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2026 Europe Interchange

THE FUTURE IS CONNECTED: STANDARDS AND AI POWERING DIGITAL TRANSFORMATION

MILAN, ITALY | MAIN CONFERENCE: 20-21 MAY | TRAININGS & WORKSHOPS: 18, 19, & 22 MAY

From A to Z – Planning and Executing an NDA Submission

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Marcus Svensson, Statistical Programming Associate Director, AstraZeneca

Speakers

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Statistical Programming Director
AstraZeneca

Marcus Svensson
Statistical Programming Associate Director
AstraZeneca

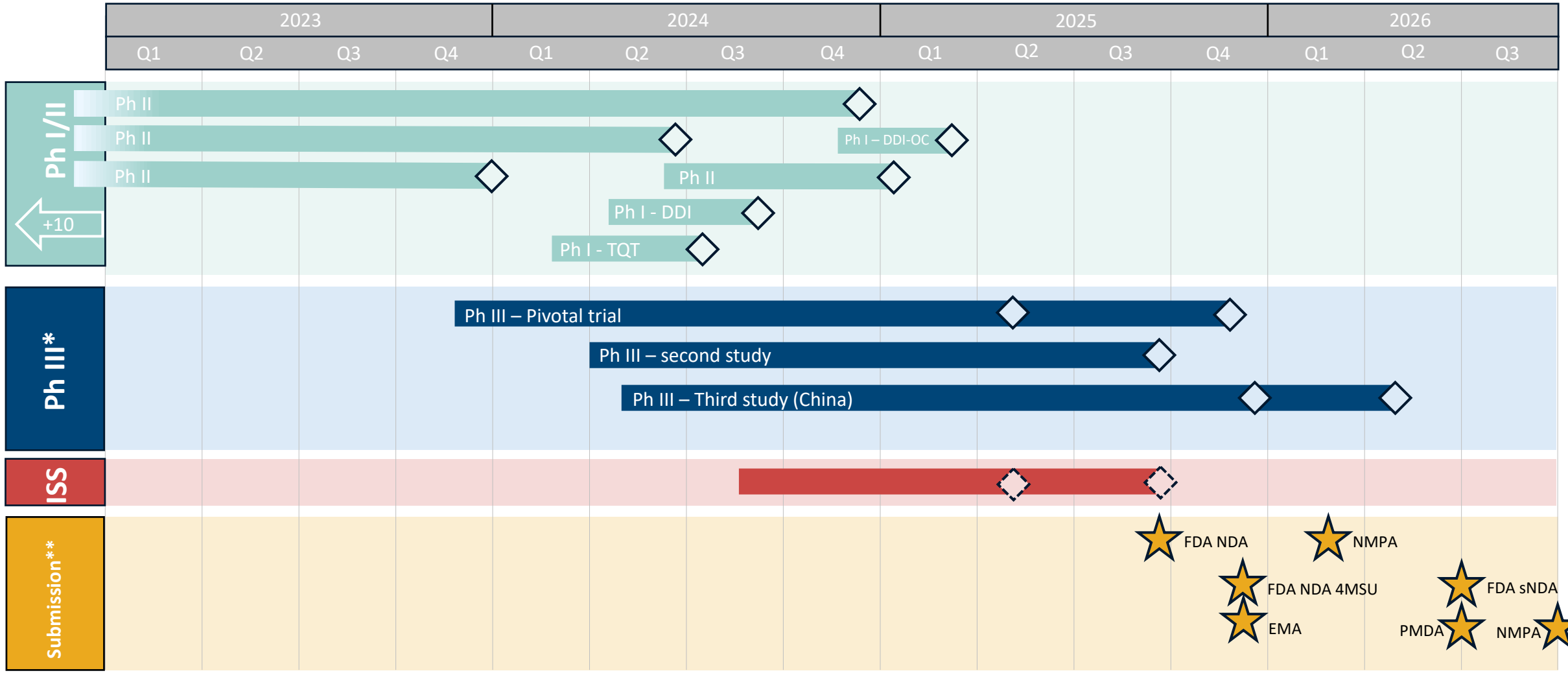
Agenda

1. Background
   - Project Introduction
   - Submission Plan
2. Submission – Biometrics Plan and Preparation
   - General project considerations
   - Deep dive: Phase III pivotal trial
3. Readout
   - Planned analysis
   - Unplanned analysis
4. Submission and Regulatory Response
5. Summary

