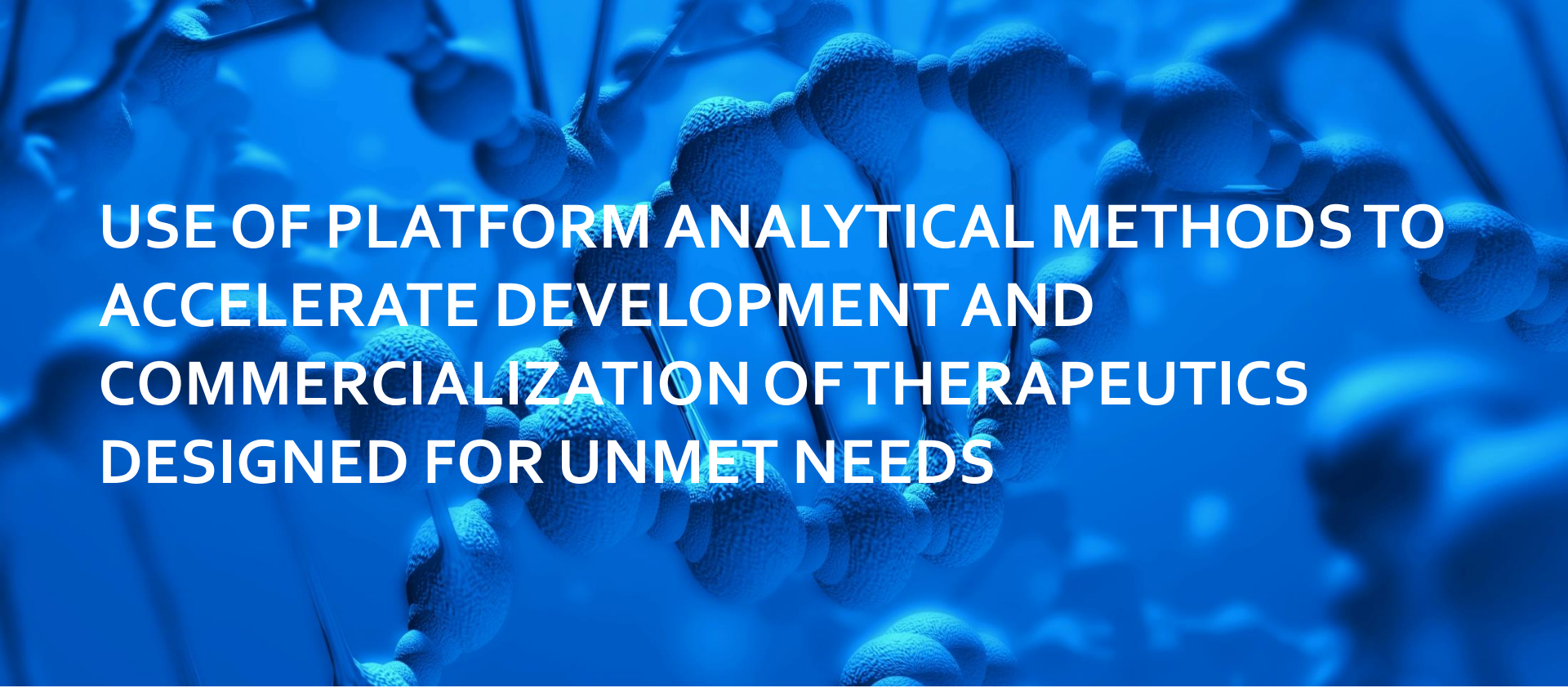


USE OF PLATFORM ANALYTICAL METHODS TO ACCELERATE DEVELOPMENT AND COMMERCIALIZATION OF THERAPEUTICS DESIGNED FOR UNMET NEEDS

TAMER ERIS

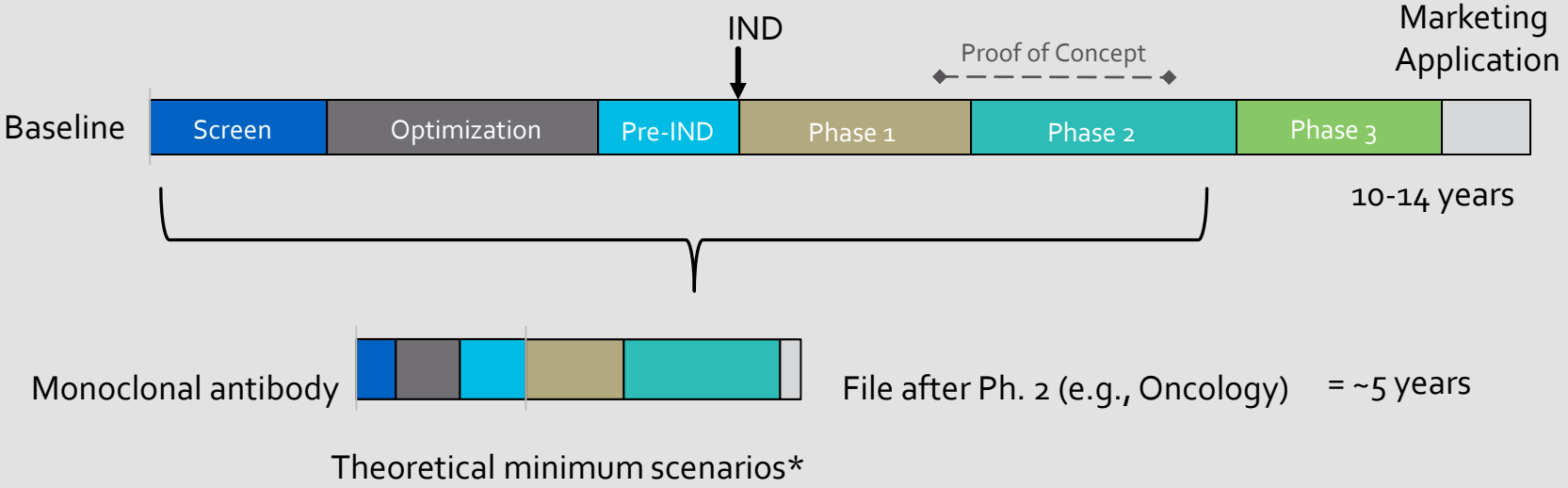
CASSS WCBP FEB 1ST, 2021

AMGEN®

PRESENTATION OVERVIEW

- Standard vs Accelerated Biologic Development Timeline
- Platform Analytical Methods
  - Method Performance Expectations
  - Fit-to-Platform Assessment
- Application of Analytical Platforms to Enable Speed
  - Candidate Screening/Molecule Selection
  - Speed to Tox and FIH studies
  - Commercialization Activities
  - Hypothetical 12 Month COVID mAb Development Timeline

