PYC Therapeutics

Life-changing science

Bell Potter healthcare conference

November 2024

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1 in every 1,000 people has polycystic kidney disease and no treatment options available

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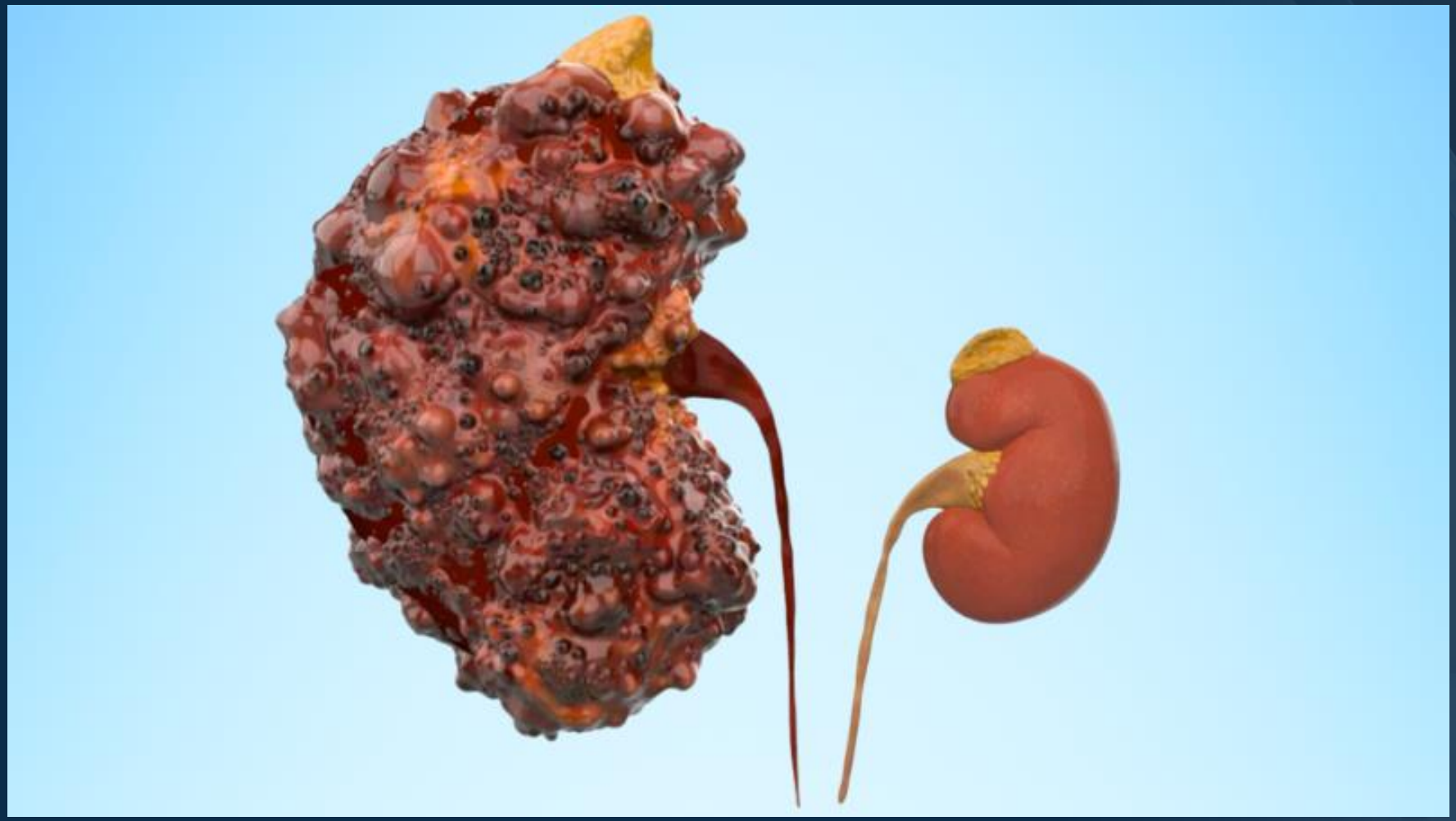

