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NDA Submission Experience: Rescue Case Study

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Think Patient!

It’s about the Science after all!

Key Topics for Discussion

- Rescue Case Study Background
- Gap Assessment
- Remediation Performed
- Lesson Learned & Recommendations

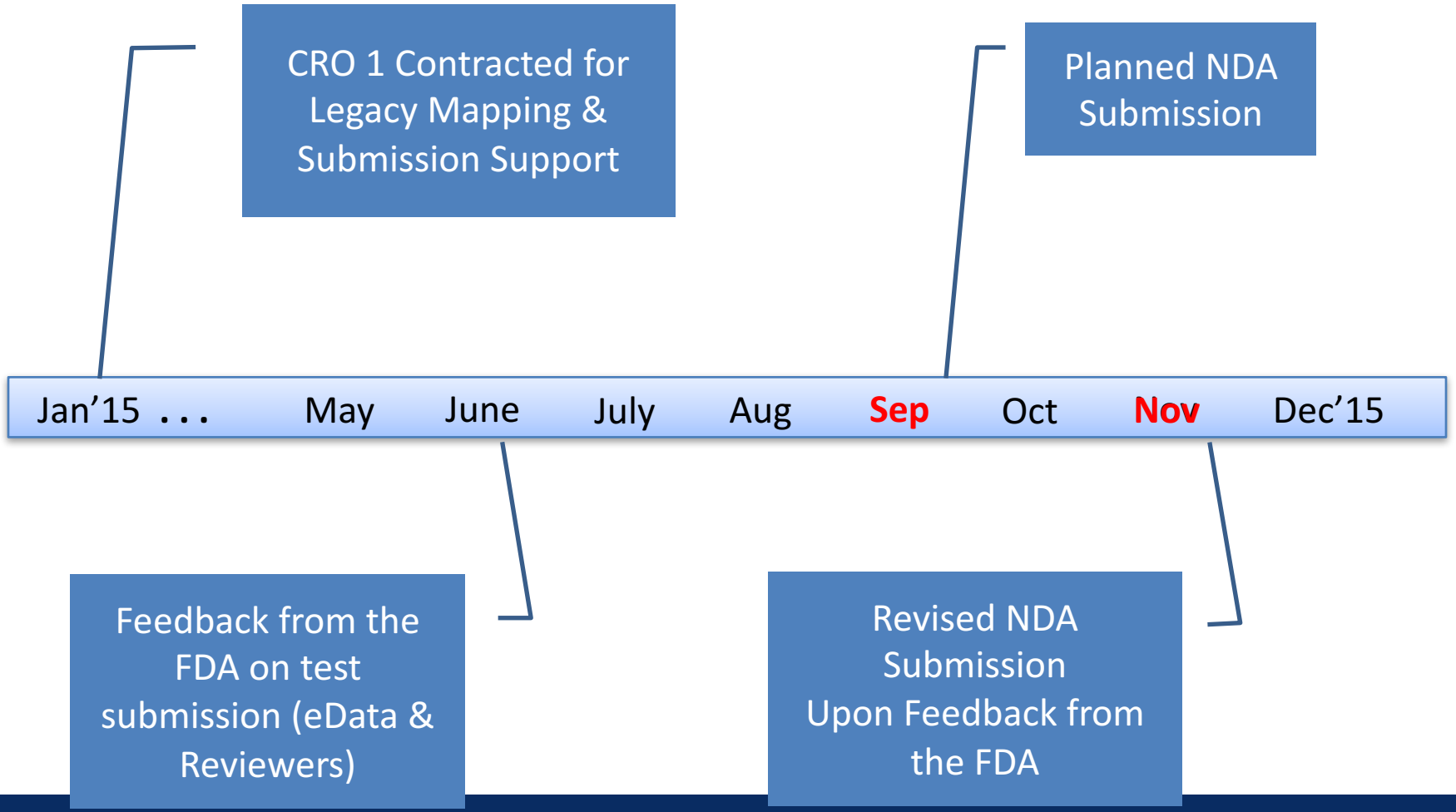
Sponsor's Background

- A mid-sized pharmaceutical company
- Sponsor's first-ever NDA submission
- Limited in-house resources
- Outsourced to 3 different global CROs to work on their late stage studies and submission support
- Six studies (Phases I-III) in both legacy and CDISC formats

Pre-NDA Meeting: FDA Expectations

- CDISC SDTM format for all submitted studies
- Phase II-III analysis datasets in CDISC ADaM format
- ISS in CDISC ADaM format
- BIMO dataset and Site Level Subject Data Listings
- All datasets as per the Study Data Technical Conformance Guide

