



From Outsourced to Open Source: Denali's R-
Driven Transformation in Biometrics

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 - Study Lead
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All the views shared in this presentation are my own and do not reflect the opinions of my company

OVERVIEW

- What We Did
- How We Did It
- Where We're Headed

OVERVIEW

- What We Did
- Our Journey to Filing
- Our Future

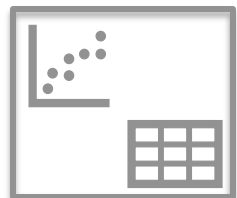
What Did We Do?



Our First Successful BLA Filing in May 2025
via AA Pathway

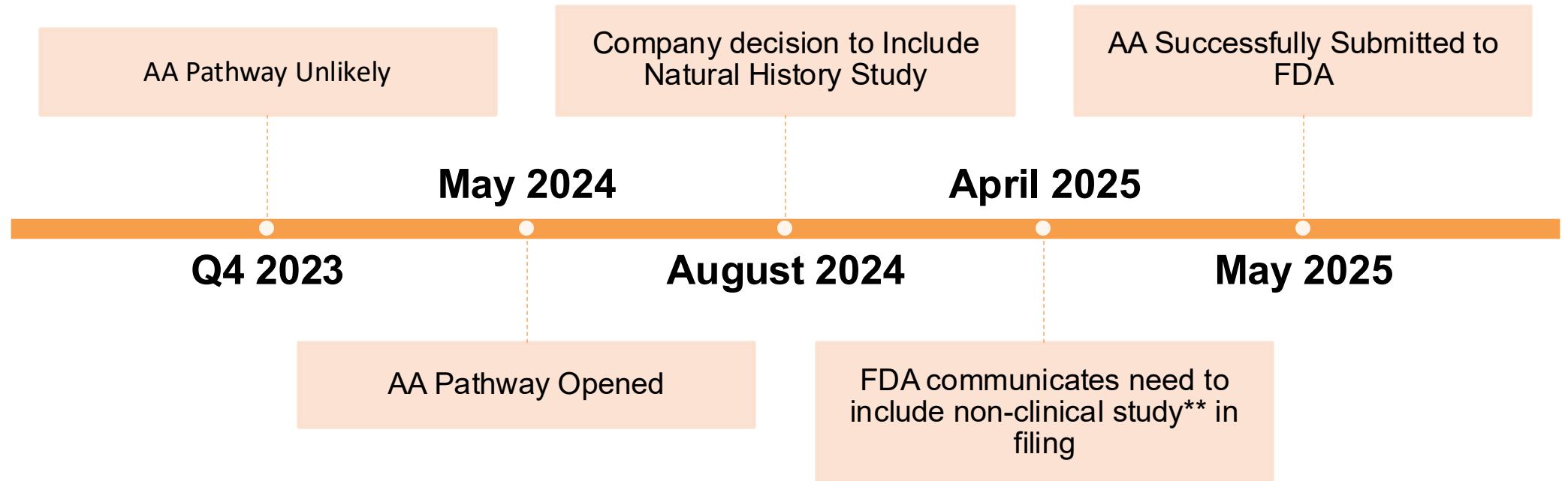


2 Clinical Studies Reports (Natural History + Phase I/IIB)
1 Integrated Summary of Efficacy
1 Biomarker Reference Range Study***



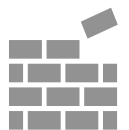
~1000 In-House TLFs + Datasets (R)
~640 Vendor Produced TLFs + Datasets (SAS)

Our Filing Timeline



OVERVIEW

- What We Did
- How We Did It
- Where We're Headed



Our Foundation



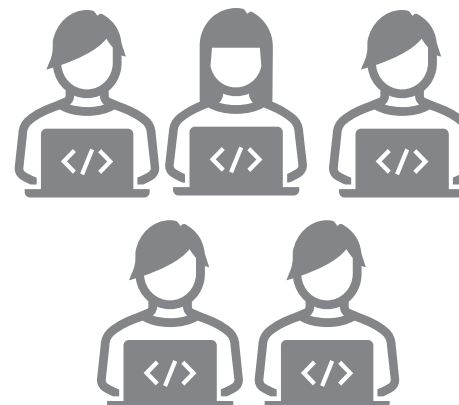
Internal Exploratory Analyses
In-House (R)



Regulatory Work/Reporting Events
Outsourced (SAS)



