

# GeneTether



Increasing Efficiency in  
Gene Editing

A preliminary prospectus containing important information relating to the securities described in this document has been filed with the securities regulatory authorities in each of the provinces of British Columbia, Alberta and Ontario. A copy of the preliminary prospectus, and any amendment, is required to be delivered with this document. The preliminary prospectus is still subject to completion. There will not be any sale or any acceptance of an offer to buy the securities until a receipt for the final prospectus has been issued. This document does not provide full disclosure of all material facts relating to the securities offered. Investors should read the preliminary prospectus, the final prospectus and any amendment for disclosure of those facts, especially risk factors relating to the securities offered, before making an investment decision.

Corporate Presentation | November 4, 2021



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## Reference to Prospectus

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This presentation is qualified in its entirety by reference to, and must be read in conjunction with, the information contained in the prospectus. A prospective investor is not entitled to rely on parts of the information contained in this presentation to the exclusion of others. An investor should rely only on the information contained in the prospectus. The Company has not, and Research Capital Corporation (the “Agent”) has not, authorized anyone to provide investors with additional or different information. If anyone provides an investor with additional or different or inconsistent information, including statements in media articles about the Company, the investor should not rely on it. Except as specifically provided herein, this presentation may not be copied or otherwise distributed, in whole or in part, by or to any person or in any medium whatsoever. Any unauthorized use of the presentation is strictly prohibited.

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# Disclaimer

## Forward Looking Information

This Presentation contains forward looking statements with respect to GeneTether. By their nature, forward looking statements are subject to a variety of factors that could cause actual results to differ materially from the results suggested by the forward looking statements. In addition, the forward looking statements require GeneTether to make assumptions and are subject to inherent risks and uncertainties. There is significant risk that the forward looking statements will not prove to be accurate, that GeneTether's assumptions may not be correct and that actual results may differ materially from such forward looking statements. Accordingly, readers should not place undue reliance on the forward looking statements. Generally, forward looking statements can be identified by the use of terminology such as "anticipate", "will", "expect", "may", "continue", "could", "estimate", "forecast", "plan", "potential" and similar expressions. Forward looking statements contained in this Presentation may include, but are not limited to statements with respect to the outlook for the gene editing industry and related industries; challenges and opportunities related to the gene editing industry; the completion and timing of preclinical and clinical studies; the ability of any patents resulting from GeneTether's patent applications to protect the commercial prospects of its assets; the achievement, and the timing of, certain development milestones and the successful execution of GeneTether's business strategy (including its business model and mission); the use and benefits of GeneTether's products and services; demographic and market size/trends; forecasts of revenue and financial projections/growth potential; GeneTether's ability to obtain marketing exclusivity for any of its approved therapies; anticipated capitalization, projected milestones and the go-forward management of GeneTether; the potential impact of the COVID-19 pandemic on GeneTether's business or operations; and other expectations, beliefs, plans, objectives, assumptions, intentions or statements about future events or performance, expected regulatory filings, review and approval dates, and start-up timelines and schedules, and statements related to the continued overall advancement of GeneTether's business.

These forward looking statements are based on a number of assumptions which may prove to be incorrect including, but not limited to: general economic, market and business conditions, the outcome of research studies, the ability to obtain certain approvals, the accuracy of cost estimates, ability to obtain sufficient capital on satisfactory terms, availability of equipment and supplies, changes in customer demand, currency exchange rates and the impact of changes in applicable laws and regulations. The forward looking statements contained in this Presentation are made as of the date hereof or the dates specifically referenced in this presentation, where applicable. Except as required by law, GeneTether undertakes no obligation to update publicly or to revise any forward looking statements that are contained or incorporated in this Presentation. All forward looking statements contained in this Presentation are expressly qualified by this cautionary statement.

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# GeneTether

We are on a mission to develop new, curative therapies for patients with devastating genetic diseases using our GeneTether platform technology



# Investment Highlights

## Experienced Team

- Focused on harnessing next generation technology to significantly increase efficiency of gene editing and potentially cure serious and life threatening genetic diseases
- Extensive public life science company experience
- Global capital markets experience and extensive investor network

## Disruptive Platform Technology

- Highly efficient insertion of DNA into the genome for gene correction and complementation strategies
- Proof of concept studies showed ~7x higher gene editing efficiency using GeneTether compared to unmodified Cas9
- Expected to result in superior efficacy, safety, and flexibility

## Rare Genetic Diseases

- Pursuing curative therapies for rare genetic diseases
- Genetic kidney diseases that progress to chronic and end-stage kidney disease
- Life-threatening genetic skin diseases