Image credit: the PKD Foundation

PYC is developing a disease-modifying drug candidate for these patients

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Program	2025	2026	2027	2028
RP11 / VP-001 Monogenic blinding eye disease of childhood Gene: *PRPF31*	Ph1/2 study → Registrational study → NDA 1 Clinical proof-of-concept		Registrational efficacy	Product launch and transition to commercial-stage company
ADOA / PYC-001 Monogenic blinding eye disease of childhood Gene: *OPA1*	Ph1/2 study Human safety	2 Clinical proof-of-concept Registrational study → NDA	Registrational efficacy	
ADPKD / PYC-003 Most common lethal single-gene disorder in the world Gene: *PKD1*	Regulatory approval to commence FIH studies Ph1/2 study Human safety	3 Anatomical surrogate (TKV) efficacy Registrational study → NDA	Surrogate/Registrational efficacy	
PMS / PYC-002 Monogenic CNS disease of childhood Gene: *SHANK3*	GLP toxicology studies	Regulatory submission for FIH studies Ph1/2 study Human safety 4 Clinical proof-of-concept	Registrational study	

Based on management forecasts as at 13 November 2024 and subject to the risks set out in the company's ASX disclosures of 14 March 2024

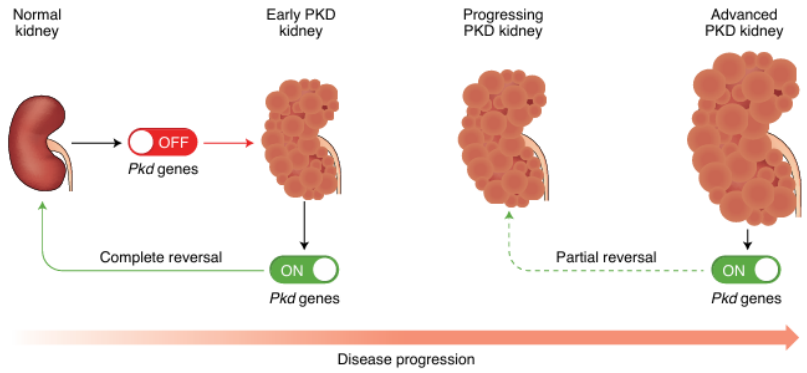
DISEASE MODELS

Reversing polycystic kidney disease

A new study shows that re-expressing *PKD* genes early in the course of the disease can fully reverse polycystic kidney disease in mice. These results reveal an unexpected ability of the kidney to regenerate following genetic rescue of polycystin function.

Alessandra Boletta

Polycystic kidney disease (PKD) is the most common human monogenic disorder[1,2]. Inherited as autosomal dominant, the disease ensues when expression of the *PKD1* or *PKD2* genes drops to low levels in individual renal tubular cells, mostly due to loss-of-heterozygosity, which causes clonal cyst initiation[3]. Increased proliferation, epithelial flattening, excessive inflammation and matrix deposition are histological hallmarks of the disease, which exacerbate with time and lead to irreversible loss of renal function[1] (Fig. 1). Recently developed interventions aimed at slowing this process significantly benefit patients and delay the



"Re-expressing the polycystins might ultimately remain the best — or possibly the only — way to revert the disorder"