DEVELOPMENT OF THERAPEUTICS CAN BE ACCELERATED SIGNIFICANTLY WITH UNLIMITED RESOURCES

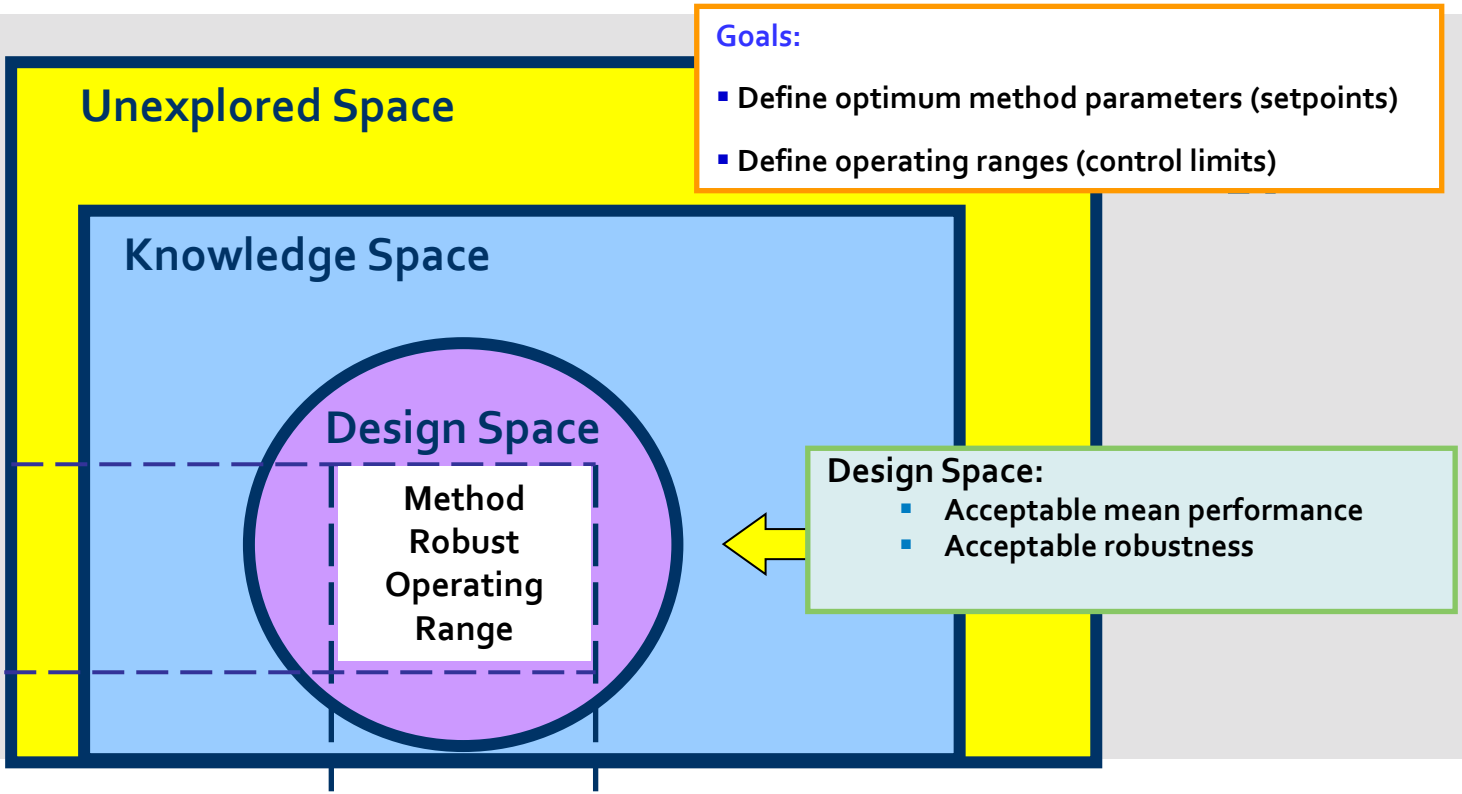


***Theoretical minimums scenarios (unlimited resources, immediate decision making)**

Source: CMR International, a Thomson Reuters business
Baseline data from CMR database 2006 - 2015

