

Shortening the Regulatory Submission Critical Path via MIDD Acceleration: A Multi-Trial Phase 3 Case Study

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BACKGROUND

Regulatory submissions for new drugs (NDAs/BLAs) increasingly rely on MIDD (model-informed drug development) analyses to support dosing, labeling, and design of post-approval trial commitments. 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 and access for patients.

OBJECTIVE

To develop a MIDD acceleration (MIDD-A) strategy that will result in a meaningful reduction in the NDA submission critical path (CP) for an ongoing Phase 3 drug development program.

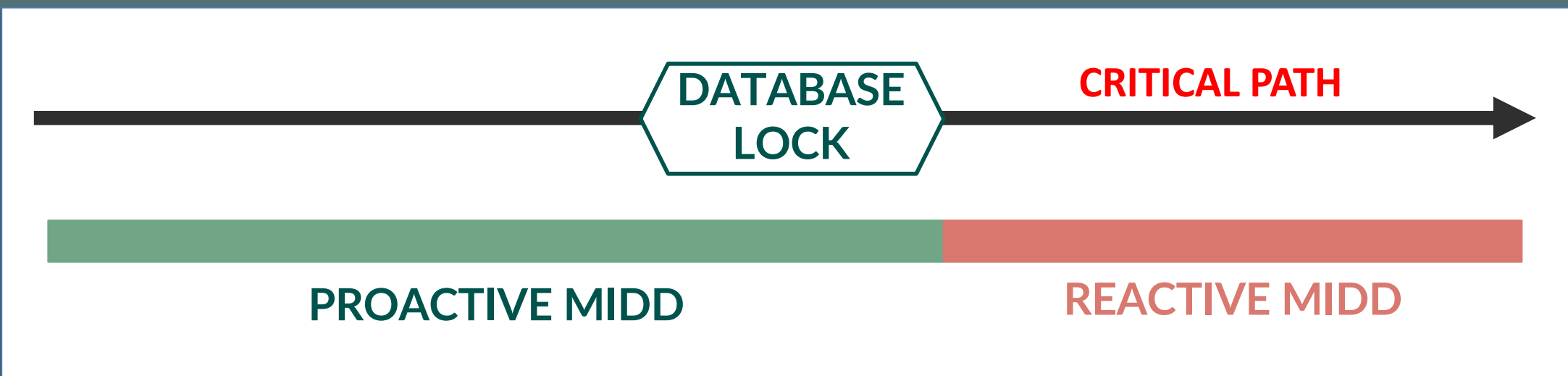
METHODS

- Building on a general approach for MIDD-A (1) and principles of CP project engineering (2,3), novel MIDD-A strategies and associated implementation plans were evaluated.
- The MIDD scope included 5 Phase 3 trials, plus supporting Phase 1 & 2 trials, and 7 total endpoints.
- The nominal (non-accelerated) development program CP timeline was 16 weeks post database lock (DBL).
- Key components of the MIDD-A strategy included:
 - standardization** of modeling tools, packages, data structures, tables, figures, and reports
 - automation** of fully code-based MIDD activities in a high performance cloud computing environment (Metworx™), and
 - proactive implementation** of high impact MIDD tasks given simulated or actual trial data.
- The approach leveraged multi-level parallel processing across the team, endpoints, and within MIDD tasks.
- Scenarios were evaluated using task, time, and dependency-based process simulations which estimated time from final DBL to final deliverables.