## IP Portfolio

- Wholly-owned intellectual property; no 3<sup>rd</sup> party financial obligations
- 1 issued patent (Australia), 8 others pending, including in the U.S.
- Oct. 2021 USPTO Office Action indicating allowance of claims covering current embodiment of GeneTether technology



# Experienced Life Sciences Team

	<p>Roland Boivin, MBA Chief Executive Officer &amp; Director</p>	
	<p>R. Geoffrey Sargent, PhD Co-Founder &amp; Chief Scientific Officer</p>	
	<p>Jean Jen, CPA, CA, MPAcc Chief Financial Officer</p>	
	<p>Peter Sampson, PhD Vice President, R&amp;D</p>	
	<p>Kuldeep Neote, PhD Chair – Scientific Advisory Board Innovation/Strategy Consultant</p>	



# Experienced Board of Directors

	<p>William J. Garner, MD Co-Founder &amp; Executive Director</p>	
	<p>Andre Fraga, Int. MBA Director</p>	
	<p>P. Gage Jull, PEng, MBA, CFA Director</p>	
	<p>Daren Graham, JD Chairperson</p>	

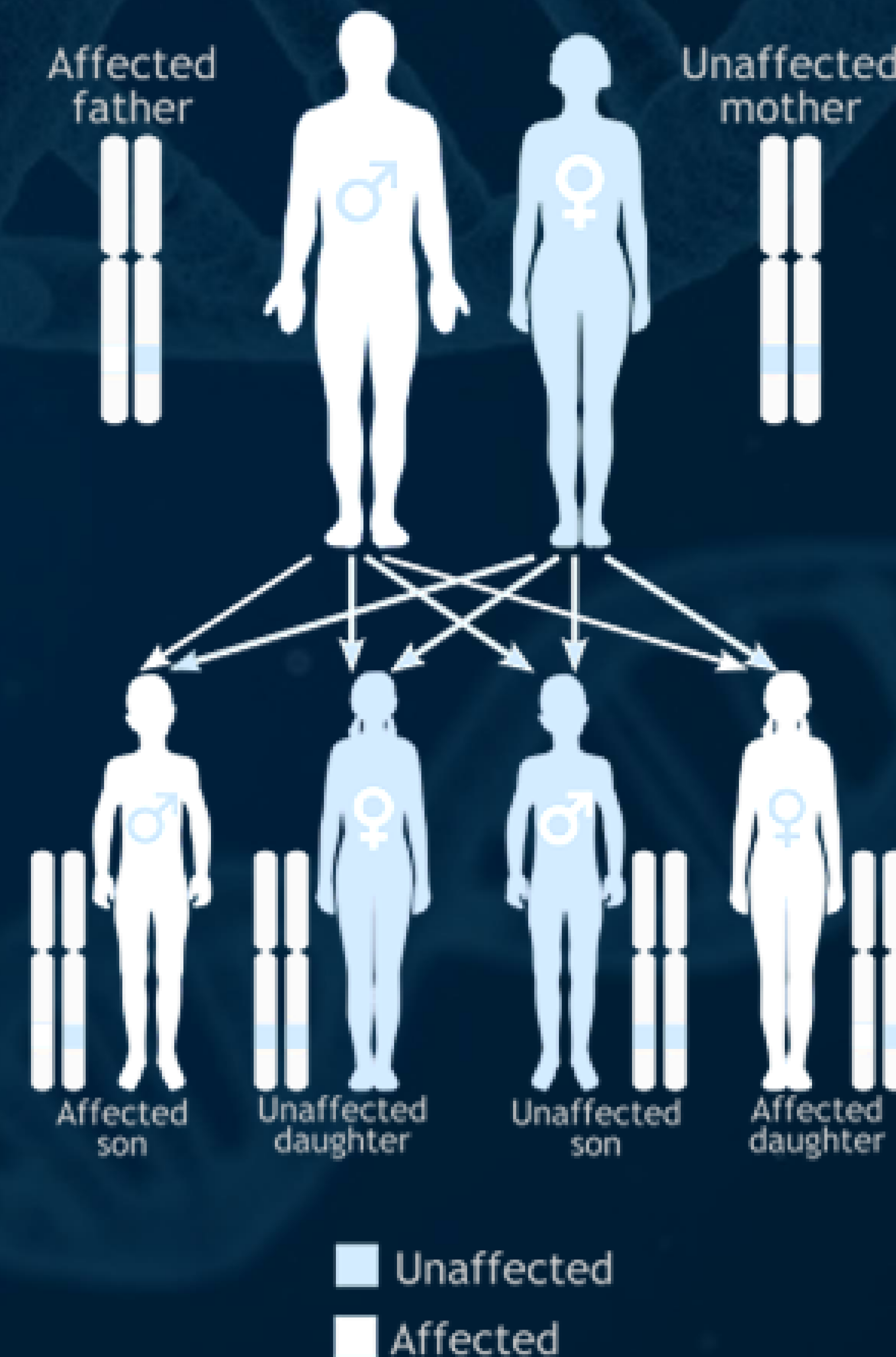


# Genetic Diseases

Approximately 10,000 diseases are known to be caused by aberrant DNA sequences that are inherited by one or both biological parents.