Background

Project Introduction & Submission Plan

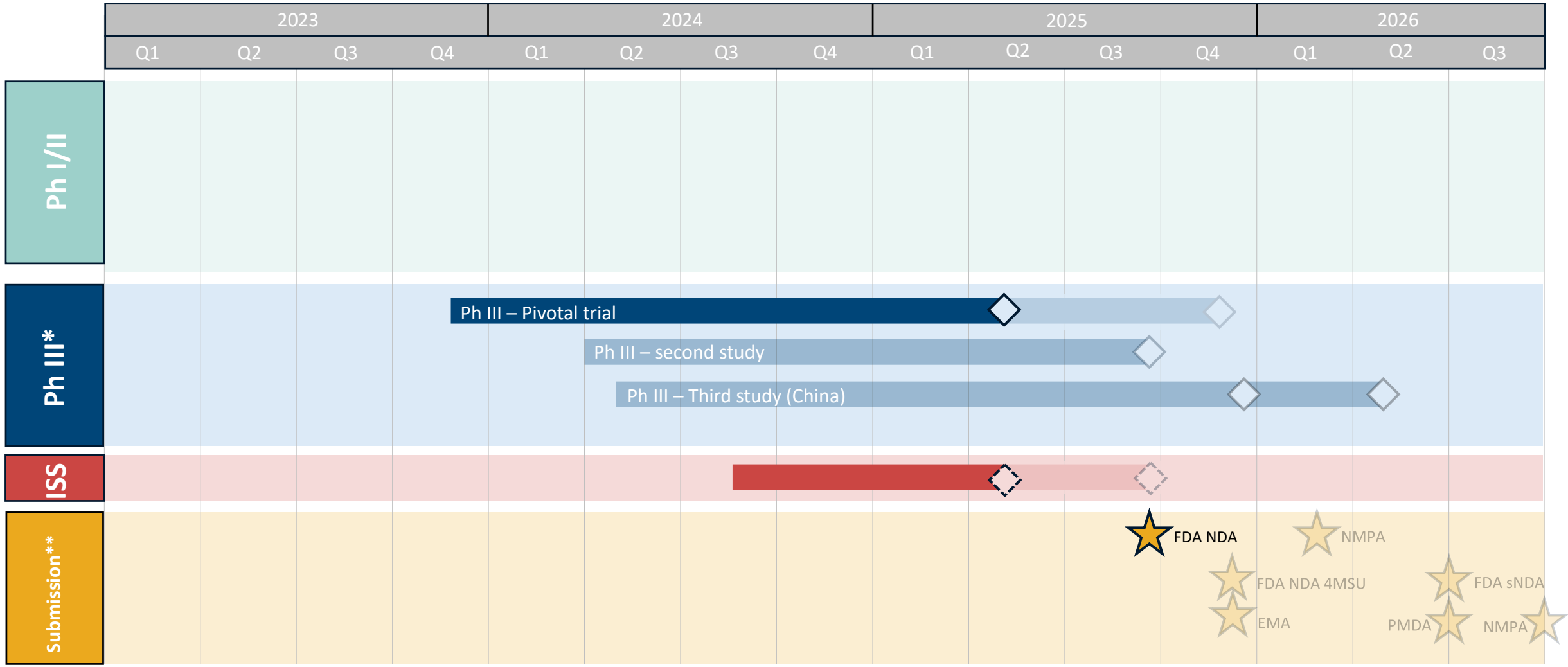
Project Introduction & Submission Plan



4MSU = 4 Month Safety Update

*Limited to Phase III studies in the submitted indication
**Limited to major markets

Project Introduction & Submission Plan



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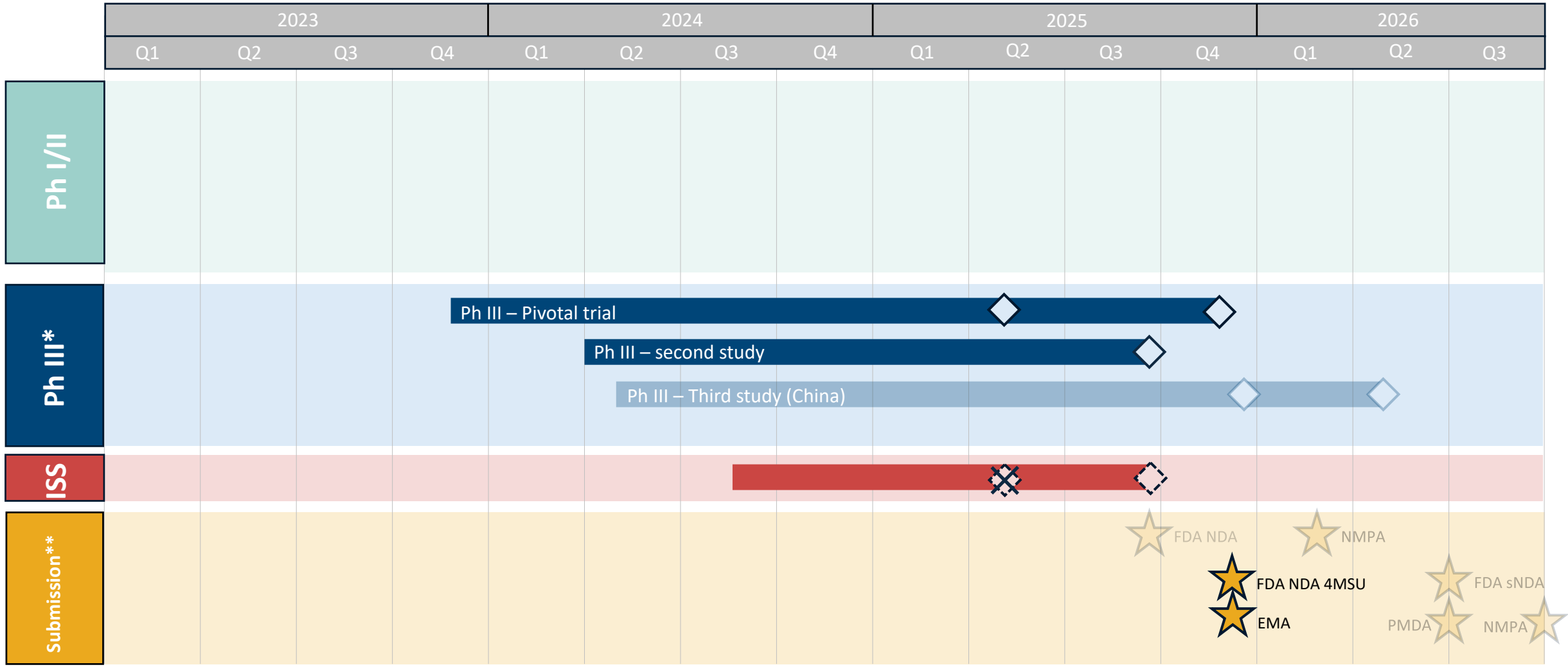

FDA NDA 4MSU does not contain the Second Ph III study

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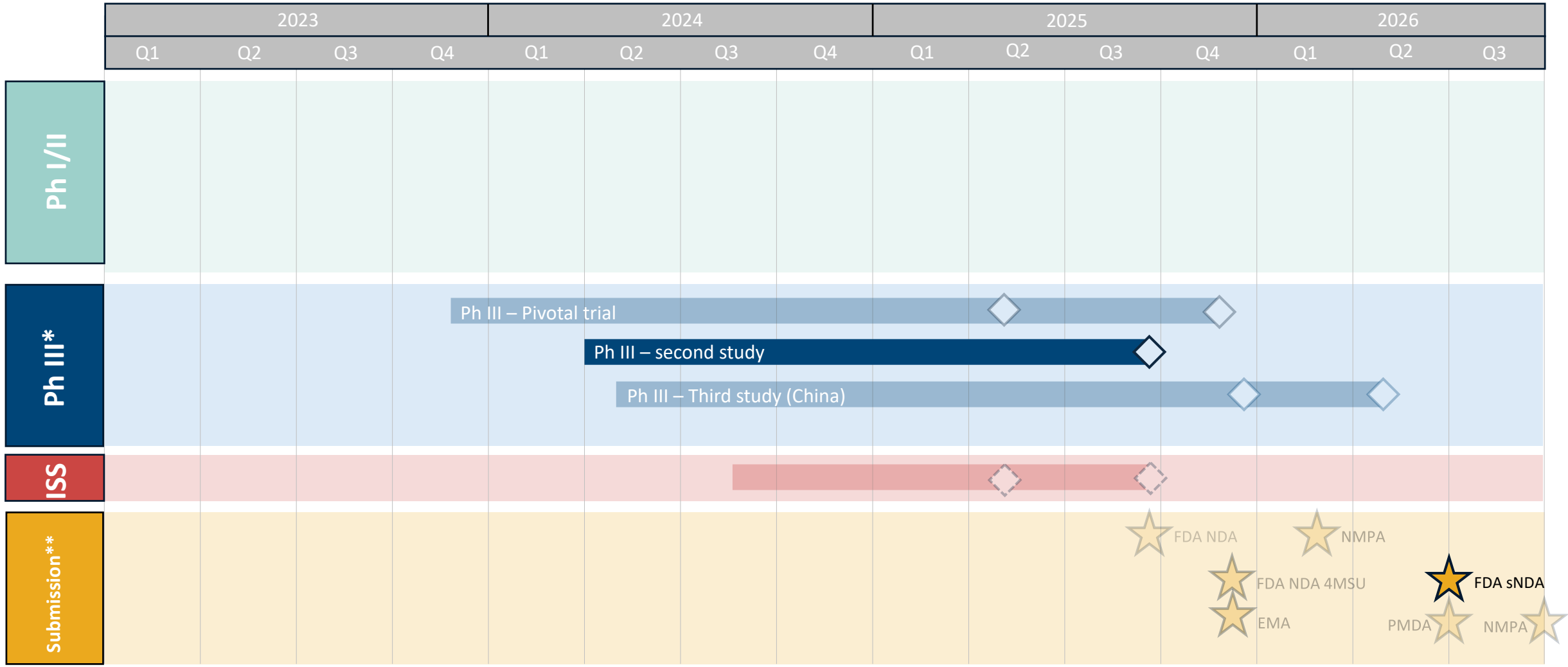

