Overview and Current Status of the BsUFA III Regulatory Science Program

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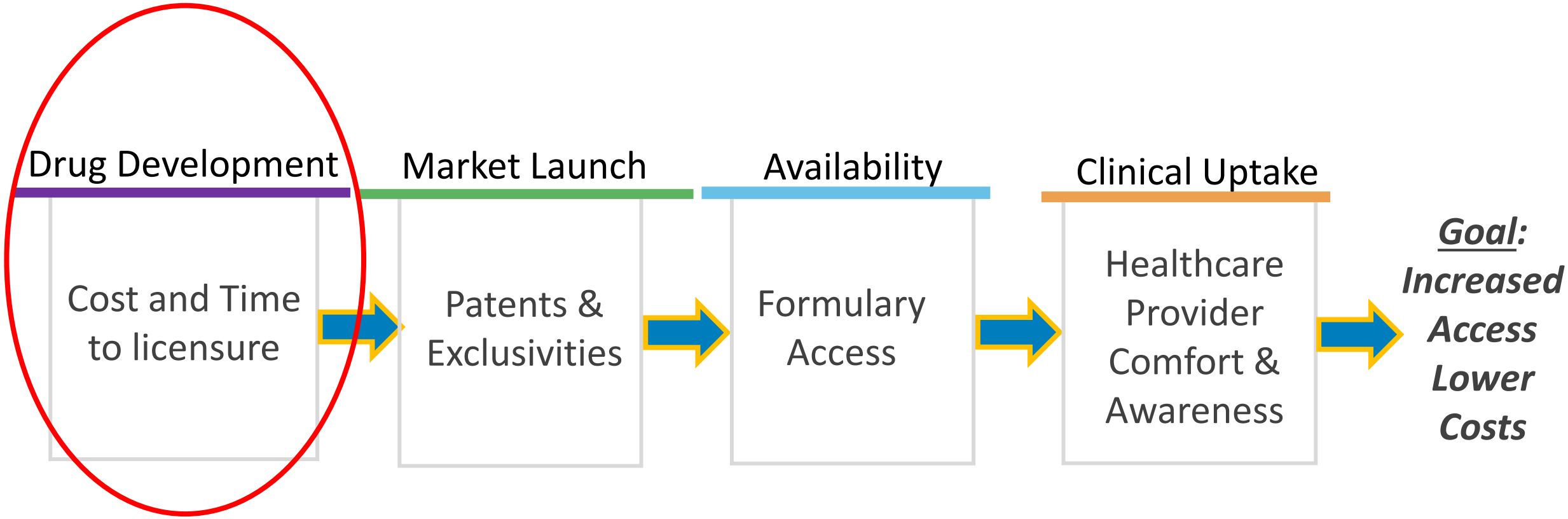
SBIA BsUFA III Regulatory Science Pilot Program October 16, 2023

Challenges and Barriers for Biosimilars in the U.S.



Biosimilars in the United States 2023-2027 – IQVIA
https://www.biosimilarscouncil.org/wp-content/uploads/2019/09/AAM-Biosimilars-Council-Failure-to-Launch-2-web.pdf
Comparison of Uptake and Prices of Biosimilars in the US, Germany, and Switzerland | Clinical Pharmacy and Pharmacology | JAMA Network Open | JAMA Network
Biosimilar Cost Savings in the United States | RAND
https://www.cardinalhealth.com/content/dam/corp/web/documents/Report/cardinal-health-2022-biosimilars-report.pdf

Establishing Biosimilarity

"no clinically meaningful differences"

- Comparative Clinical Studies
- Clinical Pharmacology
- Comparative Analytical Assessment
- Product Quality

"highly similar"

Wikipedia Commons, Owen Lloyd, AJseagul

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BsUFA III Regulatory Science Commitment

FDA is committed to enhancing regulatory decision-making and facilitating science-based recommendations in areas foundational to biosimilar development.

