ACCELERATION OF CRITICAL PATH MODEL INFORMED DRUG DEVELOPMENT (MIDD) SUBMISSION ACTIVITIES VIA DATA AND TOOL STANDARDIZATION

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Background and Rationale

Regulatory submissions for new drugs (NDAs/BLAs) increasingly rely on pharmacometric (PK/PD) analyses to support dosing, labeling, and design of post-approval trial commitments.

More frequently, MIDD related activities (data cleaning/prep, analysis, summary document preparation) are on the filing critical path (CP) following completion of the final registration studies, with delays directly impacting time to file. These delays impact overall medicine value.

Accelerating MIDD related CP activities via methods standardization, process automation, and proactive planning offers a potential mechanism for increasing speed without compromising quality.

Methods

CP MIDD activities and timelines for a Phase III program in atopic dermatitis were broken into 4 key stages

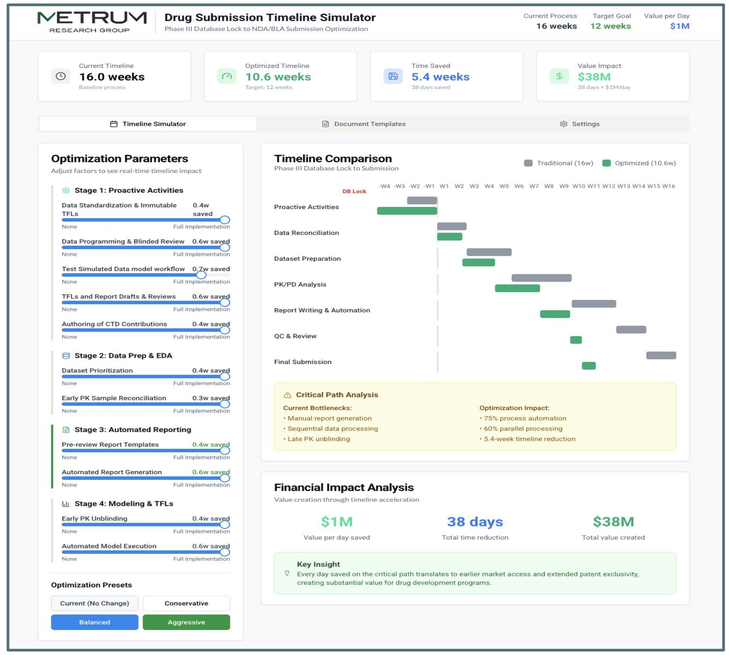
(1) Proactive Report Templating,
(2) Data Preparation & Exploratory Analysis,
(3) Modeling with Tables/Figures, and
(4) Modeling & Simulation.

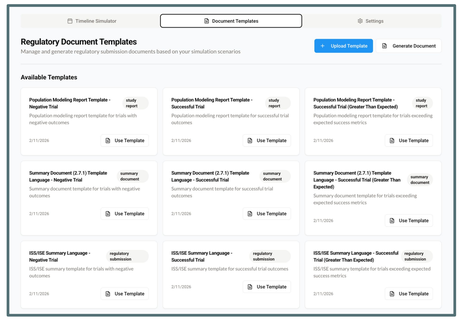
A suite of open-source tools supported by MetrumRG (MeRGE) covering data specification, model management and execution, rendering and storage of analysis-related visualizations, and trial simulations were utilized to investigate potential time savings that may be accrued from a baseline timeline for Modeling and Simulation Critical Path activities of 16 weeks.

Modeling activities were accelerated utilizing parallelization on a high performance grid on the Metworx platform

An automated tool was developed to visualize project timelines, alter assumptions regarding time saved, prioritizes critical tasks, assess risk mitigation, and improve team communication. Opportunities for acceleration were examined for each stage.

Results

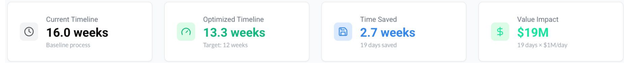




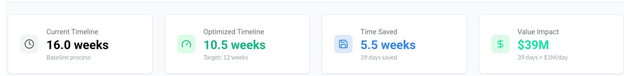
Proactive simulation, modeling, writing and review of key deliverables for each of the most likely scenarios can provide significant time savings

Savings

Scenario 1: Standardization, early PK, TRT unblinding, and post-dbase lock automation



Scenario 2: Scenario 1 plus proactive simulation, analysis, & deliverables



Conclusions

Standardization and proactive planning for potential study outcomes yields significant time savings and adds to product value.

Standardization enables rapid reproducible reanalysis. Risk from unidentified errors in first-use scripts is minimized.

Early PK unblinding can significantly decrease PMX endgame timelines.

Ensuring that PK and biomarker samples are collected prior to last visit, and proactive sample reconciliation activities yielded further reductions in timelines.

Interactive dashboards can assist in planning and communicating MIDD related critical path activities with other stakeholders.

References

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