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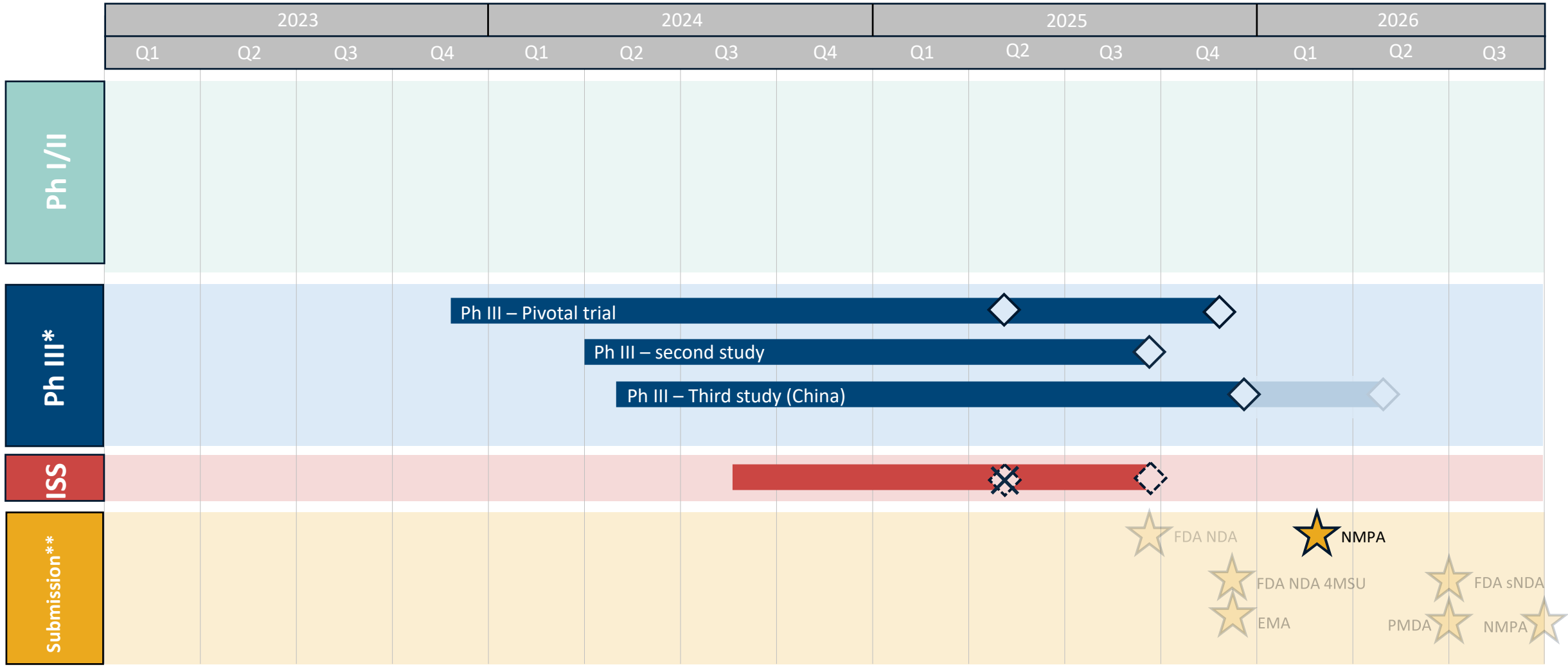