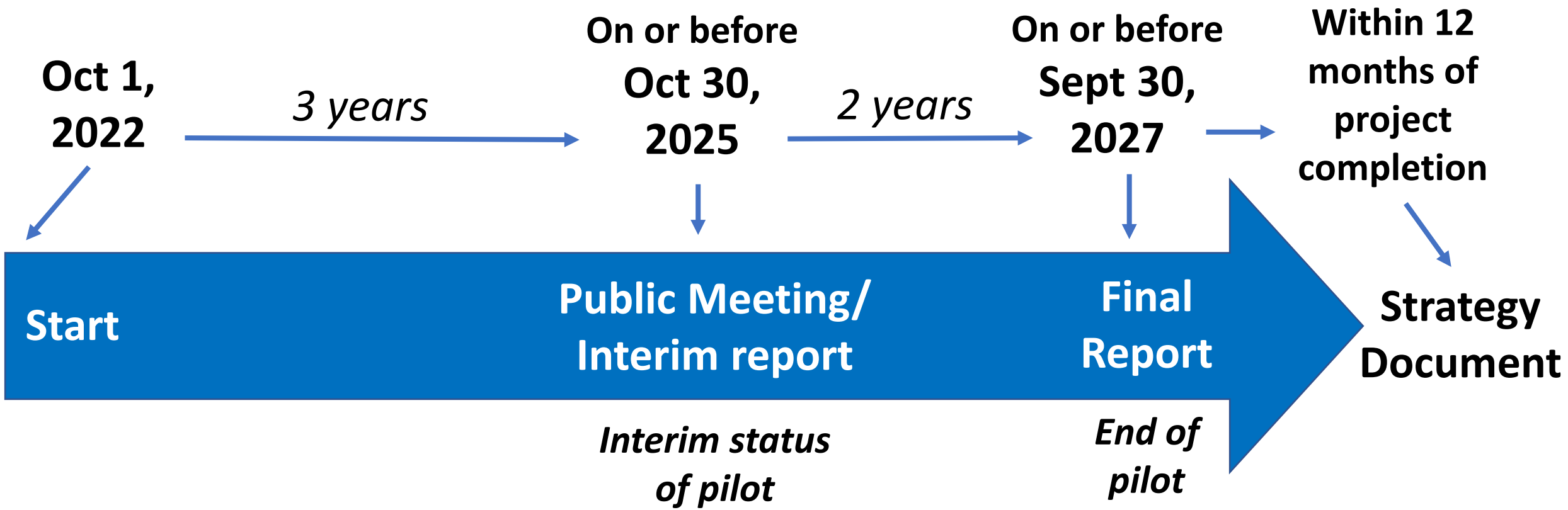
FDA will pilot a regulatory science program to facilitate ways to

(1) improve the efficiency of biosimilar product development and

(2) advance the development of interchangeable products.

Commitment Letter

Regulatory Science Pilot Program Deliverables



Regulatory Science Pilot Program Goals Focus on Composition of the 351 (k) Data Package

Current
"Abbreviated": 351(k) BLA

- Comparative Clinical Studies
- Clinical Pharmacology
- Animal
- Comparative Analytical Assessment
- Product Quality

Program Experience

Policy Development

Regulatory Research

Potential Future
"Abbreviated": 351(k) BLA

- Comparative Clinical Studies
- Clinical Pharmacology
- Animal
- Comparative Analytical Assessment
- Product Quality

Regulatory Impact #1: Increase the accuracy and capability of analytical (structural and functional) and CMC characterization

a. Define and **standardize approaches** for assessing and reporting product quality attributes

b. Characterize relationships between product quality attributes and clinical outcomes

c. Improve on and/ or develop new analytical technologies

d. Assess the impact of differences of biosimilar and reference **product presentations** (e.g., delivery device) and container closure systems on product protection, safety, compatibility, and performance

https://www.fda.gov/media/164751/download

Regulatory Impact #2: Develop alternatives to and/ or reduce the size of studies involving human subjects

e. Develop **alternatives to the comparative immunogenicity** assessment currently conducted as part of the comparative clinical study

f. Develop **alternatives to the comparative immunogenicity** assessment currently conducted as part of the switching study

g. Develop alternatives to **clinical bridging data** from a non-US approved comparator

h. Increase use of **pharmacodynamic (PD) biomarkers** instead of or in conjunction with clinical endpoints

i. Clarify which **user interface differences** that are likely to affect the safe and effective use of interchangeable products

j. Define **methodologies** to assess differences in **user interfaces** that may lead to differences in safe and effective use of interchangeable products

https://www.fda.gov/media/164751/download

Research Outcome and Regulatory Impact Reporting Structure

Regulatory Impacts: Priorities

1. Increase the accuracy and capability of analytical (structural and functional) and CMC characterization
   a. Define and standardize approaches
   b. Characterize relationships
   c. Improved/new technologies
   d. product presentations

