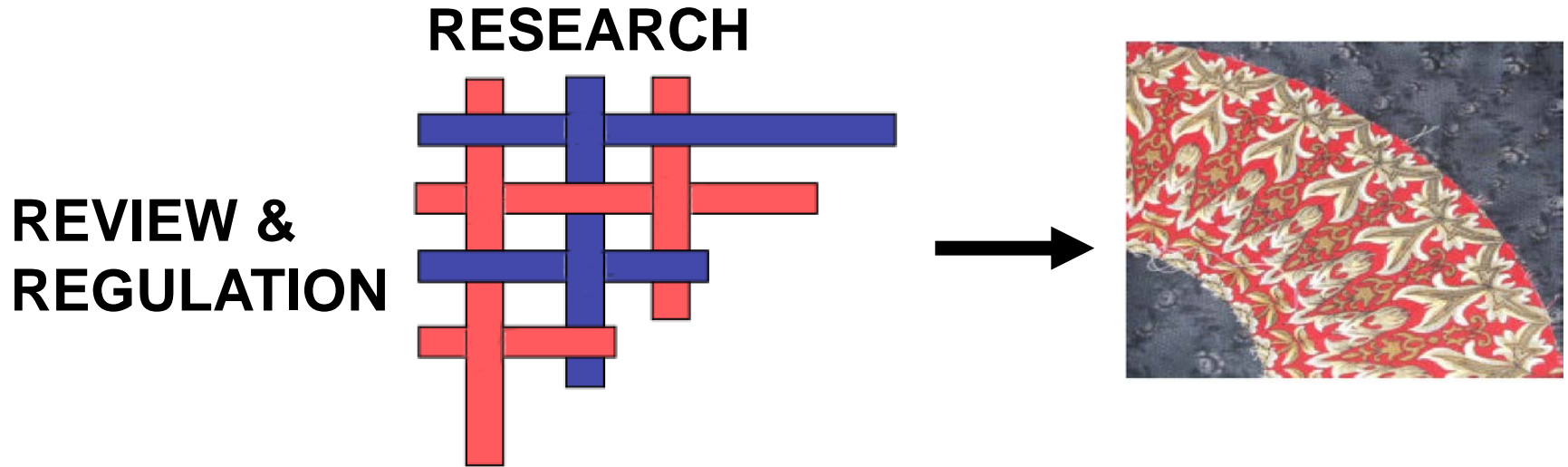
**2/3 Priority Review
11+ orphan drugs**

Challenges in OBP Product Review

- **Variety of Cell Substrates**
microbiology (virus, prion), host cell molecules
- **Heterogeneity**
glycosylation, oxidation, PEGylation
- **Higher order structure : structure**
receptor interaction and
- **Manufacturing Issues**
scale-up, selection
- **Mechanism of action** sometimes unclear
activity/potency assays
- **Immunity:**
safety and efficacy Issues
- **Comparability:** manufacturing changes
- **Counter Bioterrorism:** Animal Rule, stockpiles

BIOSIMILARS

Goals of OBP Research



- Protein manufacturing science
- Protein structure/function analysis
- Mechanism of action
 - Bioassays, Biomarkers, etc.
 - Drug resistance and toxicity
- Immunogenicity, Adventitious Agents
- Emergent problems: MCM, contamination, counterfeit

Researcher/Reviewer Model



Researcher/Reviewer Model

Advantages for all reviewers

- **Scientific knowledge to evaluate:**
 - Mechanisms of action
 - Potency assays
 - Adverse events
 - Drug-drug interactions
- **Hands-on technical experience**
 - State-of-the-Art science
 - Product development
 - Analytical techniques
 - Manufacturing methods