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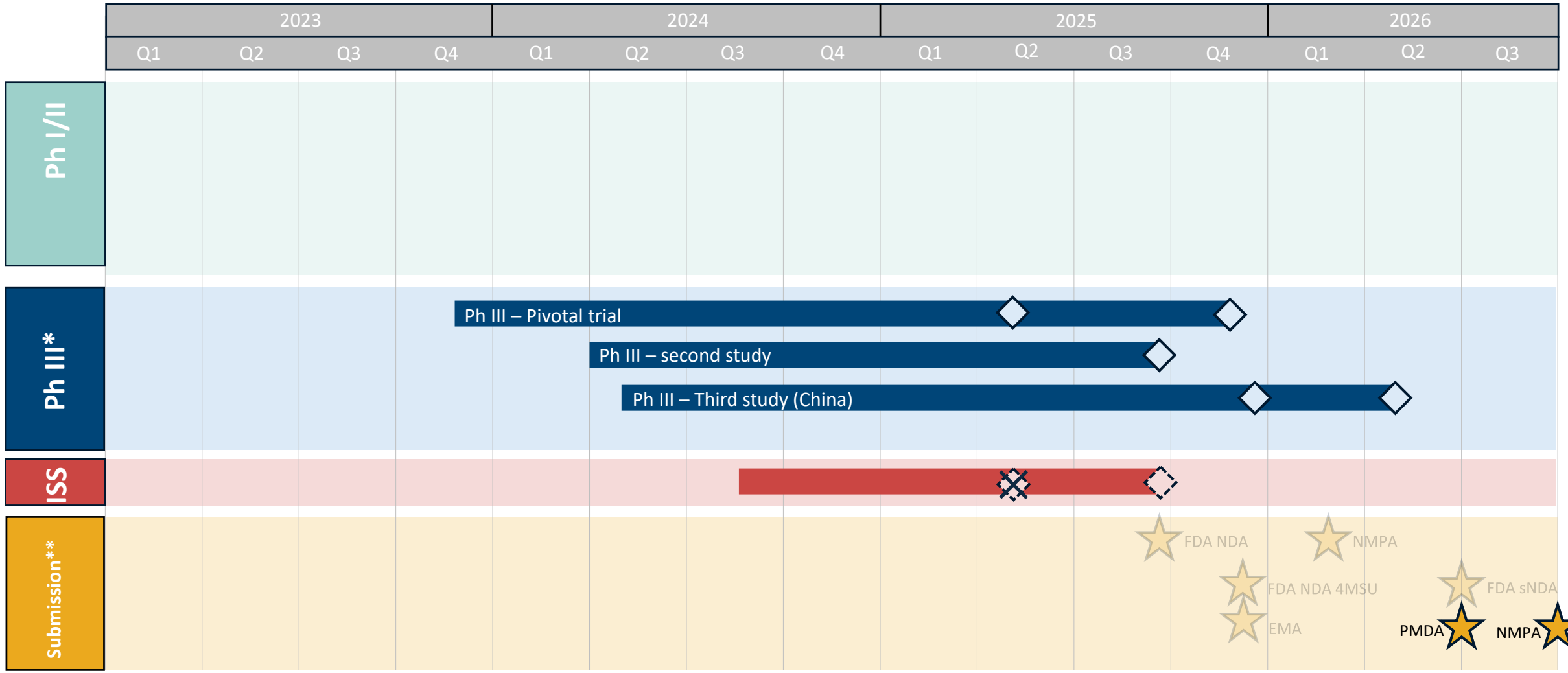

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Submission – Biometrics Plan and Preparation

Biometrics Submission Plan

Internal submission timelines

- 8 week submission (6 weeks submission from 2026)
- Biometrics deliverables following a 6 week submission plan
- Assume no updates needed to analysis/strategy following unblinding

(FDA) CRT submission scope

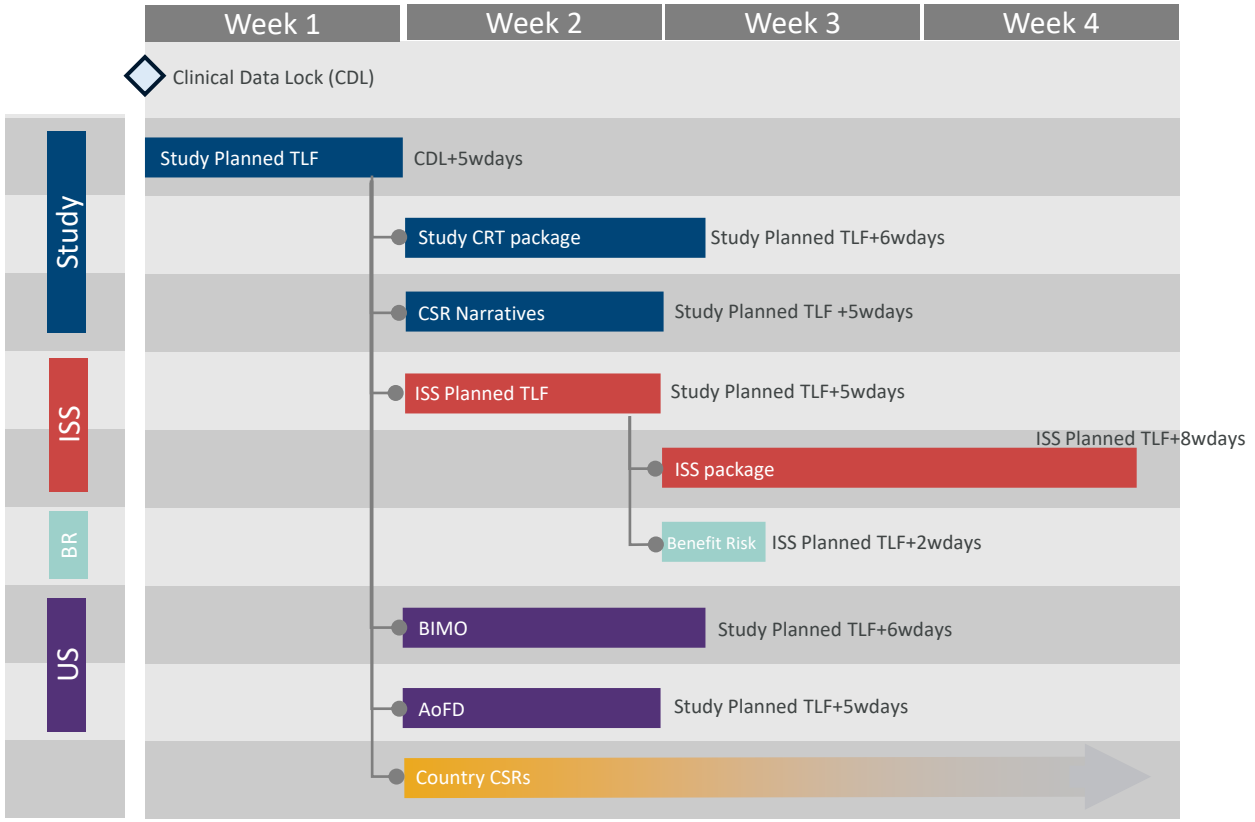
- Pivotal Phase III study: SDTM+ADaM datasets, analysis programs, aCRF, SDTM+ADaM define.xml, cSDRG, ADRG
- ISS: ADaM datasets, analysis programs, ADaM define.xml, ADRG

Key success considerations

- Planned deliverables remain within planned scope (Planned vs final)
- Programmer assignments and timelines should be bi-directionally planned
- Data dependencies is a key factor in submission planning

Identified improvements (not implemented)

- Better use and respect of time zones
- Finalization of SDTM as independent of analysis
- Ensure the scope is clear and well defined



ISS = Integrated Summary of Safety
wdays = working days

Submission requirements/guidance for CRT

Technical Rejection Criteria - Files

Data Standards Catalog

	Data Exchange Standard	Supported Version(s)	Implementation Guide Version	Exchange Format	Date Support Begins (YYYY-MM-DD	Date Support Ends (YYYY-MM-DD)
sets	SDTM	2.0	3.4	XPT	2025-04-01	
tasets	SDTM					
datasets	SDTM					