2. Develop alternatives to and/or reduce the size of studies involving human subjects
   e. Alternatives to the comparative clinical immunogenicity
   f. Alternatives to the comparative immunogenicity in switching studies
   g. Alternatives o clinical bridging data for use of a non-US comparator
   h. Increase use of PD instead of clinical endpoints
   i. Identify high risk user interface differences
   j. Methodologies to assess user interfaces for interchangeables

Research Roadmap under revision!

Demonstration Projects

- Advancing the development of interchangeable products
- Improve the efficiency of biosimilar product development

Methods to Consider

Analytical Methods

Biological Assays

Efficient clinical design

Model-informed drug development

In silico/in-vitro modeling

Machine Learning/ AI

Real World Evidence/ Data

Pharmacological studies

External Projects Funded by BsUFA III Pilot Program:

Increase the accuracy and capability of analytical characterization

Funding Year	Institution	Title
FY22	NATIONAL INSTITUTE FOR PHARM TECH/EDUC	**Platform for reliable characterization and evaluation of comparability of biosimilar drug products in lyophilized and liquid formulations**
FY22	U.S. PHARMACOPEIA	**Assessment of the performance of MAM vs conventional QC methods for evaluation of Product Quality Attributes of adalimumab and etanercept**
FY22	UNIVERSITY OF MICHIGAN AT ANN ARBOR	**Systematic Analytical Characterization of Innovator and Biosimilar Products with the Focus on Post-translational Modifications**

Internal Projects Funded by BsUFA III Pilot Program:

Increase the accuracy and capability of analytical characterization

Project Title
Bioassay - Enhanced biosimilar testing capabilities
Landscape assessment of biosimilar submissions (analytical, PK, PD, and comparative studies)
Establishment of A Feasible Method to Quantify Major Glycoforms of Human IgG1 mAb Drugs and their Biosimilars in Culture Media as a Component of Process Analytic Technology
OnePotGlycan - A chemoenzymatic method for simultaneous profiling of N and O-glycans in one-pot

External Projects Funded by BsUFA III Pilot Program:

Develop alternatives to and/or reduce the size of studies involving human subjects

Funding Year	Institution	Title
FY22	ACADEMY OF MANAGED CARE PHARMACY, INC.	**Improving the Efficiency of Regulatory Decisions for Biosimilars and Interchangeable Biosimilars by Leveraging Real-World Data**
FY22	EPIVAX, INC.	**ISPRI-HCP: CHO protein impurity immunogenicity risk prediction for improving biosimilar product development and assessing product interchangeability**
FY23	ACADEMY OF MANAGED CARE PHARMACY, INC.	**Bridging the Gap: Using Foreign Real-World Data to Inform Interchangeable Biosimilar Approvals**

Internal Projects Funded by BsUFA III Pilot Program:

Develop alternatives to and/or reduce the size of studies involving human subjects

Project Title
Validation of a non-clinical immunogenicity model
IIRMI Assay Standards - Develop acceptance parameters and standards for the Innate Immune Response Modulating Impurities (IIRMI) assays in the biosimilar space
Addressing fundamental issues for in vitro immunogenicity testing
Production & optimization of humanized mice
Translating Clinical Pharmacology Biosimilar [PD Biomarker] Research Findings into Best Practices for Industry and FDA Review Staff
Evidence-based approach to the design of clinical pharmacology studies
Critical Factors for Standardization and Accuracy of PK Assays of PEGylated Biosimilars