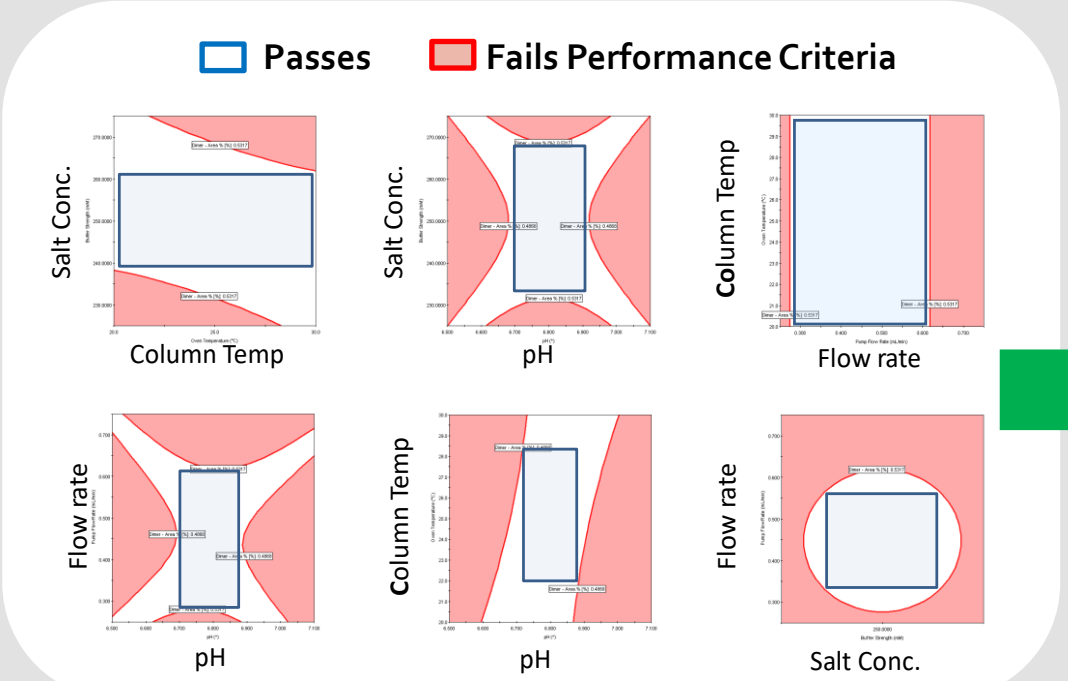
AMGEN

DEVELOPMENT OF ROBUST NEW METHODS REQUIRES SIGNIFICANT TIME & RESOURCE INVESTMENT



AMGEN

DEVELOPMENT OF PLATFORM METHODS UTILIZE DOE BASED APPROACHES TO IDENTIFY ROBUST METHOD OPERATING RANGES



HPLC Operating Parameters Assessed
Buffer pH
Flow rate (mL/min)
Column Temperature (°C)
Salt Conc. (mM)

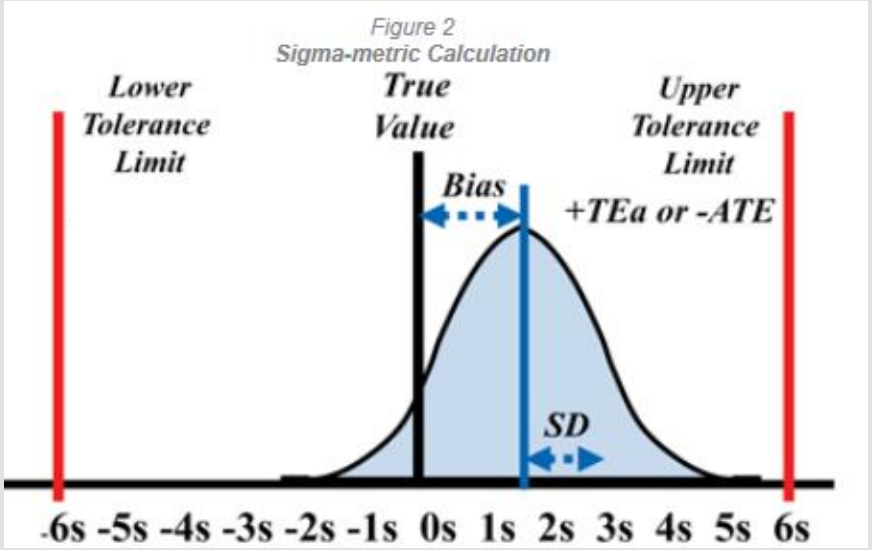
Robust Method Operating Parameters identified

Platform method performance evaluated across multiple products to identify robust method operating parameter ranges

AMGEN

METHOD PERFORMANCE TARGETS BASED ON TOTAL ANALYTICAL ERROR SUPPORT EVALUATION OF PLATFORM METHOD SUITABILITY

Total Analytical Error (TAE) - Targets for Accuracy and Precision are dependent on each other



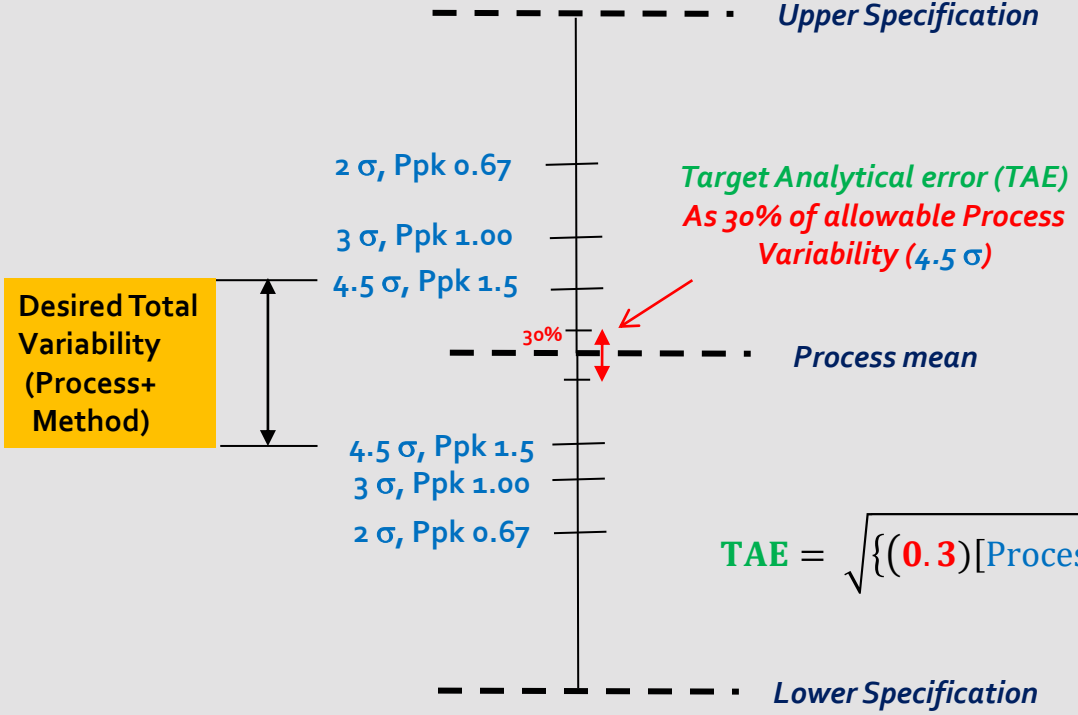
https://www.aacc.org/publications/cln/articles/2013/september/total-analytic-error