Standard	FDA Center(s)	Exchange Format	SDO	Property	Date Support Begins [8]	Date Support Ends	Date Requirement Begins	Date Requirement Ends
SDTM	CBER, CDER	XPT	CDISC	SDTMv1.4	08-18-2015	12/13/2023 [12]	03/15/2018 [1] 03/15/2019 [2]	12/13/2023 [12]
SDTM	CBER, CDER	XPT	CDISC	SDTMIGv3.2	08-18-2015	12/13/2023 [12]	03/15/2018 [1] 03/15/2019 [2]	12/13/2023 [12]
SDTM	CBER, CDER	XPT	CDISC	SDTMv1.7	07-07-2020		03/15/2022 [1] 03/15/2023 [2]	
SDTM	CBER, CDER	XPT	CDISC	SDTMIGv3.3	07-07-2020		03/15/2022 [1] 03/15/2023 [2]	
SDTM	CBER, CDER	XPT	CDISC	SDTMv2.0	12/13/2023 [12]		03/15/2025 [12]	
SDTM	CBER, CDER	XPT	CDISC	SDTMIGv3.4	12/13/2023 [12]		03/15/2025 [12]	

Technical Rejection Criteria – File Content

SDTM Rules v4.0

RULE ID	MESSAGE	DOMAINS	PMDA Severity	3.1.2	3.1.3
2001	Variable value not found in non-extensible codelist	ALL	Reject	X	X
CT2004	Variable value not found in non-extensible codelist when value-level condition occurs	ALL	Reject	X	X

Lab data in SI/Conventional units (LB/LC)

- CDISC Knowledge base
- LB Domain (Laboratory)

For clinical studies, please submit two separate domains for lab results. The LB domain should contain SI units in LBSTRESU for the SI results in the LBSTRESC and LBSTRESN fields. An additional custom domain structured identically to LB should contain conventional units in --STRESU for the results in conventional units in the --STRESC and --STRESN variables. It is ideal if both conventional and SI units come directly from the lab vendor.

June 2023

Periodic review of the FDA Study Data TCG

FDA TCG v5.4 release

LB Domain (Laboratory)

For clinical studies, please submit two separate domains for lab results. The LB domain should contain SI units in LBSTRESU for the SI results in the LBSTRESC and LBSTRESN fields. An additional custom domain structured identically to LB should contain conventional units in --STRESU for the results in conventional units in the --STRESC and --STRESN variables. It is ideal if both conventional and SI units come directly from the lab vendor.

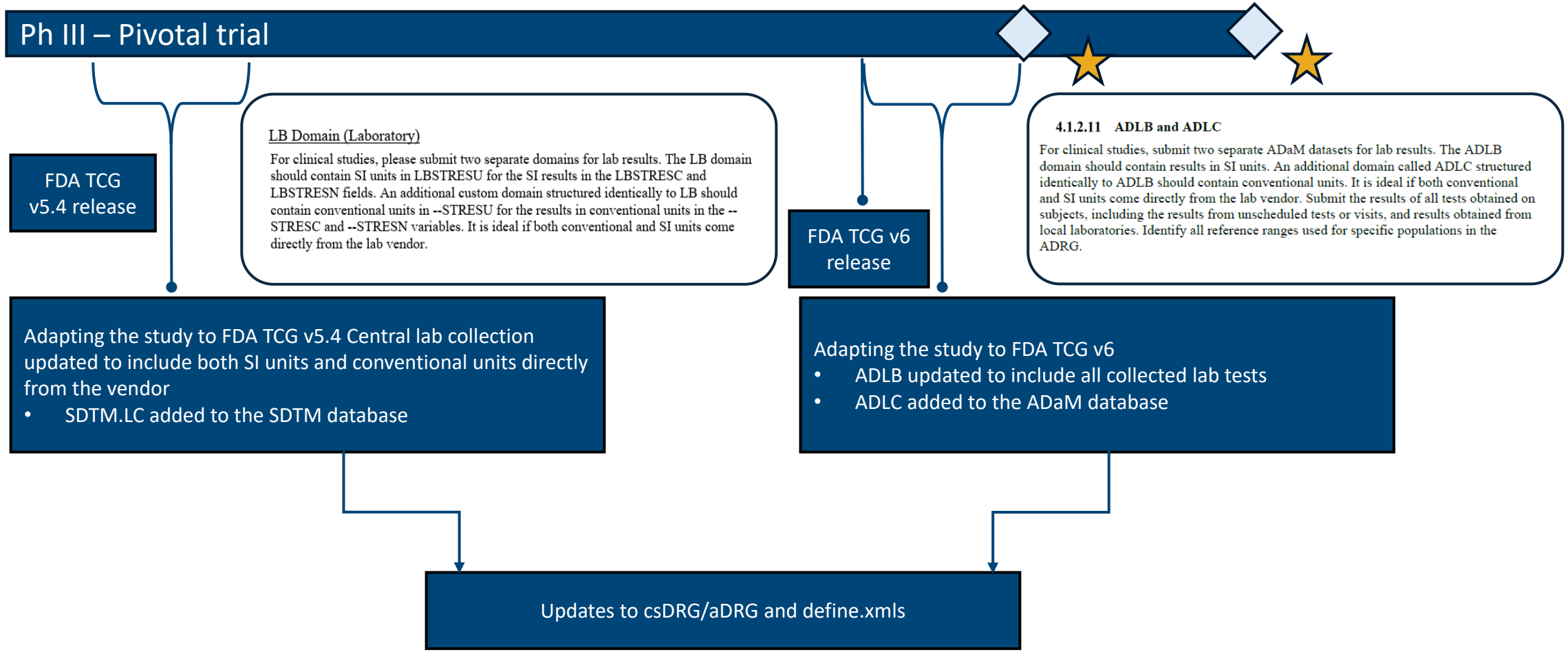
Adapting the study to FDA TCG v5.4 Central lab collection updated to include both SI units and conventional units directly from the vendor

- SDTM.LC added to the SDTM database

Updates to csDRG/aDRG and define.xmls

TCG = Technical Conformance Guide

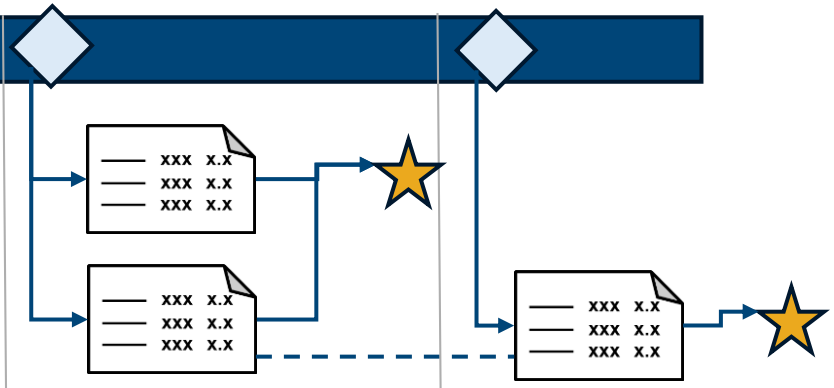
Periodic review of the FDA Study Data TCG