Nature GeNetics | VOL 53 | DecembeR 2021 | 1623–1630

PYC-003 addresses the underlying cause of polycystic kidney disease

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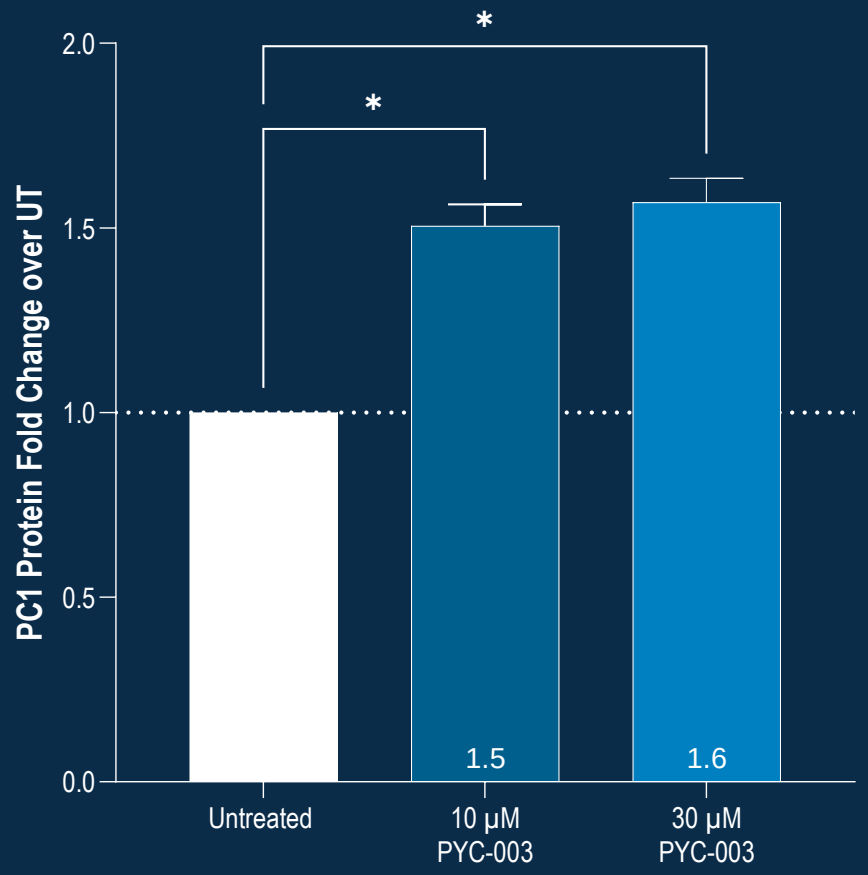
Addresses the root cause of PKD in Human Kidney Cells[1]

PYC-003 increases levels of PC1 protein (the missing protein that causes PKD) in a human cell line