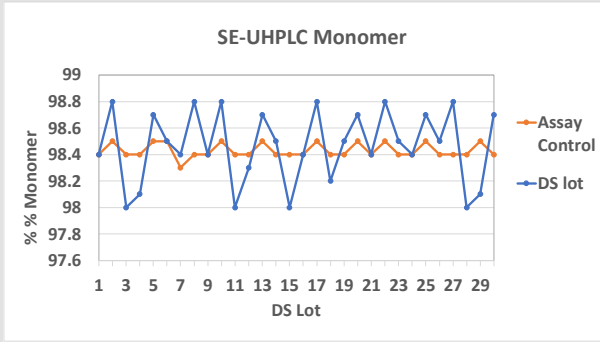
If Accuracy (of process, method, or both) is poor, we have less room for variability

If Precision (of process, method, or both) is poor, must be very Accurate

AMGEN

ASPIRATIONAL METHOD PRECISION TARGETS ENABLE PROCESS MONITORING AND APPROPRIATE SPECIFICATION SETTING



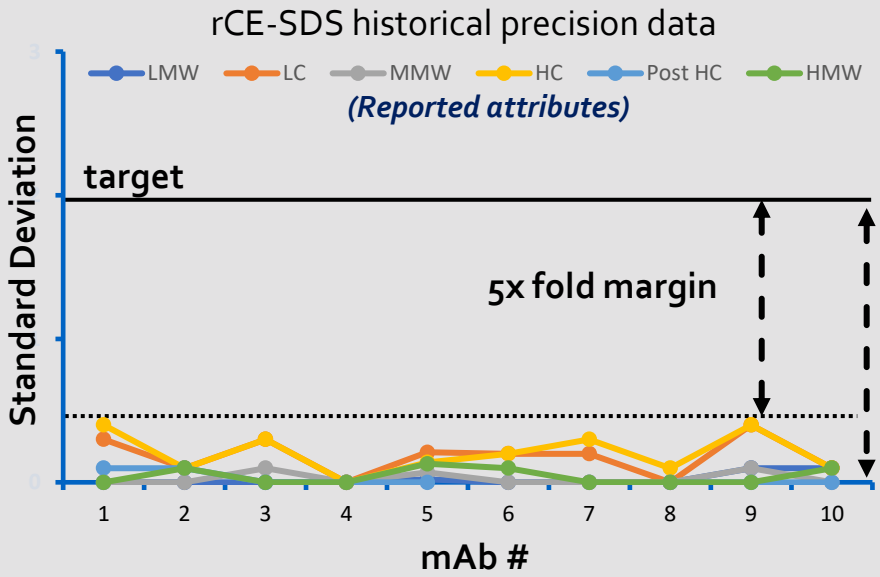


Platform SE-UHPLC method is fit-for-purpose for monitoring Process Variability

$$\mathbf{TAE} = \sqrt{\{(\mathbf{0.3})[\text{Process SD Target}]^2\}}$$

Desired State: Target Analytical (method) error (variance) (TAE) will be limited to ≤ 30% of the allowable Process Variance

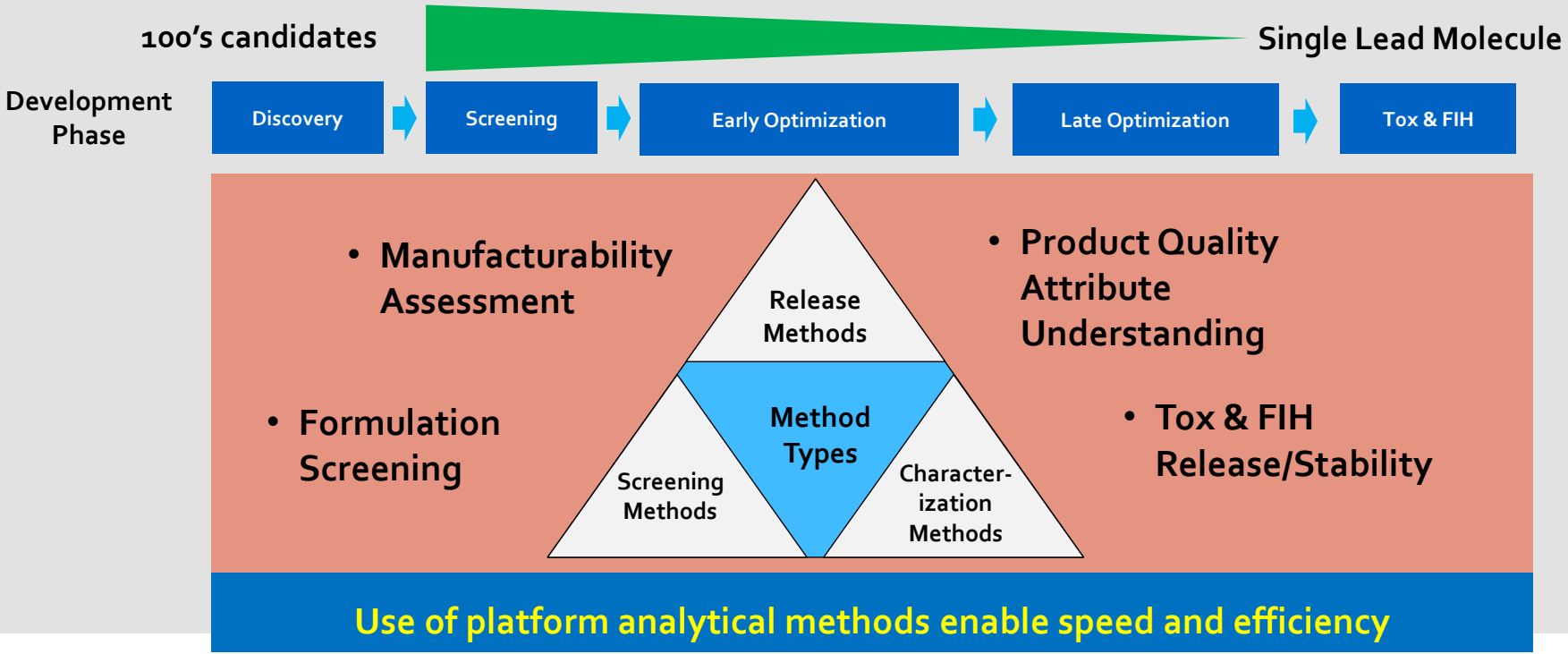
PRIOR KNOWLEDGE FROM PLATFORM METHOD QUALIFICATIONS DEMONSTRATES FIT-FOR-PURPOSE FOR TESTING MAB MODALITY