TCG = Technical Conformance Guide

Preparing for multiple database locks

Ph III – Pivotal trial

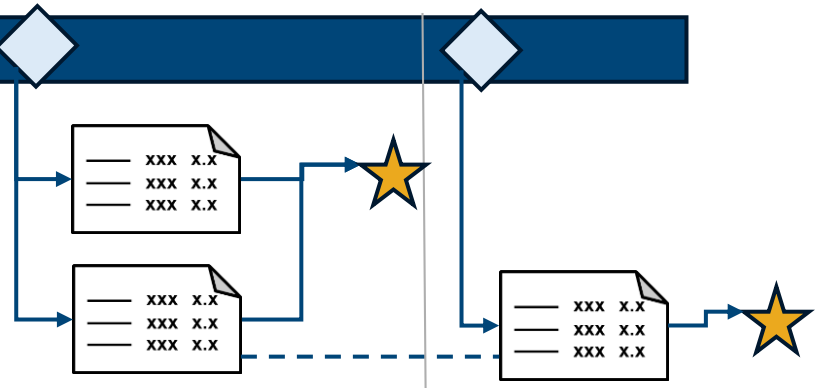


Component	Interim CDL	CDL
All data (SDTM, ADaM)	Final	Final
Efficacy and short term safety TLFs	Final	Not included
Long term safety analysis TLFs	Preliminary	Final

CDL = Clinical Data Lock

Preparing for multiple database locks

Ph III – Pivotal trial

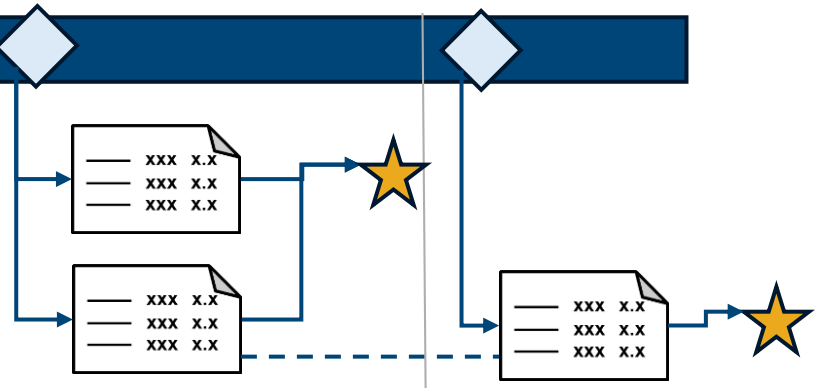


Reason for change	Interim CDL	CDL
Temporary interim CDL derivations	Temporary derivation	Derivations updated
Addition of SDTM device domains	Not included	Domains added
Information Request (IR) FDA: Request to provide additional ADaM variables	Not applicable	Variables added

CDL = Clinical Data Lock

Preparing for multiple database locks

Ph III – Pivotal trial



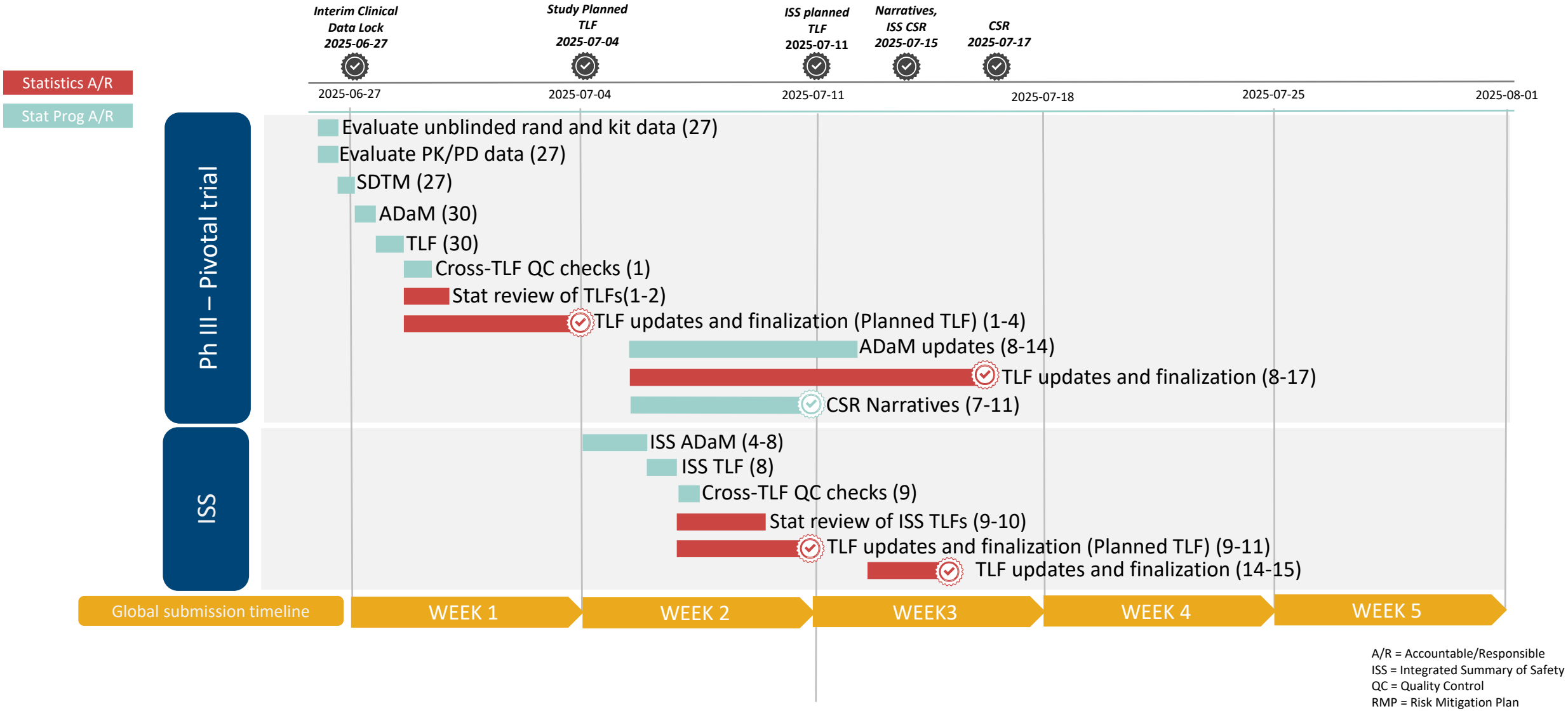
Output	Program	Interim CDL	CDL	
14.1.10.3.1 Concomitant medication by ATC classification and generic drug name - Double-blind period (Full analysis set)	tcm01.sas	Final	Not included	
14.1.10.3.4(P) Concomitant medication by ATC classification and generic drug name - 52-week period (Safety analysis set)	tcm02.sas	Preliminary	Final	Numbered as 14.1.10.3.4P in the interim CDL. Numbered as 14.1.10.3.4 in the CDL.
14.2.1 Efficacy variables, overview of key results	tover01.sas	Final	Not included	
14.3.2.1.1 Overall summary of adverse events - Double-blind period on-study (Safety analysis set)	tae01.sas	Final	Not included	
14.3.2.1.4(P) Overall summary of adverse events - 24-week period on-study (Safety analysis set)	tae02.sas	Preliminary	Final	Numbered as 14.1.10.3.4P in the interim CDL. Numbered as 14.1.10.3.4 in the CDL.