Traditional small molecule and biologic therapies have had limited success in treating many of these diseases because they fail to address the underlying genetic causes.

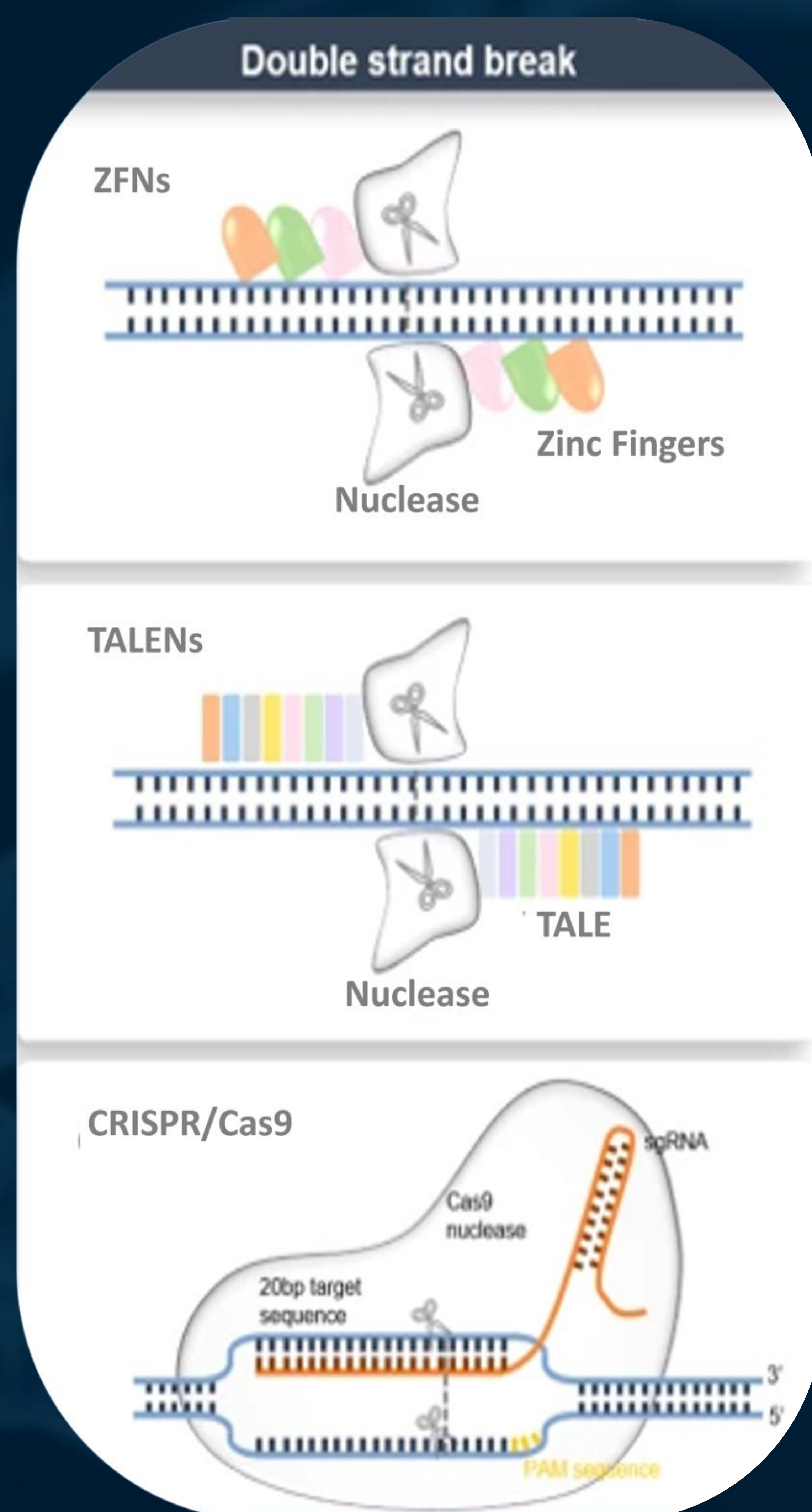
Recent advances in gene editing technologies provide the potential for curative therapies for many genetic diseases.





# Gene Editing – How it Works

## Creating double-strand breaks



A gene editing nuclease, CRISPR/Cas9 for example, is guided to a precise, predefined location in a cell's DNA where it creates a double-strand break (DSB).