Performance Parameter	Early Phase Method Qualification Strategy
Specificity	Verify for each new mAb
Repeatability	
LOD/LOQ	
Intermediate Precision	Use Prior knowledge from mAb modality
Linearity	
Accuracy	

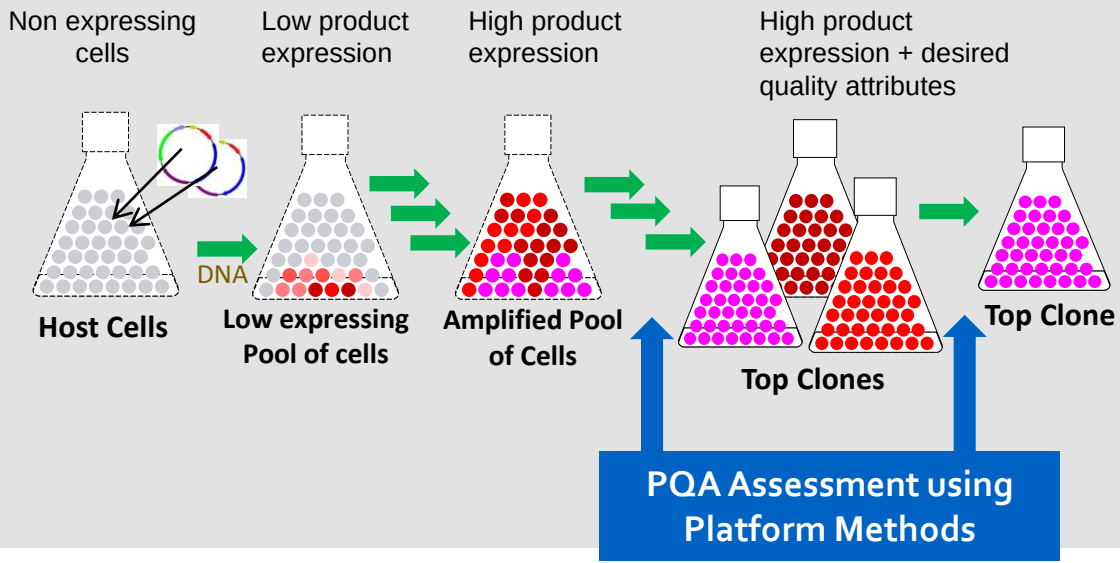
Consistent/acceptable method qualification results were observed across 10 mAb products using platform rCE-SDS method

MULTIPLE METHOD TYPES ARE EMPLOYED TO DRIVE MOLECULE SELECTION AND DELIVER PRODUCT TO CLINIC



PLATFORM METHODS ARE UTILIZED TO SELECT CLONE EXPRESSING DESIRED PRODUCT QUALITY ATTRIBUTES (PQAs)

Transfection → Pool Selection → Amplification → Subcloning & screening

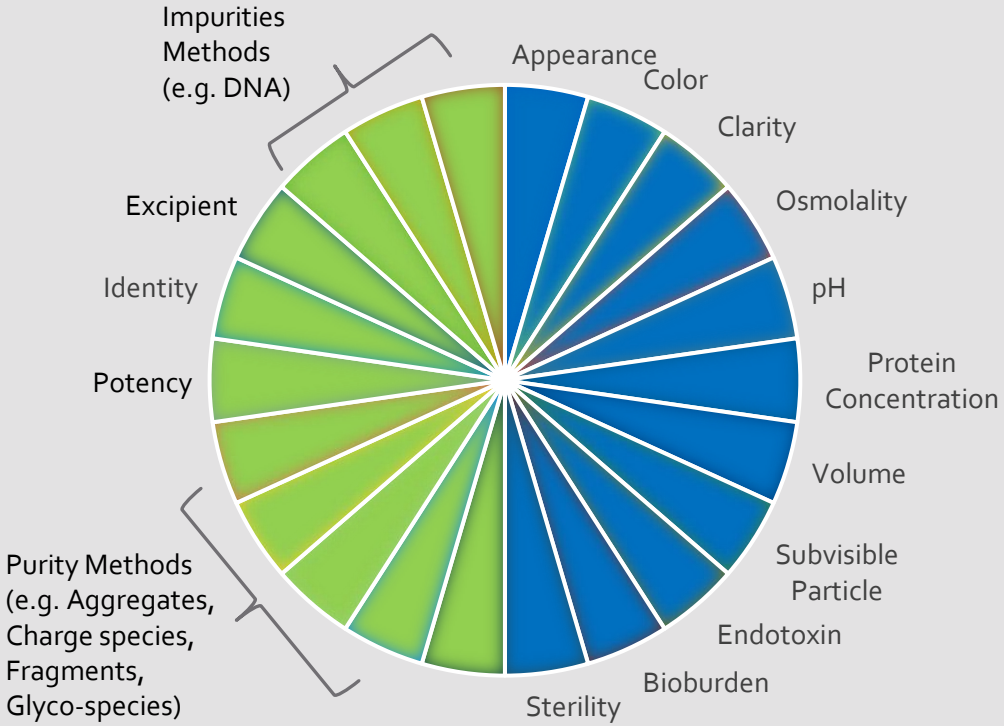


Monoclonal Antibody (mAb) Platform Methods for Clone Selection

Platform Method	Typical Attribute	Target
Titer UHPLC	Product Expression	> X g/L
SE-UHPLC	Aggregates	< X%
Glycan map	High Mannose	<X%
	Afucosylated	<X%
	Sialylated	<X%
CE-SDS	Fragmentation (Clips)	< X%
	Non-Glycosylated HC	< X%
MAM (LC/MS quantitative Peptide map)	CDR Deamidation/ CDR Oxidation	<X%
	Mutations	<X%