CDL = Clinical Data Lock

Readout

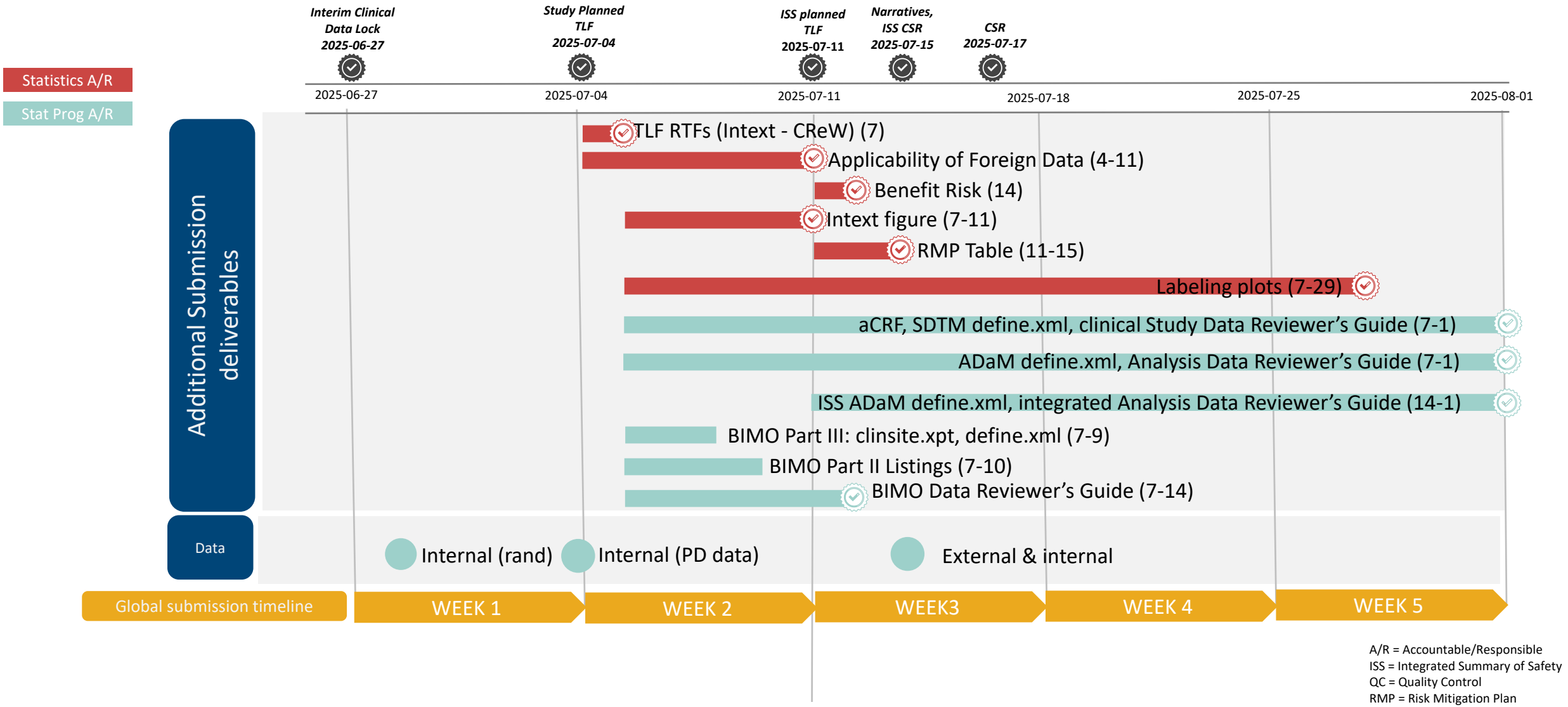
Planned Analysis
Unplanned Analysis

Ph III – Pivotal Trial Readout Timelines



A/R = Accountable/Responsible
ISS = Integrated Summary of Safety
QC = Quality Control
RMP = Risk Mitigation Plan