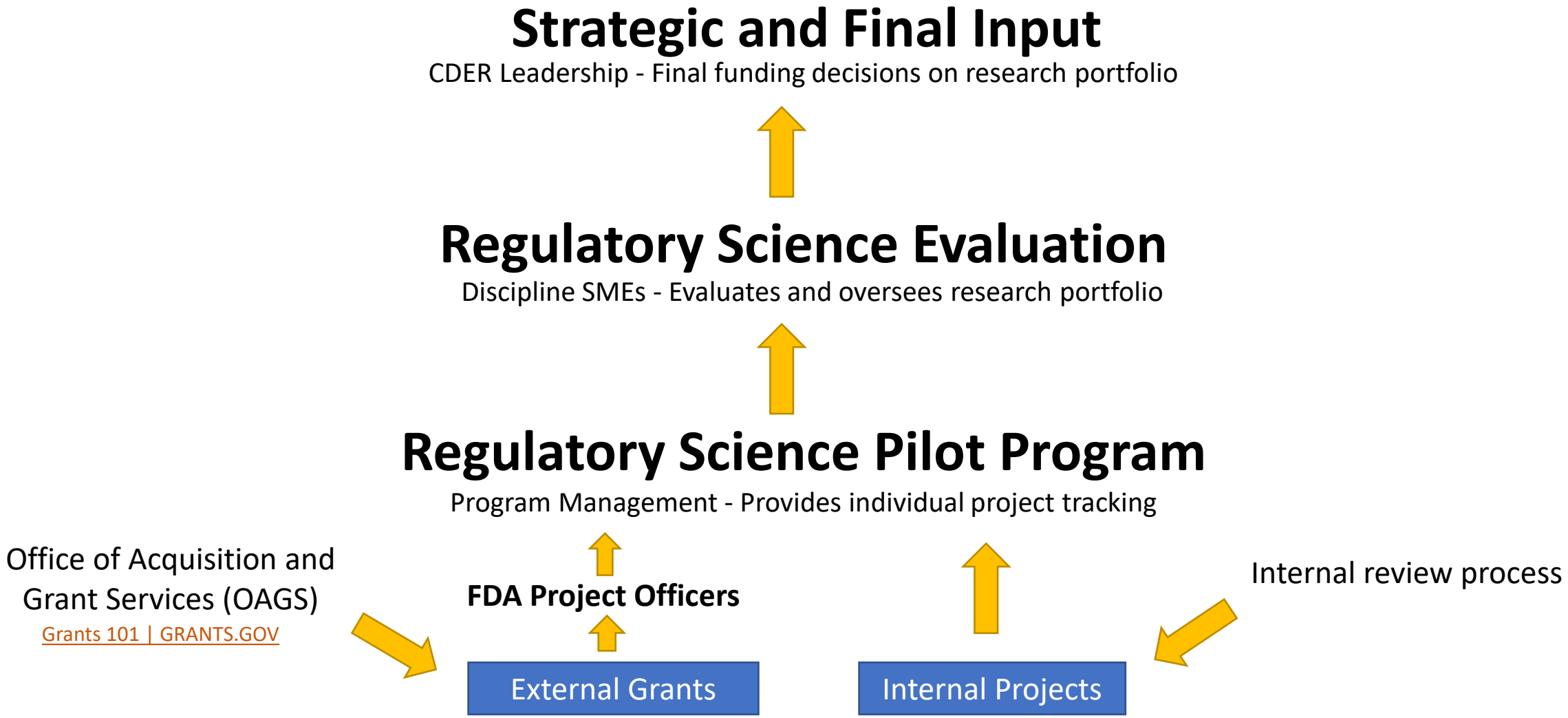
Research Priorities Addressed by Awarded Funds

Internal (FY24)	■	■	■		■	■		■		
Internal (FY23)	■	■	■		■					
External (FY23)						■				
External (FY22)	■		■	■	■	■				
Research Priorities	**A:** Standardize CAA	**B:** Clin outcome of PQA	**C:** Improve methods for CAA	**D:** Impact of device/ contain closure	**E:** Predict immunog. for CCS	**F:** Predict immunog. for switching	**G:** Non-US-comparat. bridging	**H:** PD biomarkers	**I:** Impact of user interface on interchang.	**J:** Methods to assess user interface

Enhance the efficiency of the analytical and CMC characterization

Develop alternatives to and/or reduce the size of studies involving human subjects