AMGEN

TYPICAL MONOCLONAL ANTIBODY (MAB) QC RELEASE TEST PANEL LEVERAGES PLATFORM METHODS



Product Specific Platform Methods

- Modality Specific Platform (e.g. mAb SE-UHPLC)
- General Platform (e.g. Excipient)
- Cell Line Platform (e.g. CHO DNA)

Compendial Platform Methods

AMGEN®

NEW MAM* PLATFORM METHOD INCREASES EFFICIENCY AND PROVIDES IMPROVED ATTRIBUTE SPECIFIC CONTROL STRATEGY

Current Method	Attribute	Proposed Method
rCE-SDS	Purity - Clips	Multi-Attribute Method (MAM) Quantitative LC/MS Peptide Map
CEX-HPLC	Purity – Charge Variants	
Glycan Map	Glycans	
Immunoassay	Identity	


HPLC-FLD (Glycan-map)
- Data
- Report
- LIMS


HPLC-UV (CEX-HPLC)
- Data
- Report
- LIMS


CE-UV (rCE-SDS)
- Data
- Report
- LIMS


Platereader (immunoassay)
- Data
- Report
- LIMS

MAM replaces four instrument types


UPLC/MS (MAM)
- Data
- Report
- LIMS

Multi-Attribute-Method (MAM*) is being advanced to late stage filings

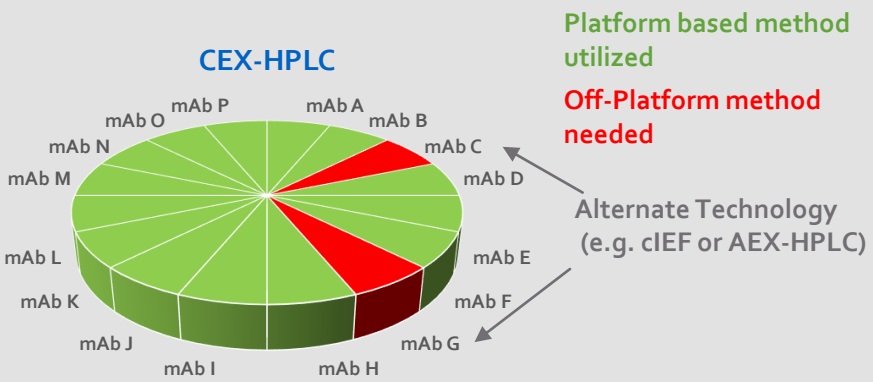
FIT-TO-PLATFORM ASSESSMENT DEMONSTRATES GOOD FIT OF PLATFORM METHODS ACROSS MULTIPLE MAB PRODUCTS

Method Component	Platform Method Parameter	mAb A Method
Technology	Technology Type (e.g. CEX-HPLC)	√
Materials & Equipment	Parameter 1	√
	Parameter 2	√
	Parameter 3	√
	Parameter 4	√
	Parameter 5	√
	Parameter 6	√
	Parameter 7	√
	Parameter 8	√
	Parameter 9	√
	Parameter 10	√
	Parameter 11	√
	Parameter 12	√
	Parameter 13	√
Method Execution	Parameter 1	√
	Parameter 2	√
	Parameter 3	√
	Parameter 4	√
	Parameter 5	√
	Parameter 6	X
	Parameter 7	√
	Parameter 8	√
	Parameter 9	√
	Parameter 10	√
Data Analysis	Parameter 1	√
	Parameter 2	√
	Parameter 3	√
	Parameter 4	√
	Parameter 5	√

Instrument type & configuration, HPLC Column, Buffers, Reagents etc.

Sample Preparation and Method Operating Parameters; e.g. Flow Rate, Column Temp, etc.

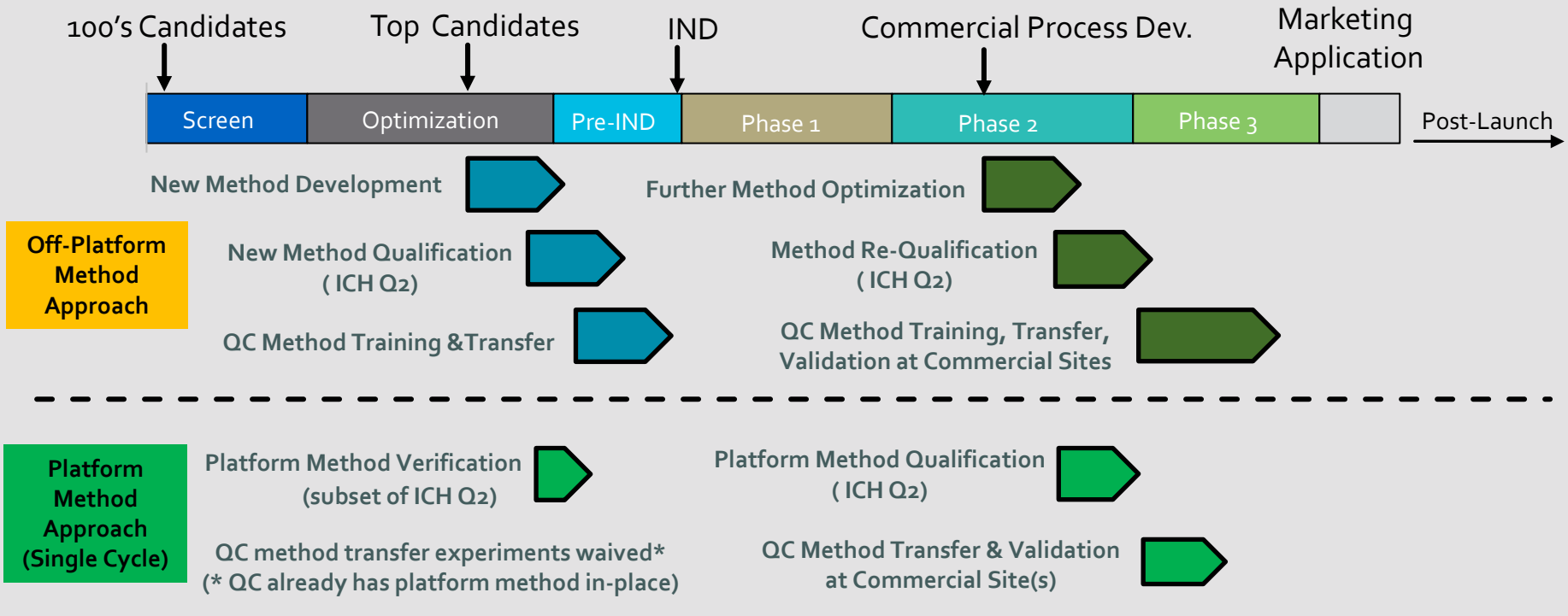
Data Calculations, Results Reporting, System Suitability