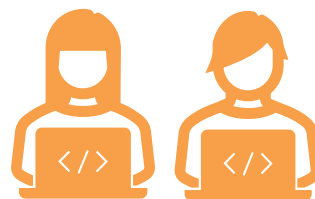
Our Goal



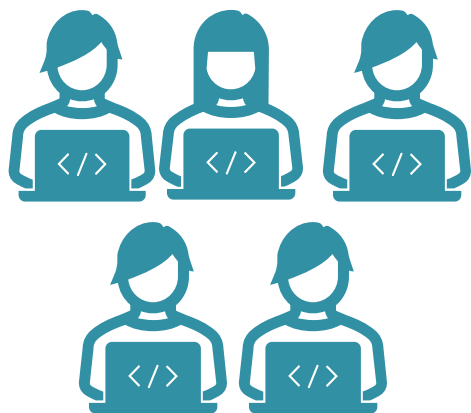
Build an In-House Team
capable of supporting our
regulatory needs



The Road to Achieving Our Goal



Internal R Team



Contractors (SAS)



CROs



The Road to Achieving Our Goal





The Road to Achieving Our Goal





The Road to Achieving Our Goal



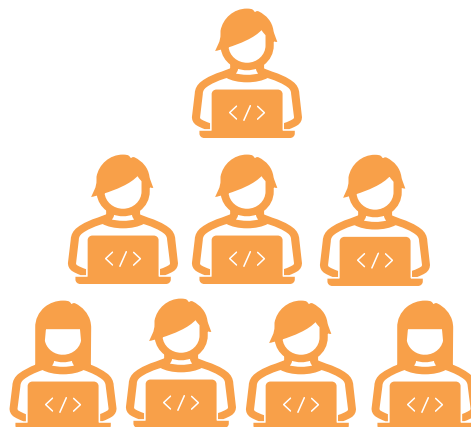
**An extensive library of
open-source packages**



The Road to Achieving Our Goal



SAS
Contractors



Internal R Team



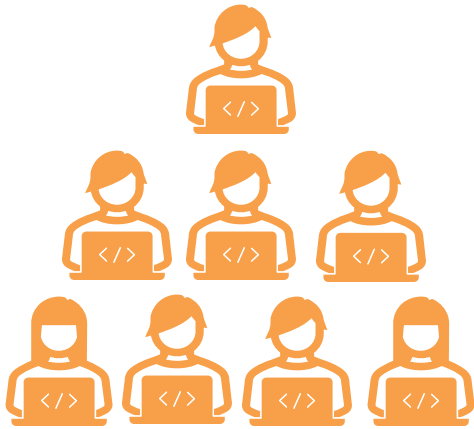
CROs



R Contractors



Key Drivers of Success – Our Team



Our Internal R Team

Experienced R Programmers

- 3 pharmaverse contributors
- 3 R Pilot submission contributors
- Programmers with extensive experience using R to support clinical trials



Key Drivers of Success – Systems Investments



Statistical Computing Environment

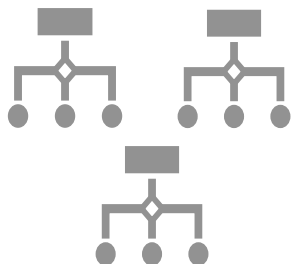
- Cloud based
- Customized GxP R environment



