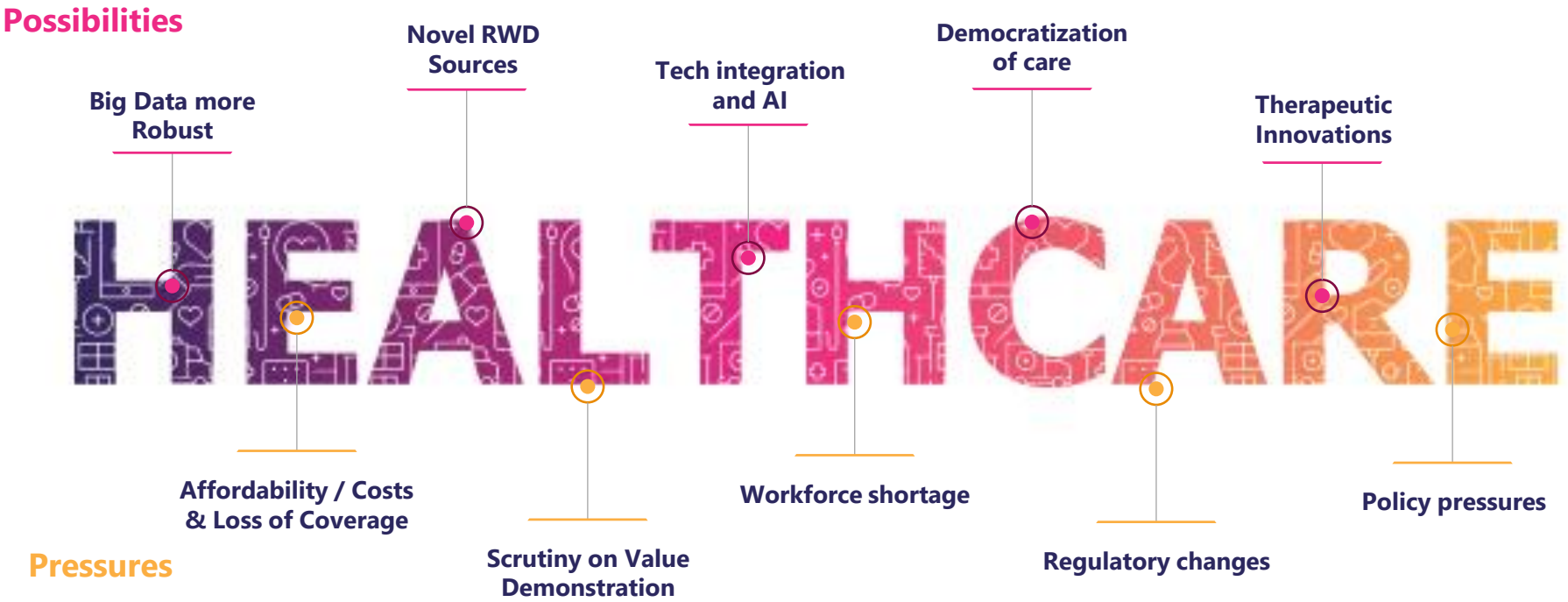
Beyond the Protocol:
Leveraging RWE to Inform Clinical Strategy and Strengthen Healthcare Decision-Making