mAb A method fits 27/28 parameters = 96% platform Fit

AMGEN

PLATFORM METHODS INCREASE EFFICIENCY AND DECREASE RESOURCES NEEDED FOR PRODUCT DEVELOPMENT



PLATFORM METHODS ENABLE EFFICIENT TRANSFER & VALIDATION OF METHODS ACROSS GLOBAL QC NETWORK

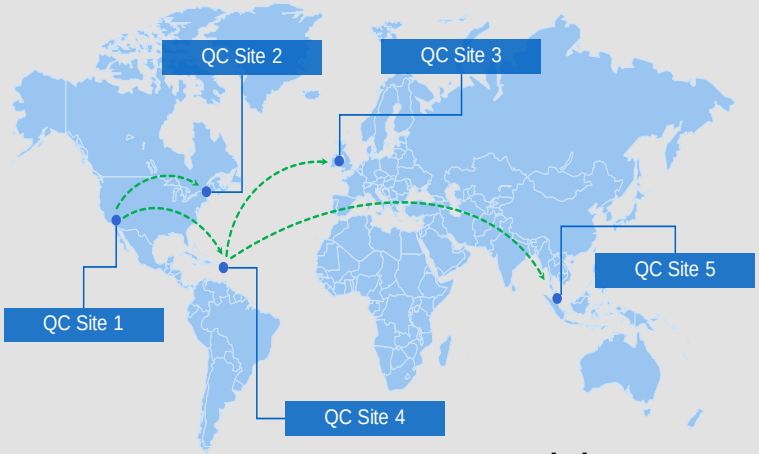
Platform Method Capabilities Exist at QC Sites

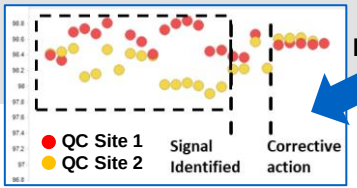
Method Category	Platform Analytical Method	Platform Method Type	QC Site 1	QC Site 2	QC Site 3	QC Site 4	QC Site 5
General	Method 1	Compendial	√	√	√	√	√
	Method 2	Compendial	√	√	√	√	√
	Method 3	Compendial	√	√	√	√	√
	Method 4	Compendial	√	√	√	√	√
	Method 5	Compendial	√	√	√	√	√
	Method 6	Compendial	√	√	√	√	√
	Method 7	Compendial	√	√	√	√	√
	Method 8	Compendial	√	√	√	√	√
	Method 9	General Platform	√	√	√	√	√
Purity	Method 10	mAb Platform	√	√	√	√	√
	Method 11	mAb Platform	√	√	√	√	√
	Method 12	mAb Platform	√	√	√	√	√
	Method 13	mAb Platform	√	√	√	√	√
Potency	Method 14	mAb Platform	√	√	√	√	√
Identity	Method 15	mAb Platform	√	√	√	√	√
Impurity	Method 16	CHO Platform	√	√	√	√	√
	Method 17	CHO Platform	√	√	√	√	√
	Method 18	mAb Platform	√	√	√	√	√
Safety	Method 19	Compendial	√	√	√	√	√
	Method 20	Compendial	√	√	√	√	√
	Method 21	Compendial	√	√	√	√	√

Reduced Method Transfer & Validation Resources for:

- Transfer Planning
- Method Equipment & Materials Procurement
- Transfer & Validation Protocols & Reports
- Analyst Training
- Investigations and troubleshooting new methods

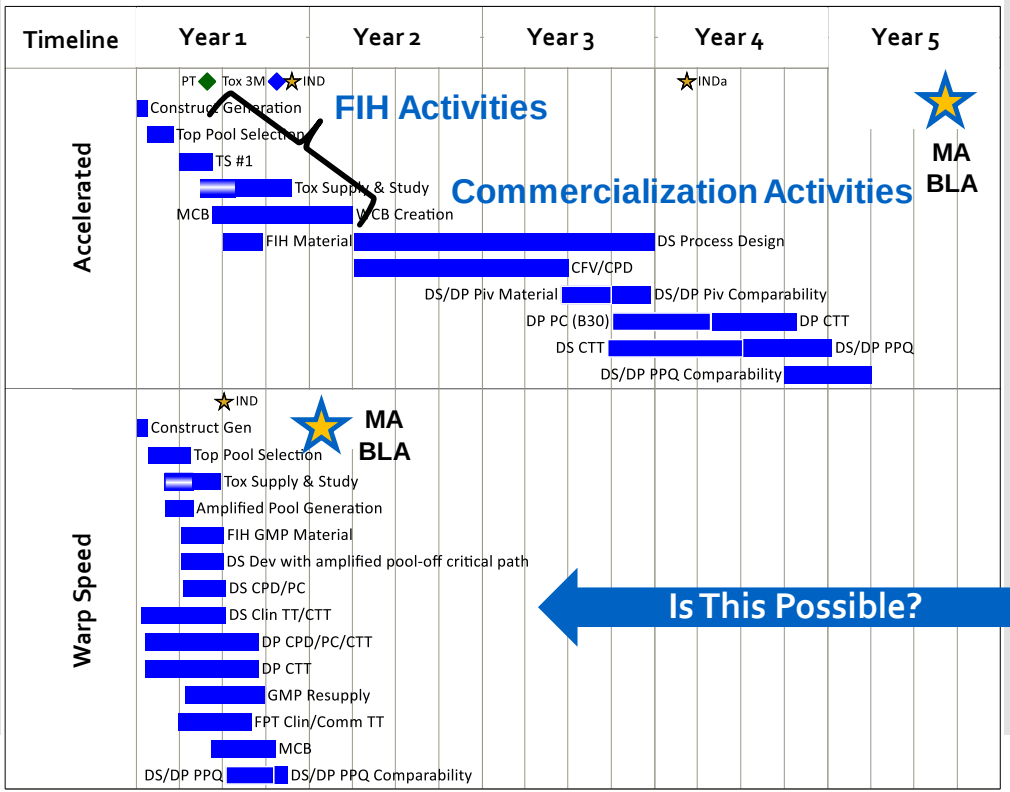
Method Transfers and Validation across Global Manufacturing and QC Network