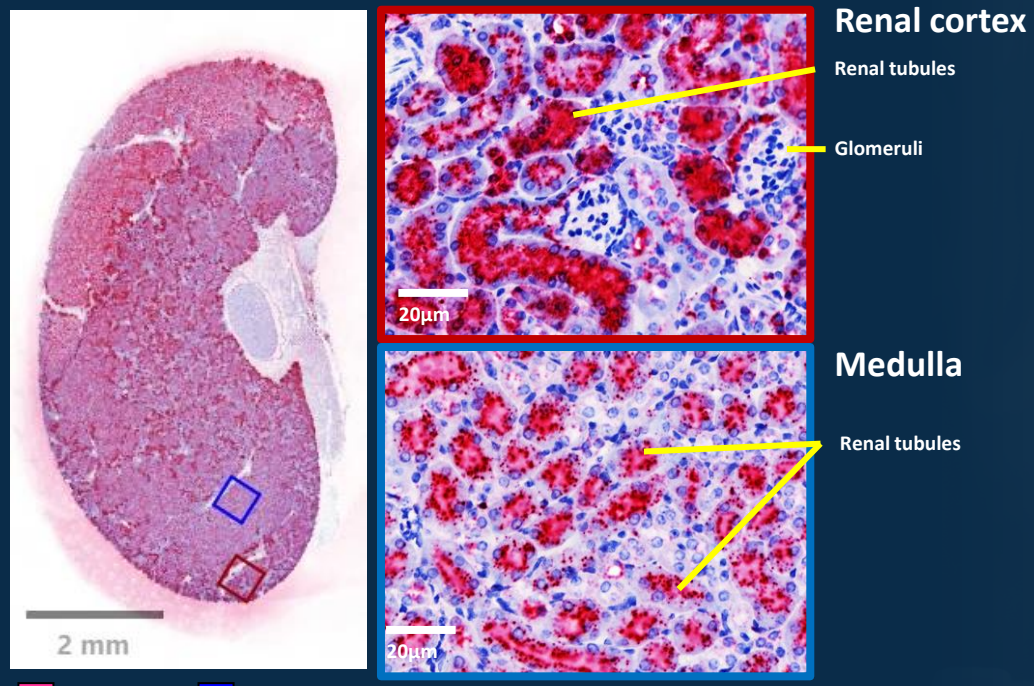


PC1 is the rate-limiting modulator of cystic disease[2]

1. PC1 full length protein fold-change over untreated (normalised to total protein) assessed at day 3 following treatment with either 10 µM or 30 µM PYC-003. Data presented mean+S.D (n=2 for protein). The data show a statistically significant (Dunnett's post-hoc test *** = <0.001, * <0.05) difference between treatment groups. Assessed in HEK293 cells.
2. Lee SH, Somlo S. Cyst growth, polycystins, and primary cilia in autosomal dominant polycystic kidney disease. Kidney Res Clin Pract. 2014;33(2):73-8.
3. Ferreira FM, Watanabe EH, Onuchic LF. Polycystins and Molecular Basis of Autosomal Dominant Polycystic Kidney Disease. In: Li X, editor. Polycystic Kidney Disease [Internet]. Brisbane (AU): Codon Publications; 2015 Nov. Chapter 7.

PYC-003 reaches all of the cells affected by polycystic kidney disease

WT/C57BL6 kidney

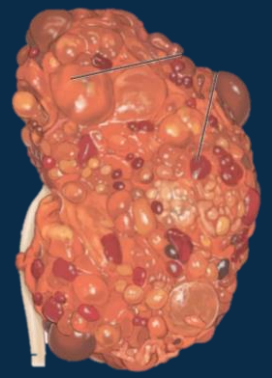


Distribution of PYC-003* to healthy mouse kidney
Single intravenous 10 mg/kg dose.
Images 3 days post-dose measured by miRNAscope.

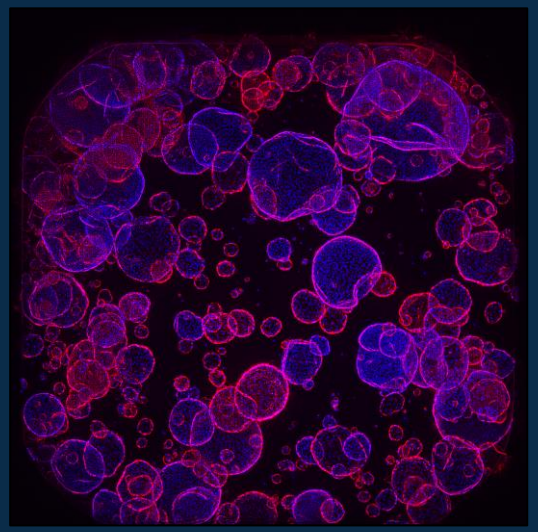
PYC-003 mouse surrogate used due to difference in PKD1 sequence between humans and mice.

PYC-003 is effective in the ‘killer experiment’ – 3D models from patients with end-stage renal failure due to PKD