Key Drivers of Success – Process Investments

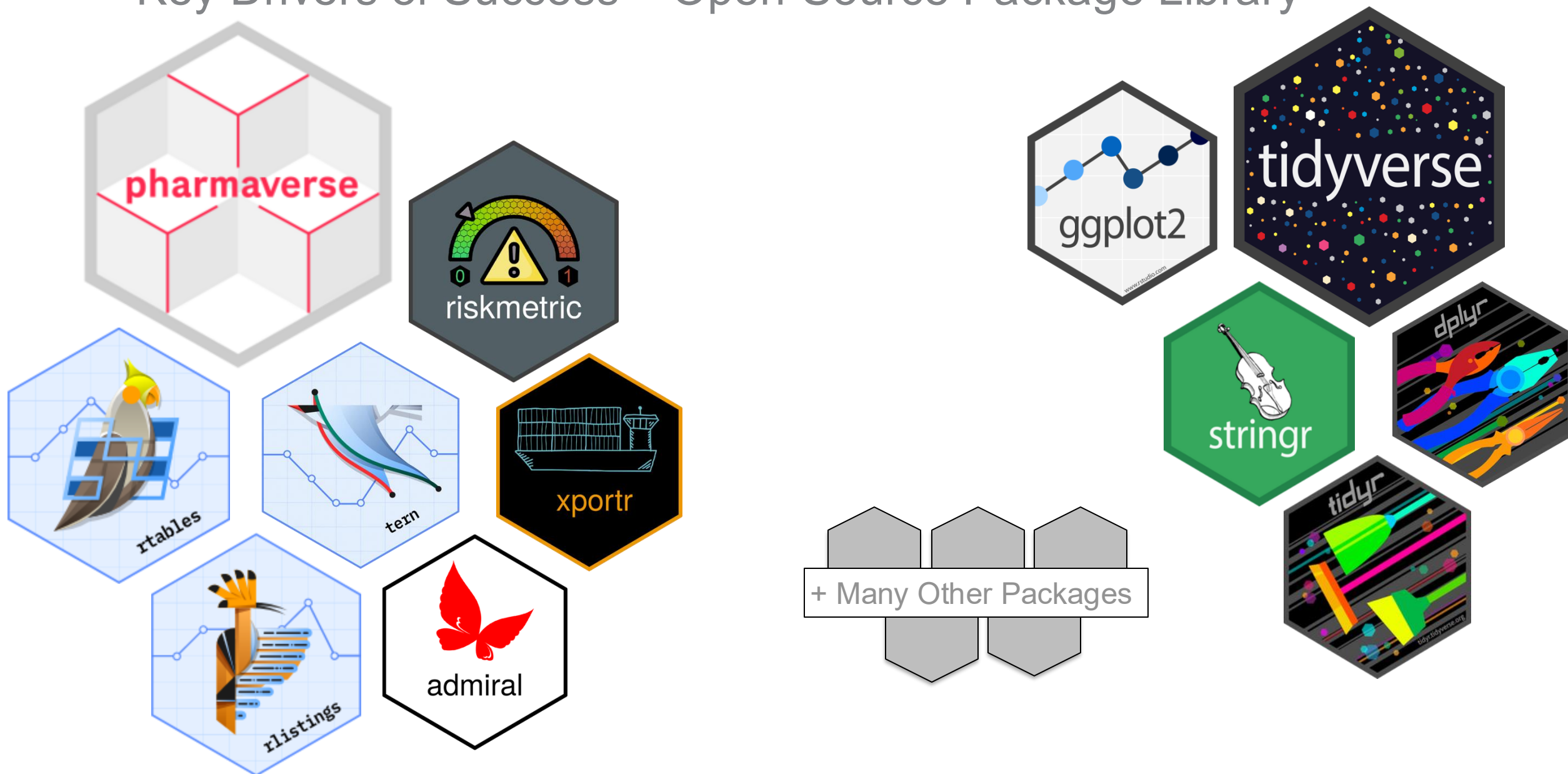


R Package Validation Process



Parameterization of Programs

Key Drivers of Success – Open-Source Package Library





Lessons Learned



Vendor oversight was a
time consuming task



Lessons Learned



Start your define package early

CRO generated package with
significant
oversight, management and
editing from our team