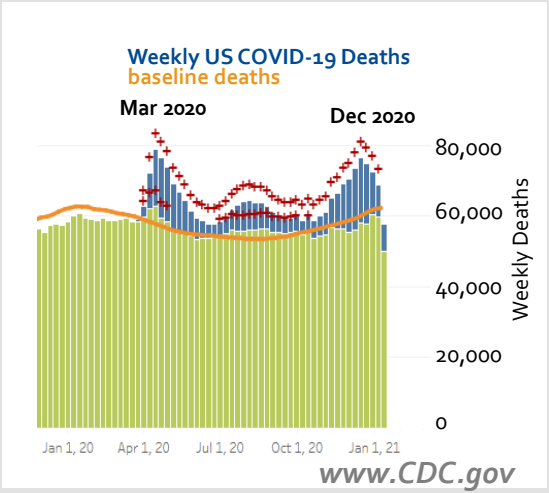




Real time method trending across sites

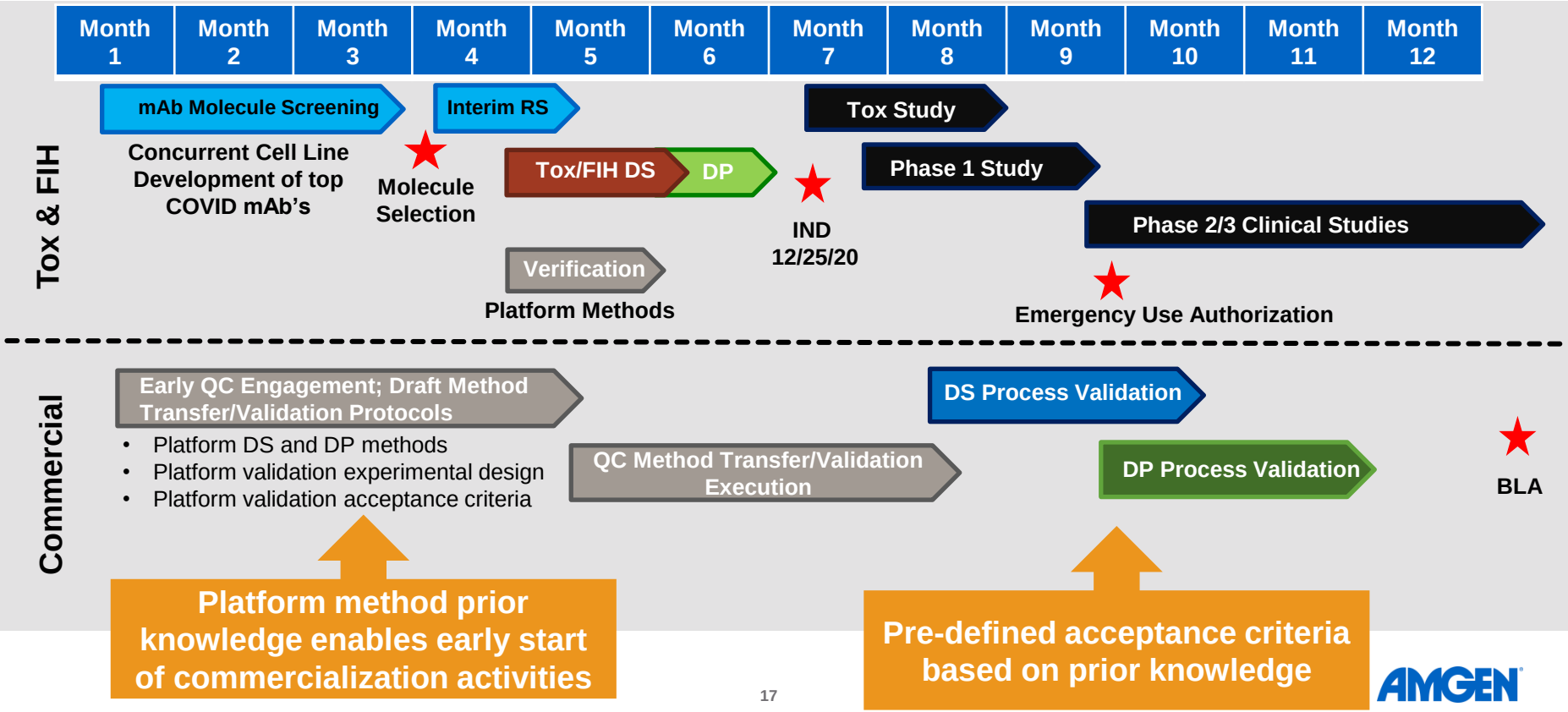
HOW DO WE FURTHER ACCELERATE THERAPEUTIC DEVELOPMENT TO FIGHT A GLOBAL PANDEMIC?





- Requires early investment in commercialization activities
- Fully leverage platform technologies, processes, & methods

HYPOTHETICAL SCENARIO LEVERAGES PLATFORM METHOD PRIOR KNOWLEDGE TO ENABLE 12 MONTH COVID MAB DEVELOPMENT



SUMMARY

- Establishment and use of platform methods enable speed and efficiency of end-to-end product development
- Platforms methods enable a single cycle approach to method development (i.e. same method used throughout development)
- Setting appropriate method performance targets helps ensure platform methods are fit-for-purpose
- Accumulated prior knowledge from platform methods provides a foundation for risk-based acceleration of product development activities (e.g. method transfer, validation, specification setting)

ACKNOWLEDGEMENTS

Amgen Attribute Sciences

Nic Angell

Suminda Hapuarachchi

John Harrahy

Neeraj Agrawal

Anna Ip

Izydor Apostol

Tiffany Thiel

Chetan Goudar