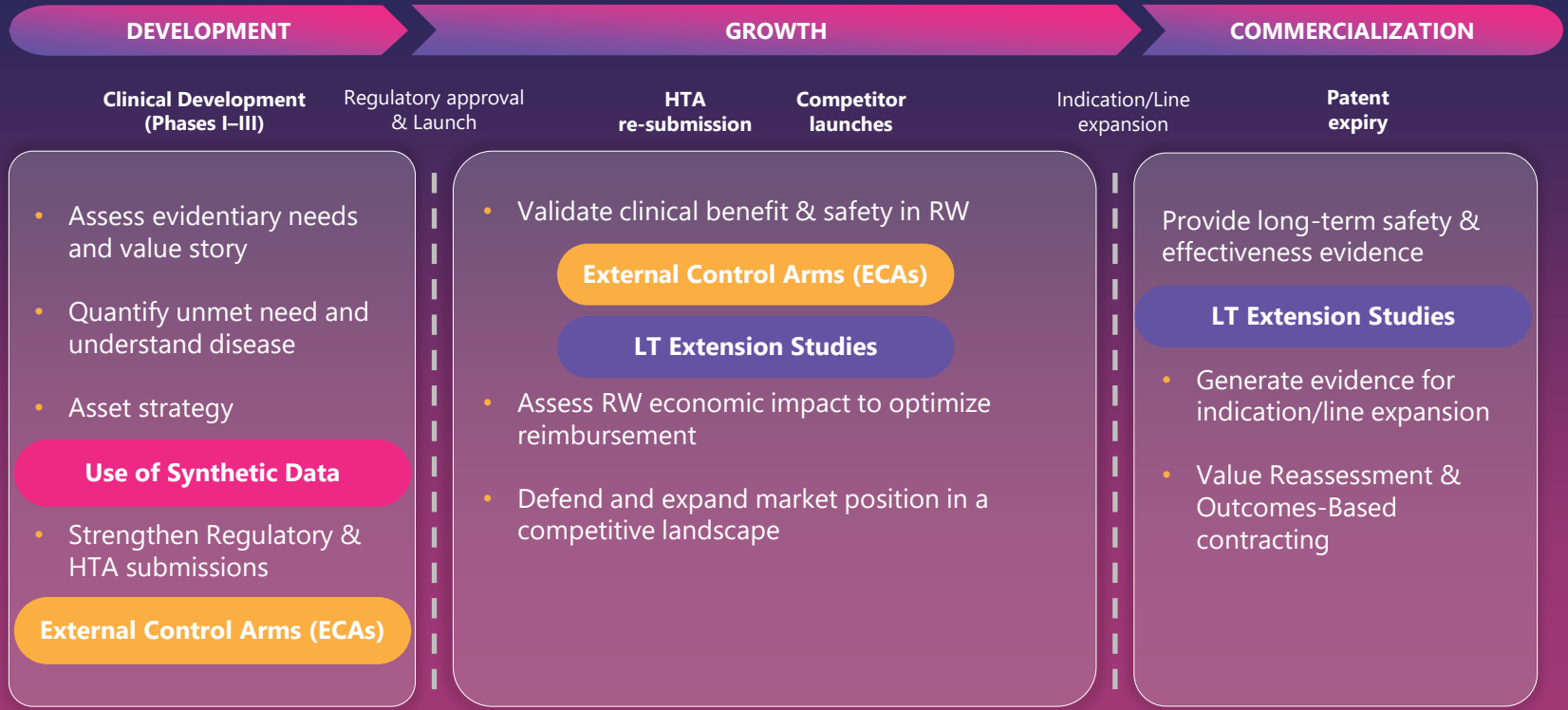
April 13th 2026

The future of Evidence Generation is being Rewritten



Leveraging Robust RWE Across the Product Lifecycle

Growing Role of Innovation Designs



Growing Acceptance of Innovative Designs (RCT-RWE)

	Use of Synthetic Data	External Control Arm	LT Extension Studies
	Artificially generated data that mimic the statistical properties of real data without containing identifiable patient information.	Data from historical RCT or RWD when randomization not feasible or ethical OR to power / accelerate study where high unmet need.	RW extension for RCT to assess long-term outcomes (safety & effectiveness) w or w/o drug provisions. The extension enables follow-up of tokenized trial patients via RW database or direct-to-patient data collection
FDA	"Synthetic data may be useful for algorithm development and exploratory analyses, but its suitability for regulatory decision-making depends on demonstrating that it reliably represents the underlying RWD." *2024 FDA workshop on AI/ML*	*"Randomized controlled trials are the most reliable way to demonstrate efficacy and safety… externally controlled studies may be considered, but they require strong justification."* *Draft Guidance Feb 2023*	*"Decentralized elements allow trial-related activities to occur remotely at locations convenient for trial participants."* *Final Guidance. Sep 2024*
EMA	"EMA bases its regulatory decisions on RWD sources… using rigorous and transparent analytics, such as advanced artificial-intelligence-driven methods." *2024 Data in Regulation*	*RCTs " are the gold standard… however, in some situations, causal conclusions may be derived from a setting where the investigational medicinal product data was collected under a clinical trial protocol while the control arm was not a randomized arm in that same protocol."* *EMA guideline 2025*	*"The DCT approach seeks to take advantage of technological progress and introduce new methodologies to make clinical trials more easily accessible and participation more convenient for trial participants."* *EMA Joint Meeting June 2023*

Use of Agentic AI to Generate Synthetic Data

Nascent Opportunities through Advanced Methods

Why Synthetic Data matters?

Inform Early Go/No-Go decisions
Cost-effective approach to optimizing asset strategy before large investments by simulating expected outcomes under various scenarios in Phase I-II

Inform CT Design
Cost-effective approach to modeling alternative controls & sample sizes and stress-test treatment effects

Privacy-Preserving Cost Effective ECAs
Build an ECA partially (+ RWD) or totally through a fully de-identified synthetic cohort. Not for regulatory purposes yet but can inform provider and payer decisions.