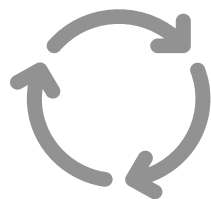
Lessons Learned



SMEs appreciated the flexibility
of generating graphics in R



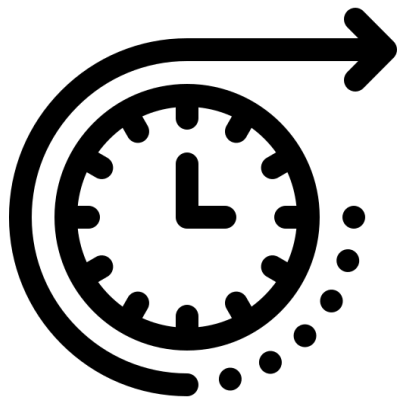
Lessons Learned



Agility of our In-House Team



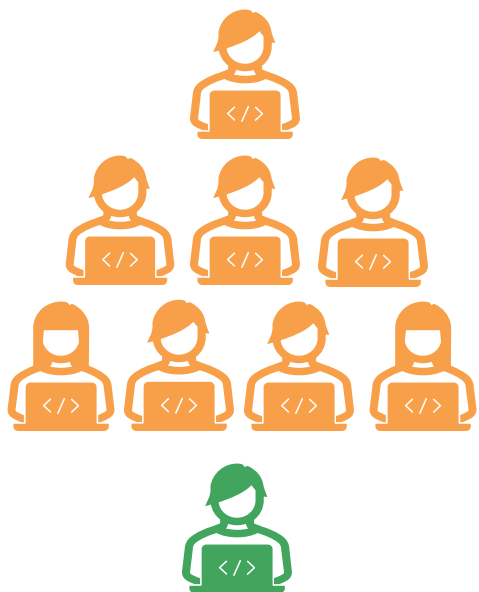
Lessons Learned



The future is R



Lessons Learned



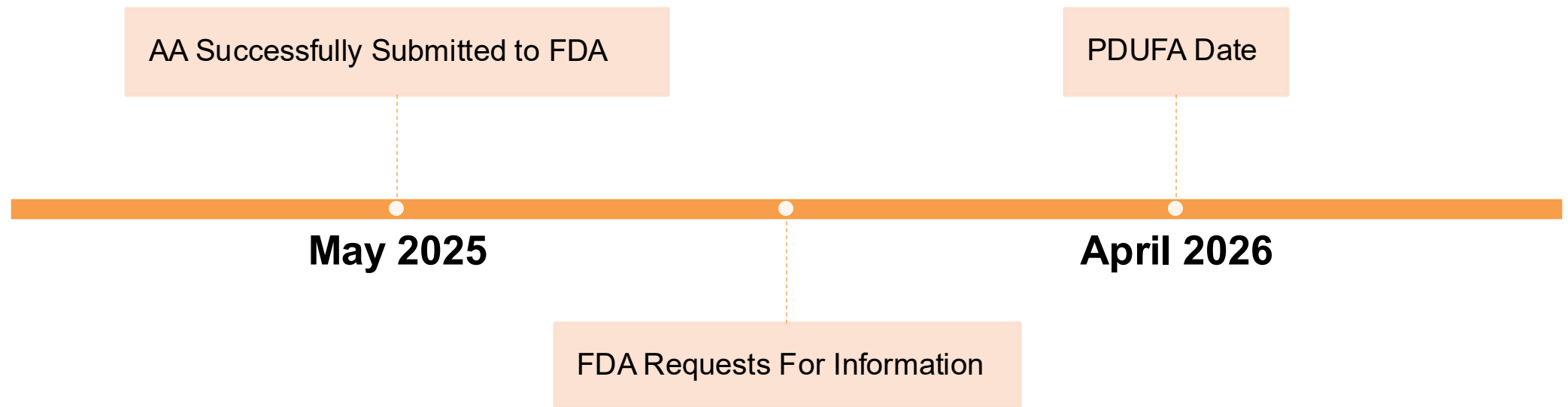
Our Team can do this!

~ 60% of Outputs
Generated In-House

OVERVIEW

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Post Filing





Where are We Headed

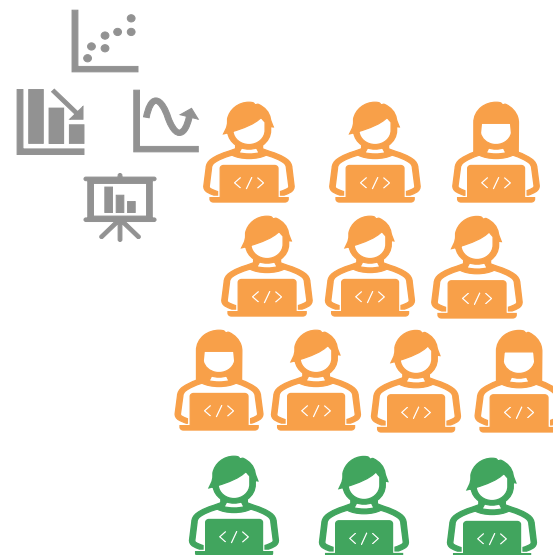




Where are We Headed

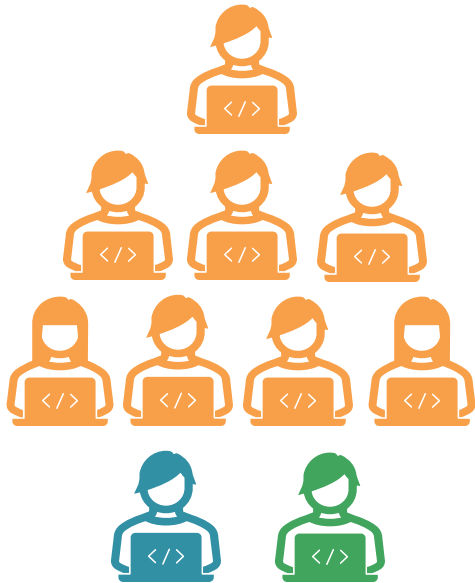


Move all regulatory
work in-house





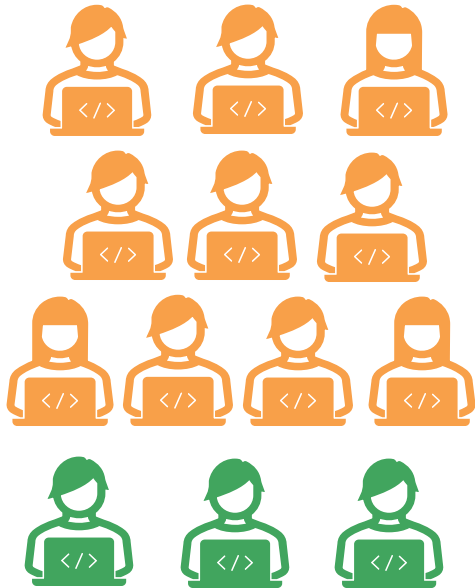
Where are We Headed



Continue to Invest in
our Internal R Team



Where are We Headed



Continue to Invest in
our Internal R Team

Questions?



