ASX ANNOUNCEMENT

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Pathkey Advances TrialKey with Drug-Level AI Features

Highlights:

- **R&D breakthrough:** Pathkey.AI's AI-powered clinical trial analytics platform, TrialKey, now incorporates drug-level features such as molecular structure and pharmacokinetics, enhancing predictive accuracy and guiding drug candidate design.
- **Peptide proof-of-concept:** TrialKey successfully analysed 42 peptide trials in type 2 diabetes and obesity, identifying key molecular & patient drivers of trial success. This medical framework is therapeutically neutral and has the capacity to be directly applied to any drug modality or clinical dataset.
- **Market potential:** Global peptide therapeutics market valued at US$117bn in 2024, forecast to grow to US$260bn by 2030 (10.8% CAGR)[1].
- **Strategic evolution:** This is the first step in TrialKey moving beyond trial optimisation into AI-driven drug discovery and repurposing - opening new commercial and clinical applications.

Pathkey.AI Ltd (ASX: PKY) ("Pathkey" or "the Company"), a leader in AI-driven clinical trial optimisation, is pleased to provide an update on research & development supporting enhancements to the Company's flagship platform, TrialKey.

Pathkey continues to advance its mission of transforming clinical trials and drug development with artificial intelligence.

Pathkey's TrialKey platform brings AI-powered predictive analytics to clinical trials, benchmarking them against a global dataset of over 500,000 clinical programs. This enables:

- Probability of success predictions tailored to trial indication and phase.
- Optimised trial design through AI-driven analysis of endpoints, inclusion/exclusion criteria and patient cohorts.

[1] https://www.grandviewresearch.com/industry-analysis/peptide-therapeutics-market

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- Capital allocation and risk assessment for insurers and investors engaging with biotech companies.

Advancing AI R&D

Through its research and development (R&D) program throughout FY25, Pathkey has expanded TrialKey's ability to analyse clinical trials beyond protocol design and patient eligibility.

For the first time, TrialKey is now incorporating drug-level features - such as molecular structure and pharmacokinetic properties - alongside traditional trial variables. This represents a significant step toward enabling AI-powered drug discovery and repurposing.

The R&D work, incorporating TrialKey's explainable AI has, for the first time, enabled researchers to quantify which molecular properties and pharmacokinetic factors (e.g., half-life, bioavailability, DPP-4 susceptibility) are most associated with clinical trial success or failure—providing transparent, feature-level guidance for candidate design and trial planning.

Peptide Proof-of-Concept Study

To demonstrate the platform's latest enhanced capabilities, Pathkey applied TrialKey to a set of 42 clinical trials in peptide-based therapies for type 2 diabetes and obesity. A detailed summary of the methodology for the proof-of concept study is set out in the Appendix to this announcement.

Through the study, TrialKey identified the optimal drug and patient characteristics most associated with successful outcomes. The study highlighted features such as peptide length, molecular weight, receptor binding and patient comorbidities as critical drivers of trial success. This approach has the capacity to accelerate the identification of viable therapeutic candidates targeting metabolic disorders such as type 2 diabetes and obesity, and facilitate the design of new, more effective drugs.

Peptides are one of the fastest-growing therapeutic classes in biotech, with applications in oncology, endocrinology, metabolic disease and rare conditions. According to industry research by Grand View Research, the global peptide therapeutics market was valued at approximately US$117 billion in 2024 and is forecast to grow to US$260 billion by 2030 at a CAGR of around 10.8%. However, peptide programs face unique challenges in drug development - from stability and delivery, to trial design heterogeneity. These factors contribute to high trial failure rates and elevated risk for sponsors, investors, and insurers.

Strategic evolution

The outcome and impact of these results shows that TrialKey has the potential to evolve into a robust decision-support tool for early-stage drug discovery, enabling researchers to rank, cluster and explore peptides more efficiently. Pathkey's case study in the peptide report indicates that this capability has the capacity to be applied to any drug category.

This provides a number of benefits for sponsors, research organisations, investors, partners and patients:

- For sponsors and contract research organisations (CROs), this means TrialKey can now extend beyond optimising clinical trial design and begin to inform which compounds and patient subgroups are most likely to succeed.
- For investors and partners, this marks Pathkey's first concrete step into the high-growth field of AI-driven drug discovery and repurposing.
- For patients, this points to a future where therapies are designed, tested and delivered more efficiently - reducing trial failures and accelerating access to life-saving treatments.

Pathkey.AI Executive Chairman, Saurabh Jain, said:

"The success of Pathkey's R&D program has proven that TrialKey is evolving from a clinical trial optimisation platform into a comprehensive AI engine for both trial design and drug discovery. These developments strengthen Pathkey's commercial position, broaden its addressable market and reinforce the Company's role as a global leader in AI for life sciences."