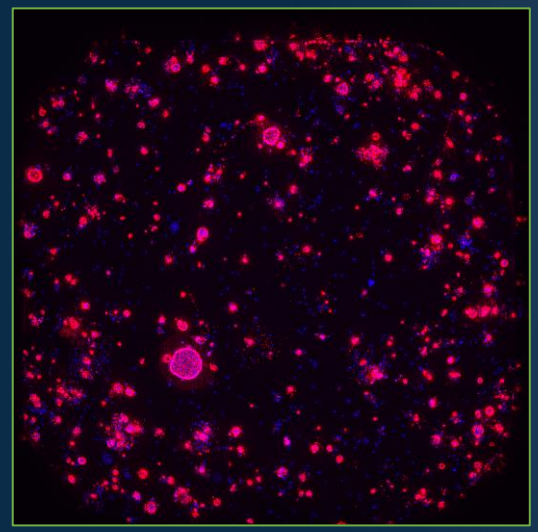
Polycystic kidney

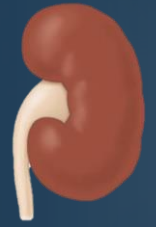


Untreated



PYC-003 treated





1. Refer ASX announcements 13 November 2023, 4 October 2023, 7 October 2020 and 16 December 2020

High-quality clinical data is king in life sciences – it is the 'coinage of the realm'

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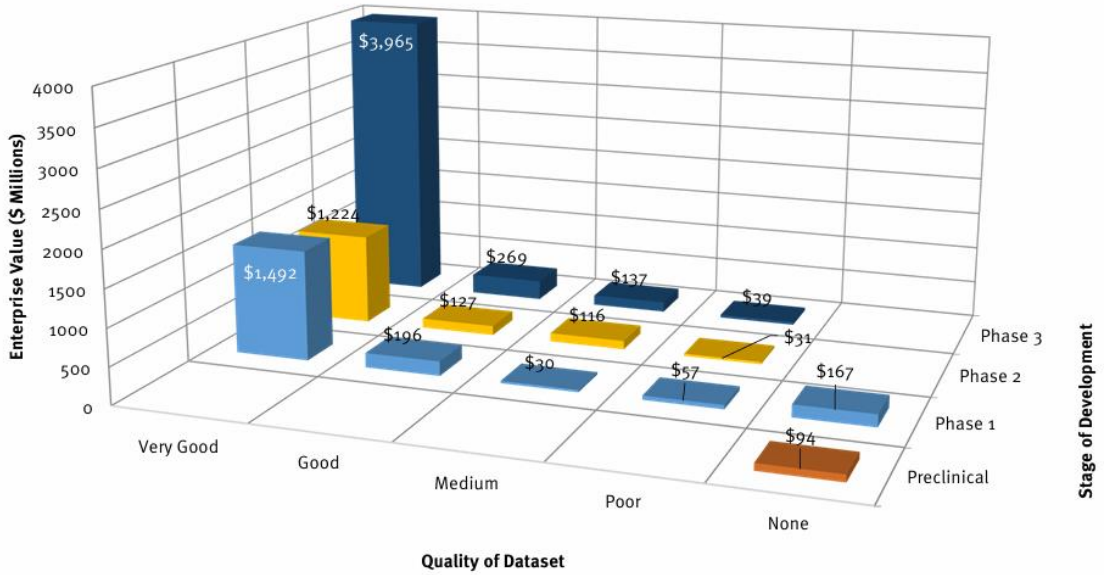
"Winner-Take-All" Mindset Re-Emerging in Biotech

Driven in part by Vaxcyte and Summit, we are seeing the average EV of Phase 3 stocks with very good datasets come close to $4 billion.

The of average value of a company with a great Phase 3 dataset today is *forty-two times higher* than a company with no data.

We have not seen a quality premium like this before in biotech.

Average Enterprise Value of a Biotech Listed on U.S. Exchanges by Stage of Development and Quality of Data, Sep 6, 2024 ($ millions)



Source: CapitalIQ and Stifel analysis. We classified datasets that indicated a high probability that the drug would meaningfully improve on the standard of care for a disease as "very good". We classified "good" data as data that might beat the standard of care. Medium data was data that was unlikely to beat the standard of care, was very early or came from a study with a mixed signal. Poor data reflects situations where a drug did not perform well at all in a clinical trial.

28

1. Stifel biopharma market update September 2024

“There’s a lot of demand right now for these types of companies…Companies that have programs with high probability of success in the clinic and the opportunity to quickly accelerate through clinical development.”