How to generate synthetic data

Start with appropriate RWD (patient-level) or RCT data source(s)

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Use AI-supported pipeline to generate a synthetic dataset

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Assess similarities to the original data to gauge success

What limitations of RWD does synthetic data overcome?

- RWD must closely resemble real patient populations
- RWD must protect patient privacy
- Costly, time-consuming and potential unethical if high unmet need

- **Do you have an early asset that you are considering multiple indications for?**
- **Would you like to stress-test your CDP using synthetic data?**
- **Do you have an asset whose value may be underestimated in the trial where an SCA could showcase the full benefits?**

Augment your CDP with an ECA to Strengthen a Submission

Growing Opportunities through Advanced Methods & Robust Data

Why ECAs matter?

Strengthen Single Arm Trials (SAT)
Provides contextual information for SAT regulatory submissions increasing probability of success

Accelerate Access to Needed Therapies
For RCT in high unmet need (e.g. accelerated approval pathway) and/or with slow recruitment; RWD can augment the control arm

Lifecycle Management Approach
Supports label expansions to new populations (e.g. to male breast cancer) or new lines of therapy for decisions by regulators, payers and providers

1- SAT: rare indication (control is unethical or unfeasible)
2- RCT with slow recruitment: high unmet need with inadequate SOC
3- RCT with open label extension (OLE) component to increase robustness of control

Yes

Is an RCT with well established SOC, in a like population + key trial endpoints available?

No

Can I match trial patients in terms of I/E criteria and key endpoints via a RW dataset(s)?

Data Used for ECA

- **Historical RCT Data** — Bayesian Borrowing
- Yes → **Patient-Level RWD (full or partial)** — Bayesian Borrowing
- No → **Aggregate RWD (benchmarking)**

- **Do you have an asset with SAT or slow recruitment RCT?**
- **Are you thinking of expanding an asset to a new population / LOT / setting?**
- **Have you identified RWD sources in your indications of interest in your key markets?**

Innovative Extension to Assess Long-Term Outcomes

Growing Opportunities through Advances in Technology & Use of Tokenization

Why LT Extensions matter?

Allows for Long-Term Follow-Up
Cost-effective data collection by reducing site and patient burden while collecting key safety and effectiveness endpoints over 10+ years

Enables Earlier Launch
For breakthrough therapies and high unmet need, launch can occur as soon as clinical efficacy is proven if the Company commits to a Phase IV study to collect LT data

Improves Representativeness
Loss to follow-up in long-term studies can lead to confounding, and RCTs often under-represent certain populations. The shift to RW endpoints makes the insights more relevant to decision-makers.

End of Parent RCT

Traditional RCT site-based amendment	Direct-to-Patient (DTP)	Via Database
Operational considerations: • Operational delivery continuity • Clinical trial requirements • High-cost approach	**Operational considerations:** • Reduced site & patient burden • Non-Interventional Study in some countries • Regional adaptations required?	**Operational considerations:** • Most cost effective • Regional adaptations required?
Scientific considerations: • Most robust data	**Scientific considerations:** • Endpoints “capturable” by patient • Select validation of key endpoints	**Scientific considerations:** • Coverage of desired endpoints, length of time (add death data) • Select validation of key endpoints
Ideal situation for application: • Shorter extensions (~1-2 years) • Small trial populations • Subtle or hard to recognize endpoints	**Ideal situation for application:** • Long-term follow-up (10+ yrs) • Endpoints reliably captured via ECOAs or Digital Health • Can follow patients who will change treatment centers	**Ideal situation for application:** • Strong national data coverage (Nordics, France, US) • Disease registries • Don’t need to follow all patients

- **Do you have a CAR-T asset or gene therapy that may require long-term follow up?**
- **Do you have a breakthrough therapy that you are considering accelerated approval for?**

Key Takeaways to Optimize Access to Therapies

RWE as Strategic Asset

- Integrate RWE early & anticipate post marketing collection of LT data
- Adopt Causal Inference Methods to protect ideals of safety & effectiveness

Invest in Robust RWD

- Invest in RWD quality and governance to ensure credibility with regulators and payers.

Comprehensive Strategy

- Adopt flexible, hybrid evidence strategies that combine synthetic data, ECAs, and long-term data collection tokenization approaches.

Cross-Functional Readiness

Medical, regulatory, biostats, and data science must operate as one evidence engine.

THANK YOU!

Any Questions? Let's stay connected!

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