NDA Submission Target at Risk & Change Order $$$



Sponsor & Niche Provider Collaboration

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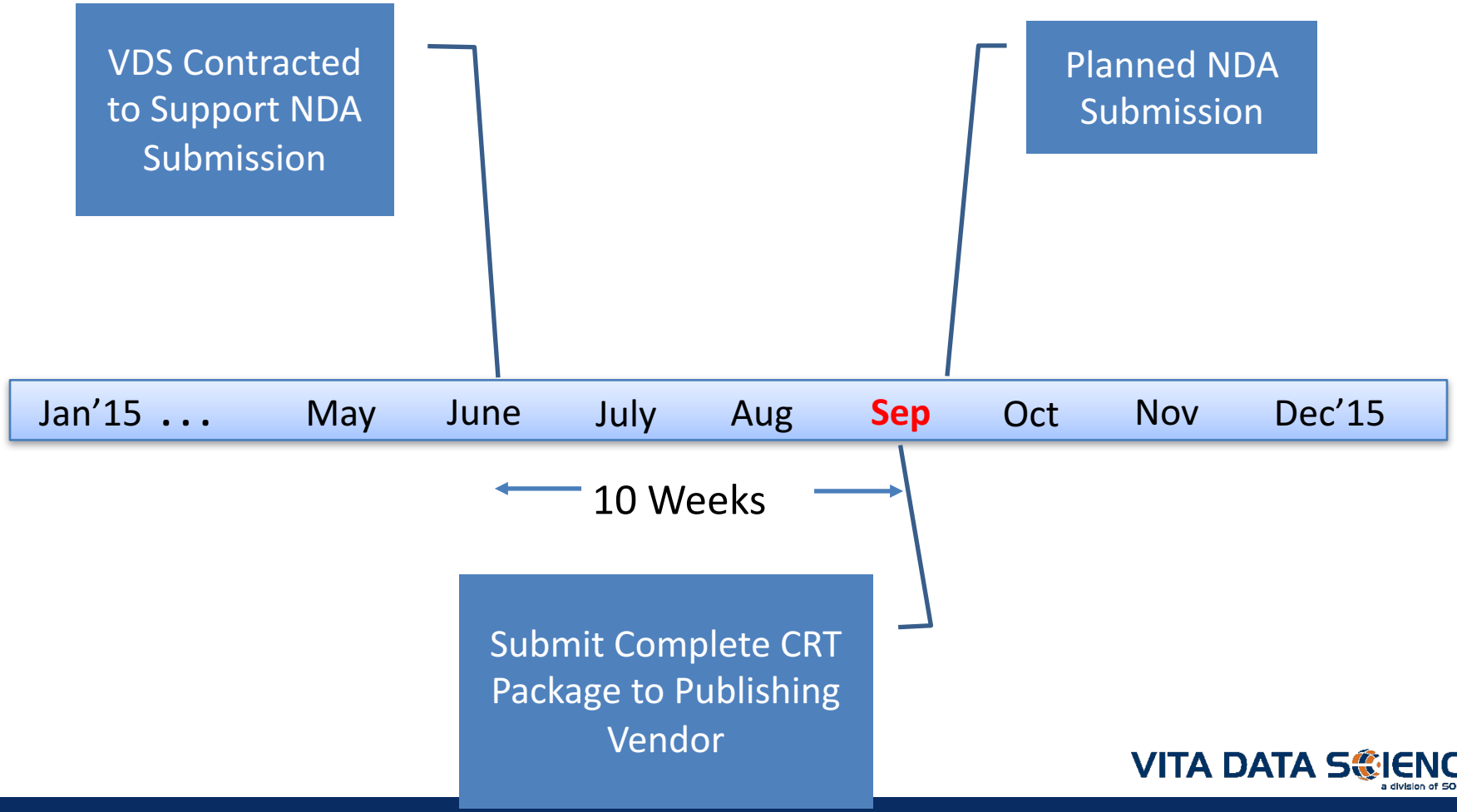
Inventory of Datasets CRT Submission Package

Submission-Ready Deliverables	Phase I Studies (CRO 1)	Phase 2 Study (CRO 2)	Phase 3 Studies (CRO 3)	ISS (CRO 3)
SDTM Datasets	✓	✓	✓	NA
SDTM aCRF	X	X	✓	NA
SDTM define	X	✓	✓	NA
SDTM reviewers guide	X	X	X	NA
ADaM/Legacy datasets	✓	✓	✓	✓
ADaM/Legacy define	X	✓	✓	✓
ADaM/Legacy reviewers guide	X	X	X	✓

Gap Assessment – Miscellaneous

- Case Report Form (CRF) was in word format
- Different versions of OpenCDISC were used across all studies.
- SAS® codes were not provided to the Sponsor for the FDA submission
- BIMO datasets and site level subject data listings were not programmed.

Rescue Project Targeted Timeline



Rescue Project – Successful!

- 'Submission-ready' CRT package in 10 weeks !
- Worked closely with the Sponsor and other CROs
- NDA submitted per original targeted timeline
- No feedback from the FDA on data compliance!
  - Helped addressed questions from the FDA review division
- Provided support on several additional projects

Key Lessons Learned/Recommendation

- Address OpenCDISC compliance issues during SDTM dataset development
- Define.xml and SDTM aCRF developed early in the SDTM development life cycle
- Ensure consistency used when multiple studies are outsourced
- Reviewers guide should have details about your primary efficacy end-points including reference to the SAS codes

Key Lessons Learned/Recommendation …contd (2)

- Clear contract with added specifics about Sponsor expectations for each deliverable
  - Dataset standards and any Sponsor specific standards
  - List of expected CDISC deliverables (XPTs, define, SDTM aCRF, SDRG/ADRG)
  - Number of Dry runs
  - Compliance checks
  - SAS Codes and associated macros
  - 'Submission-ready' CRT package
- Sponsor's oversight on outsourced deliverables

Key Lessons Learned/Recommendation …contd (3)

- Engage FDA review division early in the drug development/submission process
  - Study Data Standardization Plan (SDSP)
- Discuss datasets submission details at the pre-NDA meeting
- Submit sample/test submission to the eData team and FDA review division

Key Lessons Learned/Recommendation …contd (4)

- Choose the right service provider/vendor to work on your submission!
  - Interview and qualify project team members
  - Team members must have prior submission experience
  - Data Standards and Submission SME should be part of the team

- Remember – goal must be to have '**submission-ready**' deliverables from your vendor upfront!

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