THANK YOU

Our Filing Experience

Our Future

Our Future

Future Studies conducted 100% In-House

Contribution to open-source packages

NICOLE

- What we did
 - XXX number of total outputs across 2 clinical studies, 1 integrated study and 1 non-clinical study
 - % of outputs done inhouse
- How we did it?
 - Vendor support
 - Leveraging the pharmaverse
- Lessons learned
- Future Work

THOMAS

- Denali submitted its first BLA via the AA pathway in May 2025
- Biometrics deliverables were created using a hybrid approach: in-house R vs. CRO SAS
- How did we manage to pull this off?
- A bit of history of Denali Biometrics
- Key learnings for other Biotechs
- The outlook: Next studies 100% in-house

MICHAEL

- Data Science at Denali over the years
- BLA and AA
- Overview of the workflow
- Managing vendors – struggles and learnings
- In-house flexibility, efficiency and dependability
- SME appreciation for in-house work vs vendor work
- Future plans

OUTLINE

- What we did
 - Denali submitted its first BLA via the AA pathway in May 2025 (for Michael likely to talk about AA approval)
 - XXX number of total outputs across 2 clinical studies, 1 integrated study and 1 non-clinical study
 - % of outputs done inhouse
 - E2 Numbers
 - 682 in house
 - 488 Fortrea
- How did we do this?
 - A bit of history of Denali Biometrics
 - Original team with fully in R only intmal work [and shipped everything to vendor]
 - New management wants to do everyting internal in R but SAS contractors brought on to support this
 - Evaluation of R vs SAS to determine can we do it in R
 - R began to outperform SAS
 - Hybrid approach
 - Vendor management
 - Leveraging phamaverse
 - 3 people who worked at denali directly contributed to phamaverse
 - Memembers of pilot 3 submission
 - A bit of experience
 - Submission/communication with FDA
 - Regular meetings
 - Define package generation
 - Reference range study
 - Submitting R programs/R installation instructions
 - Org chart [pre vs post thomas] color by SAS vs R check with AJ on numbers
 - Highlight that we brought in new talent and didn't train existing talent
 - R validation + System cost
 - Higlht riskmetric pacakge [another open source package]
 - Switch from CRO to R requires initial internal investment that can pay off in the long run
 - Timeline slide
 - Hilight NoAA signal [Q4 2023]; then AA go [May 2024]; then E1 not being included then included[September/August]; then ISE[January? Check with Rupa]; then biomarker study [check with Kyle]
- Lessons learned
 - In-house flexibility, efficiency and dependability
 - Relationship with vendor [improved once they knew what we were doing]
 - Likely to expand with RFIs
 - SME appreciation for in-house work vs vendor work
 - SMEs recognized the challenges with inhouse updates/vendor outputs
 - Weighing the importance of updates based on these timeline implications
 - Highlight the benefits of in-house timelines (avoid bashing fortrea)
 - Leads into future plans and desire to do in-house
- Future plans
 - Next studies 100% in-house
 - Contribute more to open source
 - Plans to contribute to admiralpedx
- Potential Questions
 - Ok so you could have done this in SAS
 - Small team
 - We can leverage phamaverse instead of having to develop entire SAS macro library
 - Easier to parameterize the outputs
 - Graphics support in R is more flexible [SME preferred R figures vs SAS figures; in fact SAS figures were needed in R]
 - Demographics: Next generation; SAS skills limited [in history of of biometrics team]

STUDY OVERVIEW

- E-0001
 - Total Number of inhouse
 - Vendor Produced
 - In-House
- E-0002
 - Total Number of inhouse
 - Vendor Produced
 - In-House
- E-0001 + E-0002
 - Total Number of inhouse
 - Vendor Produced
 - In-House
- Biomarker Reference Range Study
 - Total Number of inhouse
 - Vendor Produced
 - In-House

PACKAGES

- Pharmaverse:
 - rtables
 - rlistings
 - logrx
- Other:
 - Ggplot2
 - tidyverse
 - Inhouse functions