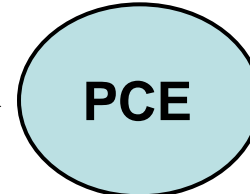
Research Career Paths

Temporary

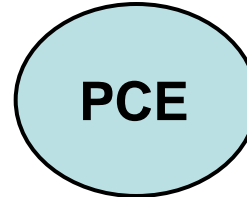
Permanent



→
7
years



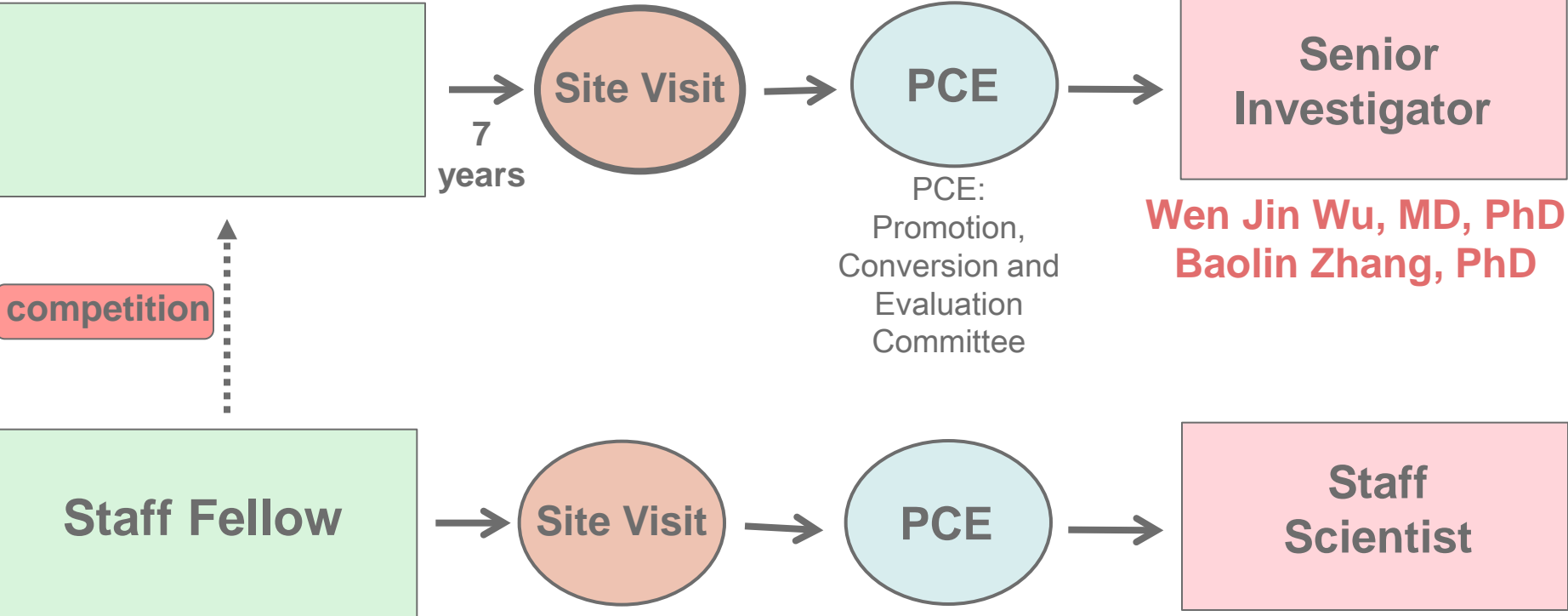
PCE:
Promotion,
Conversion and
Evaluation
Committee



Research Career Paths

Temporary

Permanent



Site-Visit Team: Evaluate individual PIs and Staff Fellows in a Laboratory Unit

- RESEARCH accomplishments since last review cycle
- RESEARCH proposals for next four years
 - Novelty and originality
 - Mission Relevance
 - Independence of the candidate
 - Productivity *relative to research support available and time for research: about 50%*
- Administrative/Management comments welcome
- Regulatory activities and regulatory work quality NOT assessed by Site Visit Team

Thank you!

To the Site Visit reviewers for your
time, expertise, and suggestions
to improve OBP's research programs

Your input is critical to fulfilling our
regulatory mission!