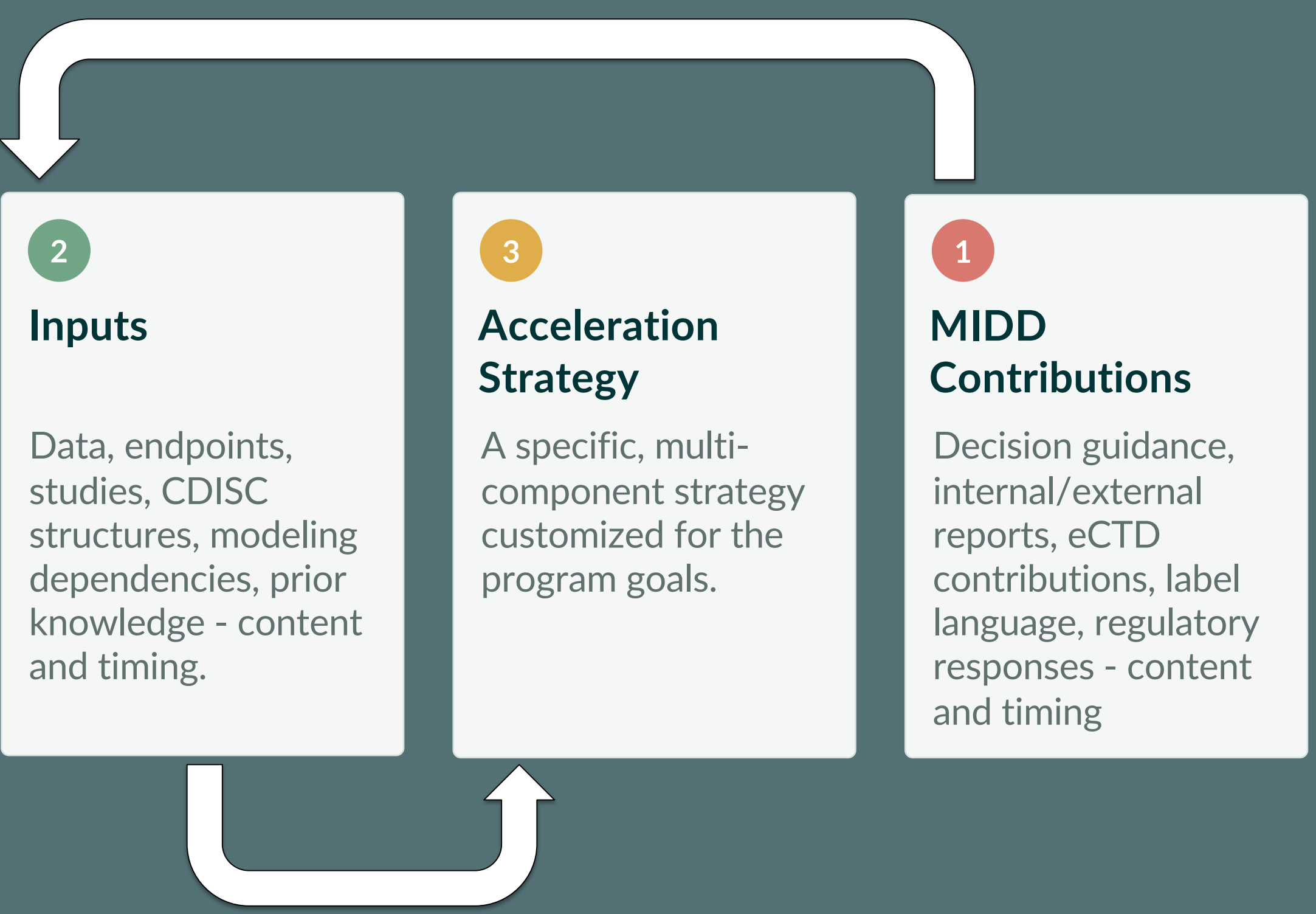
MIDD-Acceleration Impact



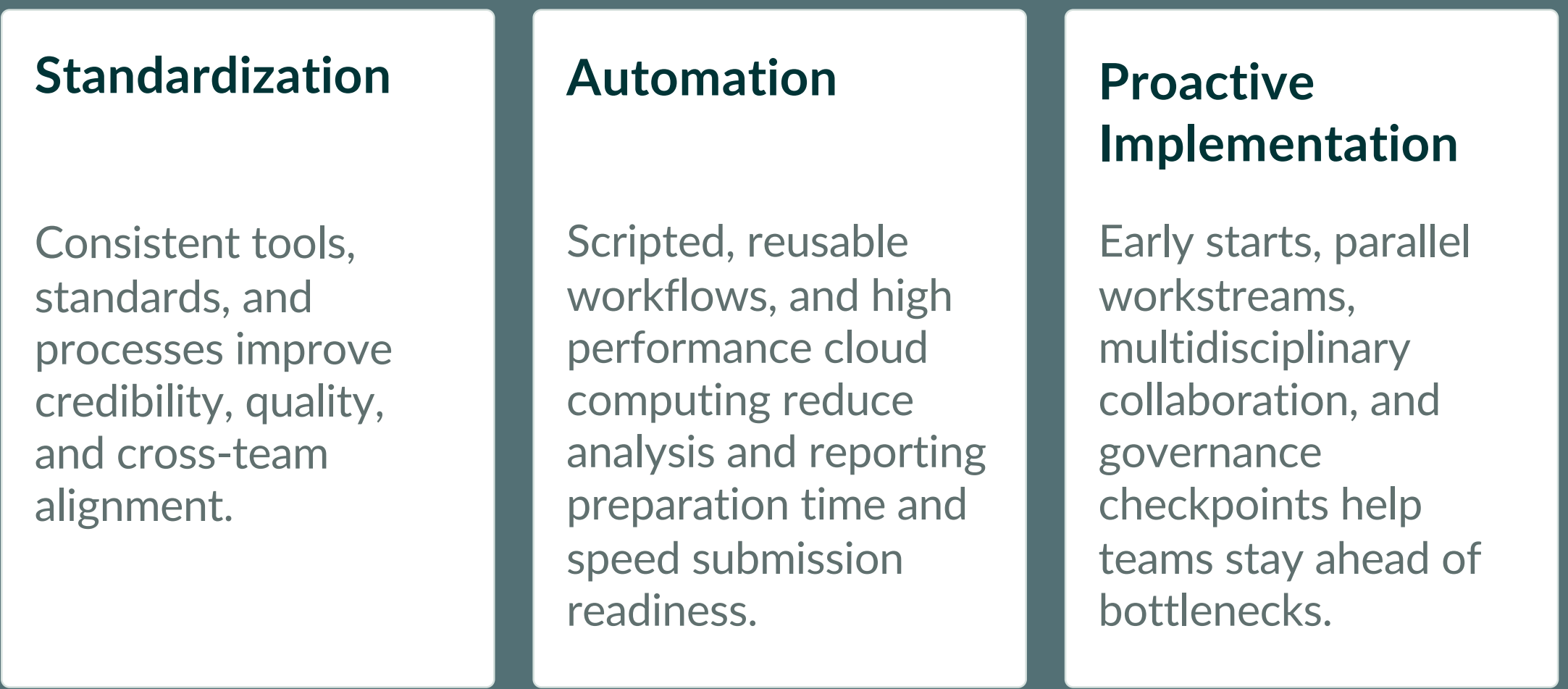
The Problem



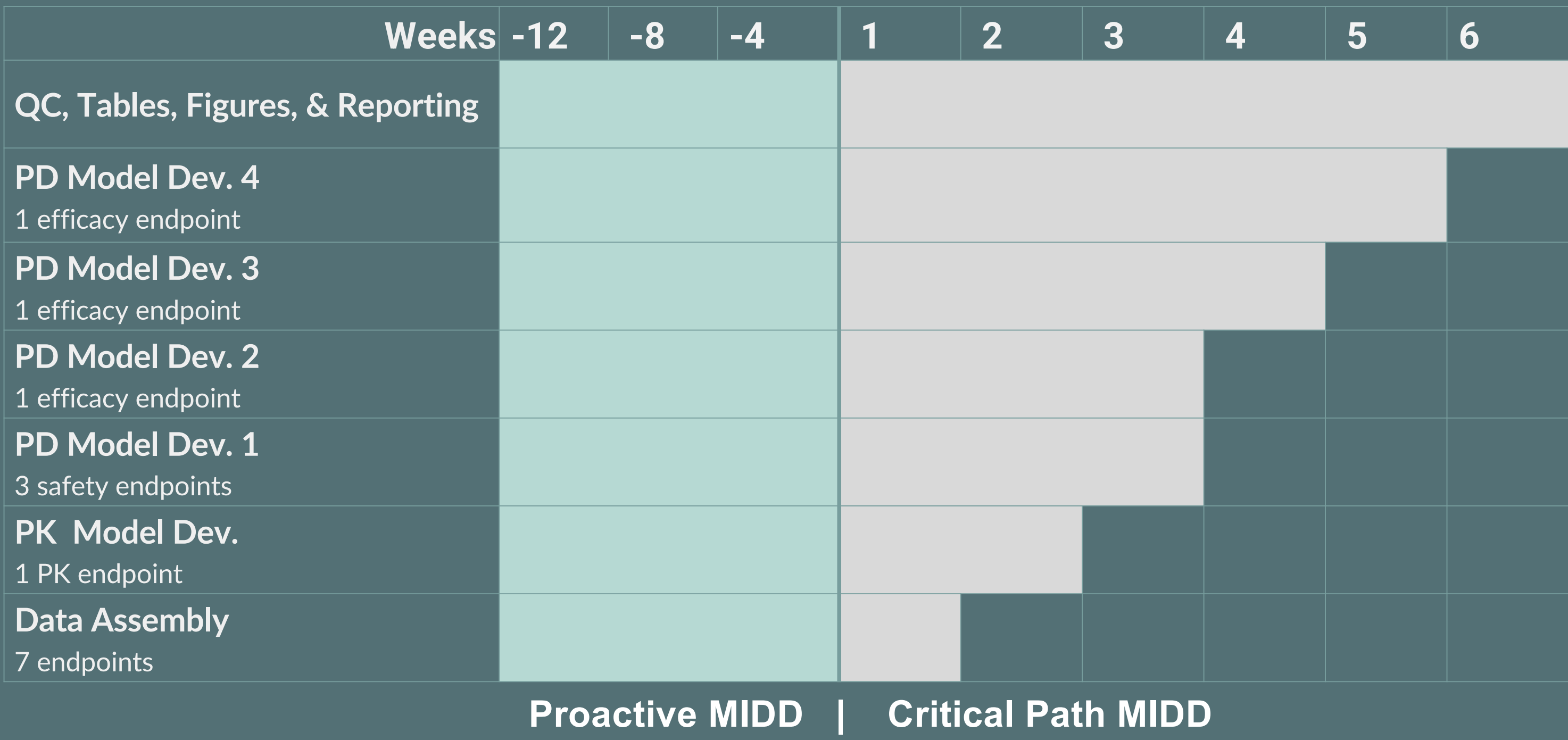
Strategy: Begin with the end in mind



Essential Components



Implementation



RESULTS

- The most impactful MIDD-A strategy resulted in a decrease of the nominal CP timeline from 16 weeks to 6 weeks.
- This 10 week savings is expected to yield at least \$70 million of value for the development program, relative to the nominal plan.
- This particular scenario included the analysis of actual emerging trial data for two of the Phase 3 trials coupled with proactive MIDD tasks based on simulated trial data for the remaining three trials.

CONCLUSIONS

- In this specific Phase 3 program, MIDD-A is expected to result in a meaningful decrease in the CP duration.
- Approaches that combine standardization, automation, and proactive implementation of MIDD activities are expected to yield significant time savings and add to product value.
- These approaches also allow for rapid reproducible reanalysis if changes in data occur and/or for responding to health authority queries.

REFERENCES

- Corrigan B. et al. Acceleration of Critical Path Model Informed Drug Development (MIDD) Submission Activities via Data and Tool Standardization. *Clinical Pharmacology & Therapeutics: Volume 119, Issue S1*, 2026.
- Kelley, J. E., Walker, M. R., & Sayer, J. S. (1989). The origins of CPM: a personal history. *PM Network*, 3(2), 7–22.
- S Atin and R Lubis 2019 IOP Conf. Ser.: Mater. Sci. Eng. 662 022031 *Implementation of Critical Path Method in Project Planning and Scheduling*.