BsUFA III Reg Sci Program Operational Structure & Decision Making



External Funding Processes

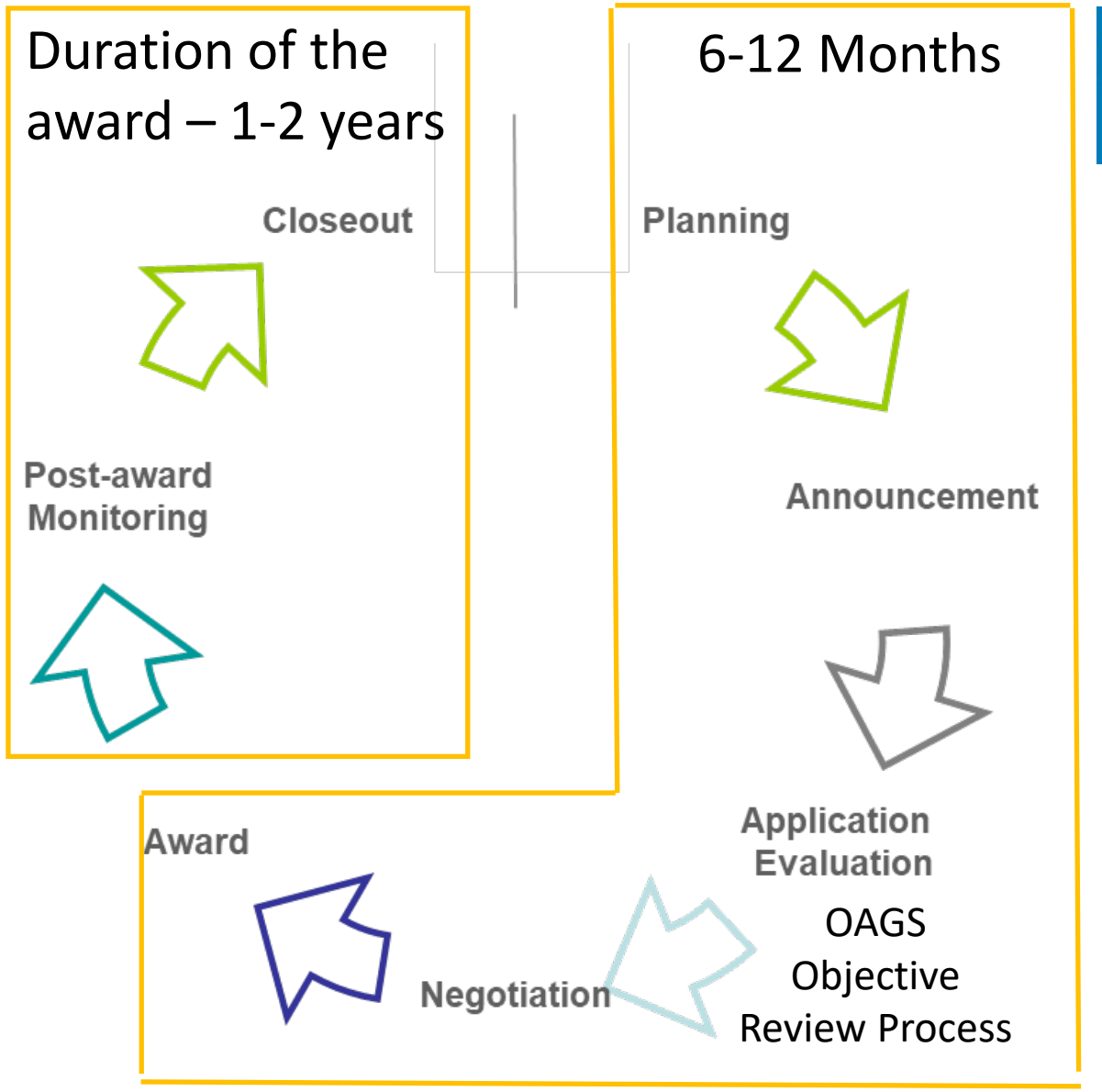
BAA

FDA funds extramural research through an agency-wide Broad Agency Announcement (BAA)

FY24 FDA Broad Agency Announcement (BAA) for Advanced Research and Development of Regulatory Science
FDABAA-24-00123
SAM.gov

The FY24 Announcement includes Biosimilar Regulatory Science Language

OAGS



Adapted from FDA Office of Acquisition & Grants Services (OAGS)

Grants 101 | GRANTS.GOV

Additional Information

For information, please reach out to:

- BsUFA Reg Sci Program

Resources:

- Biosimilars | FDA
- Biosimilars | Science and Research | FDA

Thank you!