Endpoints News 31 October 2024 - Q&A: Jade CEO talks about reverse merger and IgAN drugs

Drugs addressing diseases caused by mutations in single genes are 5x more likely to succeed[1] in the clinic

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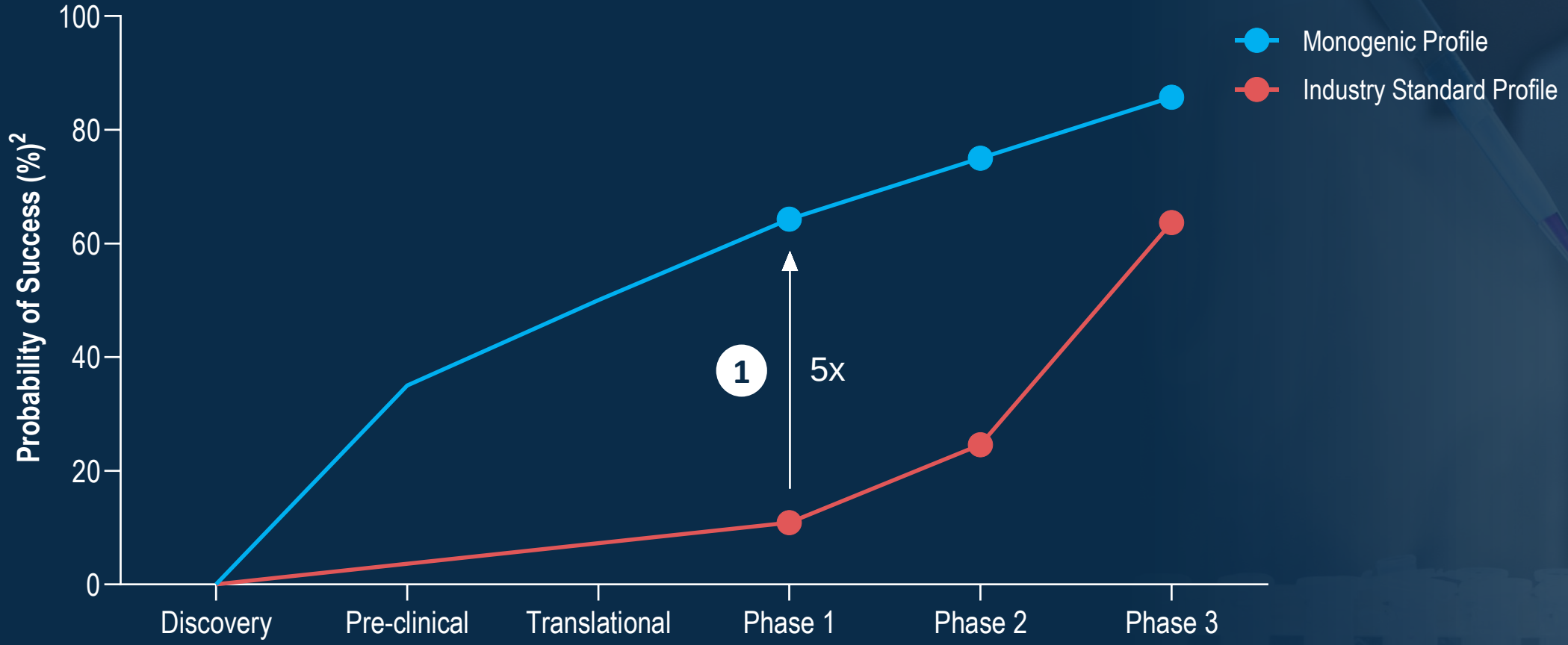

1. Advancing Human Genetics Research and Drug Discovery through Exome Sequencing of the UK Biobank. doi: https://doi.org/10.1101/2020.11.02.20222232
2. Actual probability of success numbers begin with First-in-Human (Phase 1) as described by Alnylam in https://news.alnylam.com/rnai/articles/harnessing-human-genetics-power-next-wave-rnai-therapeutics