This announcement has been authorised for release by the Board of Pathkey.AI Ltd.

About Pathkey.AI

Pathkey.AI Limited (ASX: PKY) is an Australian technology company applying artificial intelligence to improve the efficiency, success, and transparency of clinical trials. Pathkey.AI's core platform, TrialKey, is an AI-powered decision-support tool that predicts the probability of success for clinical trials and helps sponsors optimise trial design and planning. The company is committed to transforming drug development by reducing risk, improving resource allocation and unlocking data-driven innovation across the life sciences sector.

Appendix

Methodology for Peptide Case Study

Study Identification

A total of 42 clinical trials were selected for inclusion in this analysis, focused on peptide therapies in Type 2 diabetes, obesity and overweight populations. Safety-only trials were deliberately excluded to maintain consistency in efficacy endpoints. Each trial was reviewed in detail by a subject matter expert to assess clinical success against the primary endpoints. Of the 42 trials, 29 were identified as successful.

Although peptides were the initial focus, this same trial identification and expert validation process has the capacity to be applied to any therapeutic area, disease indication or drug class. The framework is indication-agnostic and scalable across clinical trial datasets of varying size and complexity.

Data Extraction and Variable Construction

Trial data were mined using TrialKey's advanced natural language processing (NLP) and data extraction pipeline. Structured and unstructured clinical trial records were transformed into analysable features. Alongside the platform's existing library of 1,300+ trial design and population variables, peptide and population-specific features were developed to capture nuances unique to this therapeutic class.

This process is adaptable: the same pipeline has the capacity to extract drug-class-specific features for other modalities (e.g., antibodies, small molecules, gene therapies) or different therapeutic areas (oncology, cardiovascular disease, neurology). By tailoring the variable set, TrialKey ensures that clinically relevant attributes are consistently captured, regardless of indication.

Peptide Characteristics Engineering

For this case study, peptide-specific variables were engineered, including sequence length, molecular weight, GLP-1 and GIP receptor binding affinity, DPP4 susceptibility, half-life, bioavailability, hydrophobicity, instability index, immunogenicity risk and chemical modifications such as Aib substitution, acylation and lipidation.

In other contexts, equivalent feature engineering would focus on mechanism-specific attributes (e.g., antibody isotype and glycosylation for biologics, chemical scaffolds for small molecules and vector design for gene therapies).

Other Variables

Eligibility criteria and biomarkers included BMI, HbA1c, fasting glucose, triglycerides, lipid levels (LDL, total cholesterol), blood pressure, heart rate, eGFR, liver function (AST) and calcitonin. Patient background factors included prior GLP-1 use, recent weight-loss drug use, steroid or antidepressant use, bariatric surgery history, comorbidities, cardiovascular disease, pancreatitis history, smoking status, alcohol use and demographics such as age and gender. Routes of administration covered oral, intradermal, subcutaneous and sublingual.

This structure highlights how population-level eligibility and background features - which vary by indication - can be incorporated into predictive models to better reflect real-world trial heterogeneity.

Modeling Approach

The dataset was modeled using XGBoost (Extreme Gradient Boosting), a high-performance algorithm chosen for its ability to handle heterogeneous, information-rich datasets while mitigating overfitting through regularisation. XGBoost's structured decision-tree framework provided robustness in capturing non-linear interactions between drug properties, trial design variables and clinical outcomes.

This modeling framework is therapeutically neutral and has the capacity to be directly applied to any drug modality or clinical dataset.

Explainable AI and Shapley Values

To address the interpretability challenge of machine learning models, Shapley values were applied. Originating from cooperative game theory, Shapley values quantify each feature's marginal contribution to a model's prediction. Within this study, they were used to decompose the relative importance of peptide attributes, assess the influence of patient background factors, and provide feature-level transparency at both the individual study level and across the dataset.

The same explainable AI framework has the capacity to be leveraged in other drug discovery and validation programs to highlight the most influential design parameters, biomarkers, or patient traits driving success.

Outcome and Impact

This methodology enabled identification of peptide features and population characteristics most strongly associated with clinical success. By combining robust predictive modeling with explainable AI, TrialKey's approach provides transparency, strategic development insights and guidance for identifying subgroups most likely to benefit from peptide-based therapies.

More broadly, the methodology demonstrates a generalisable system for drug discovery and validation across any therapeutic class or indication. Whether applied to peptides, biologics, small molecules or advanced modalities, the same framework supports:

- Transparent identification of the key drivers of trial success.
- Optimised drug design and formulation strategies.
- Biomarker-guided targeting of responsive patient populations.

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