Ph III – Pivotal Trial Readout Timelines



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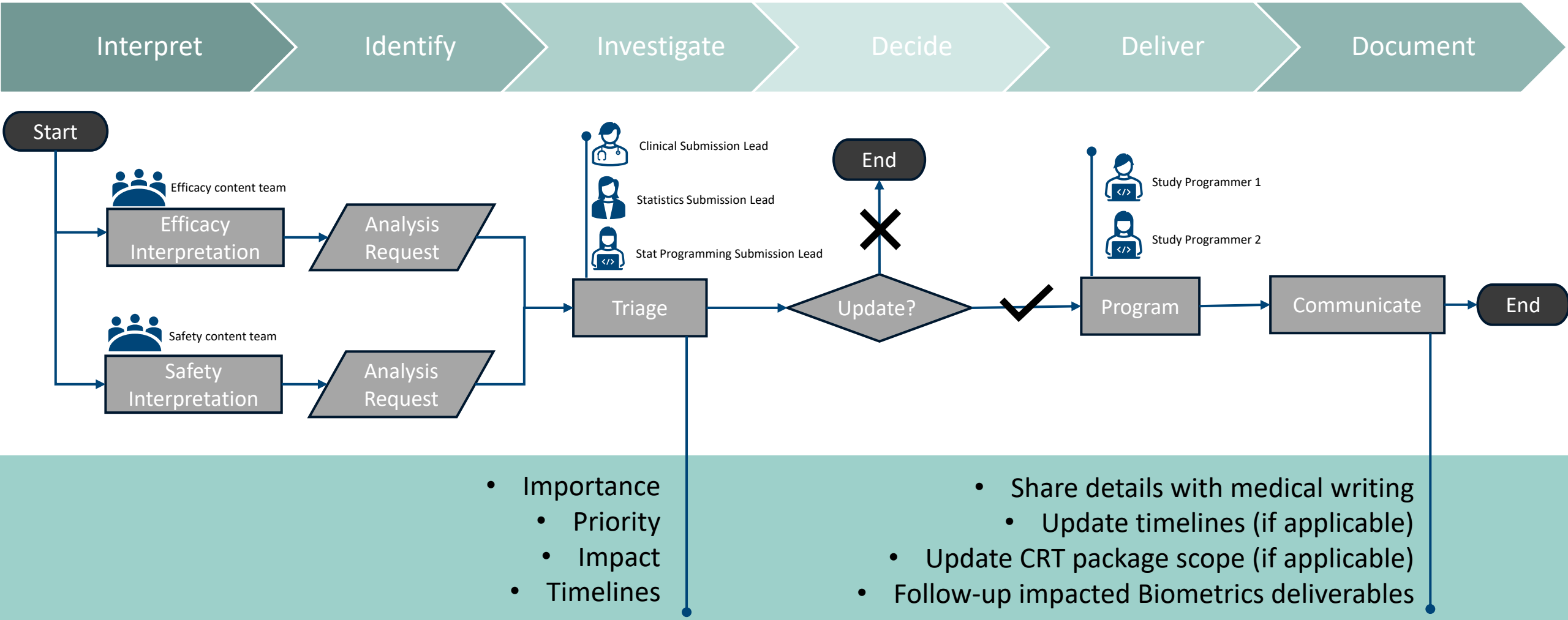
Analysis triage – changes to planned analysis



- Importance
- Priority
- Impact
- Timelines

- Share details with medical writing
- Update timelines (if applicable)
- Update CRT package scope (if applicable)
- Follow-up impacted Biometrics deliverables

Submission and Regulatory Response

CRT Package in Regulatory submission

Study	**File**	**NDA** Sequence A	**IR #1** Sequence B	**4MSU** Sequence D	**Future IR #X** Sequence Y
Pivotal Ph III	adsl.xpt	New		New (duplicate Sequence A)	*Replace (Sequence A and/or D)*
Pivotal Ph III	adae.xpt	New	Replace (Sequence A)	New (duplicate Sequence B)	*Replace (Sequence B and/or D)*
Pivotal Ph III	adlb.xpt	New		New (duplicate Sequence A)	*Replace (Sequence A and/or D)*
Pivotal Ph III	adlc.xpt	New		New (duplicate Sequence A)	*Replace (Sequence A and/or D)*
Pivotal Ph III	define.xml	New	Replace (Sequence A)	New (duplicate Sequence B)	*Replace (Sequence B and/or D)*

CRT Package in Regulatory submission

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File Tracking and Status

- Tracking of CRT package submissions on file level
  - Include status (New, Replace, Delete)
- Ensuring data properties/status is correctly reflected in submission

CRT Package in Regulatory submission

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Submission to multiple agencies

- Tracking of all agencies and branching of files over time
- Additional countries/agencies may request data

CRT Package in Regulatory submission

Study	File	NDA Sequence A	IR #1 Sequence B	IR #3 Sequence C	4MSU Sequence D	Future IR #X Sequence Y
Pivotal Ph III	adsl.xpt	New			New (duplicate Sequence A)	*Replace (Sequence A and/or D)*
Pivotal Ph III	adae.xpt	New	Replace (Sequence A)		New (duplicate Sequence B)	*Replace (Sequence B and/or D)*
Pivotal Ph III	adlb.xpt	New			New (duplicate Sequence A)	*Replace (Sequence A and/or D)*
Pivotal Ph III	adlc.xpt	New			New (duplicate Sequence A)	*Replace (Sequence A and/or D)*
Pivotal Ph III	define.xml	New	Replace (Sequence A)		New (duplicate Sequence B)	*Replace (Sequence B and/or D)*
Study X	adsl.xpt			New		
Study Y	adsl.xpt			New		
…+15	…+2000			New		

File Tracking and Status

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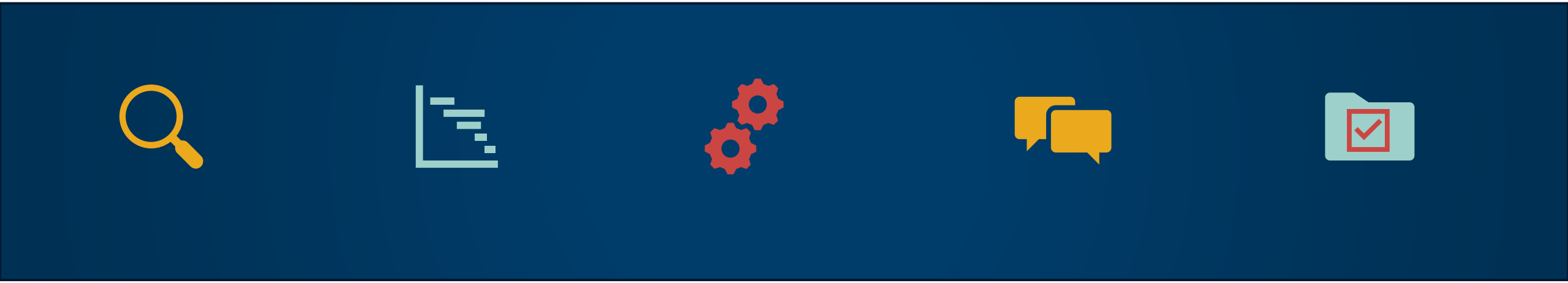
Reg response resilience

- The planned scope is subject to change
- Know the gaps to react and act quickly

From A to Z – Planning and Executing an NDA Submission



ASSESS

Assess early on the **quality** and **readiness** of your studies relative to submission

Act on items as applicable to the submission plan

PLAN

Account for **data dependencies** and make smart **resource allocations**

Have full **awareness of all sections (modules)** in the submission

Prepare CRT packages meeting **regulatory requirements** and supporting **efficient regulatory review**

EXECUTE

No new changes to the Planned TLF delivery

Conduct **efficient, cross-functional triage** of changing analysis needs

Know the **status** and relationship of your data files in submission

RESPOND

Be **prepared** and **resilient** to responses that require a change of plans

Track progress for each and all agencies

Know the **status** and relationship of your data files

APPROVE?

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Thank You!