Creating double-strand breaks is like a biological "find and delete" function.



# Major Gene Editing Technologies

## For creating double-strand breaks



CRISPR – A component of certain bacterial immune systems that is capable of guiding the system to matching sequences of DNA.

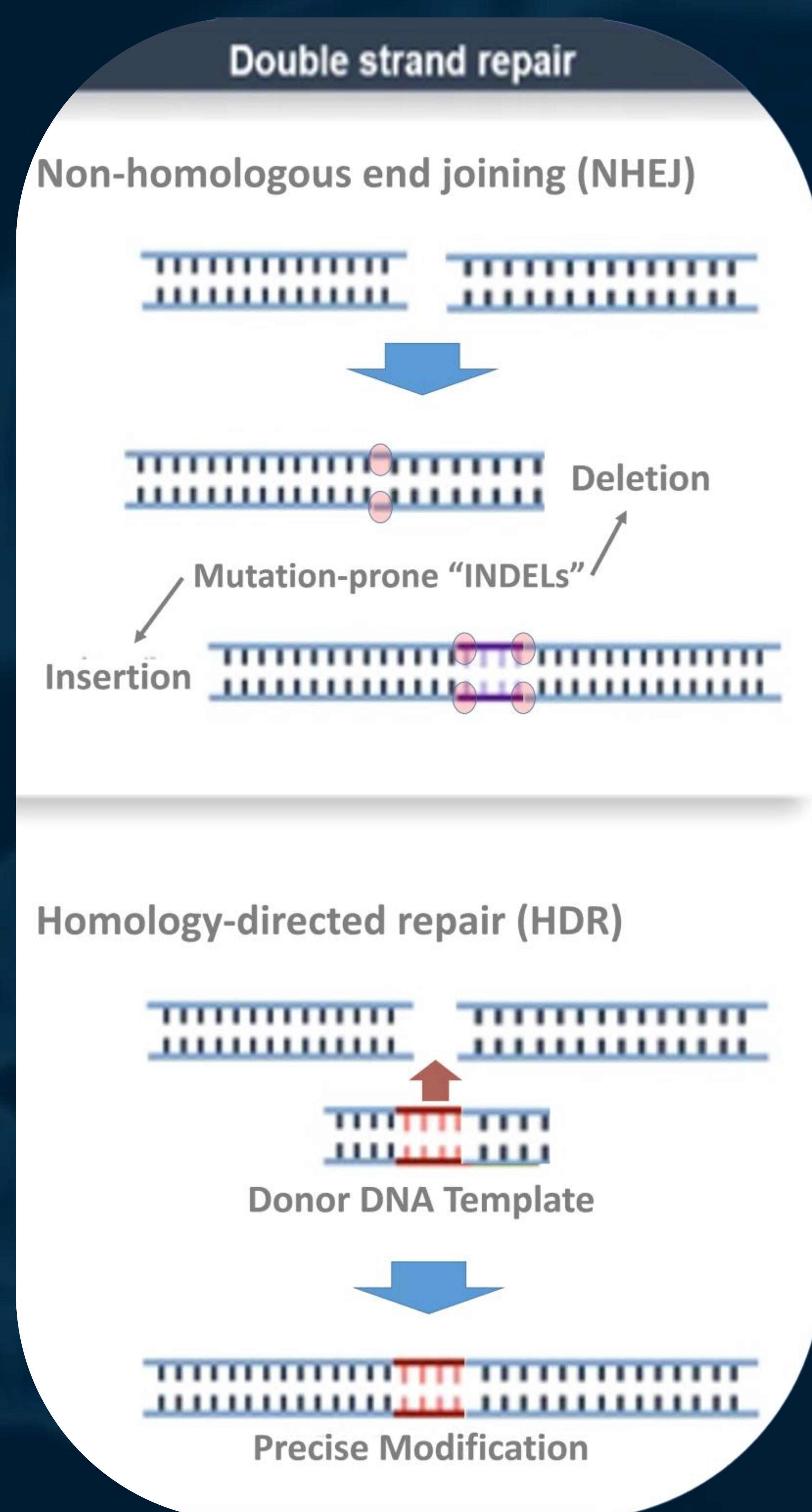
ZFN – Sequence-specific restriction enzymes generated by fusing a zinc finger DNA-binding domain to a DNA-cleavage domain.

TALEN – Sequence-specific restriction enzymes generated by fusing a transcription activator-like effector domain to a DNA-cleavage domain.



# Gene Editing – How it Works

## Repairing double-strand breaks



Double-strand breaks are repaired by one of two competing cellular repair mechanisms: non-homologous end joining (NHEJ) or, in the presence of a DNA repair template, homology-directed repair (HDR).

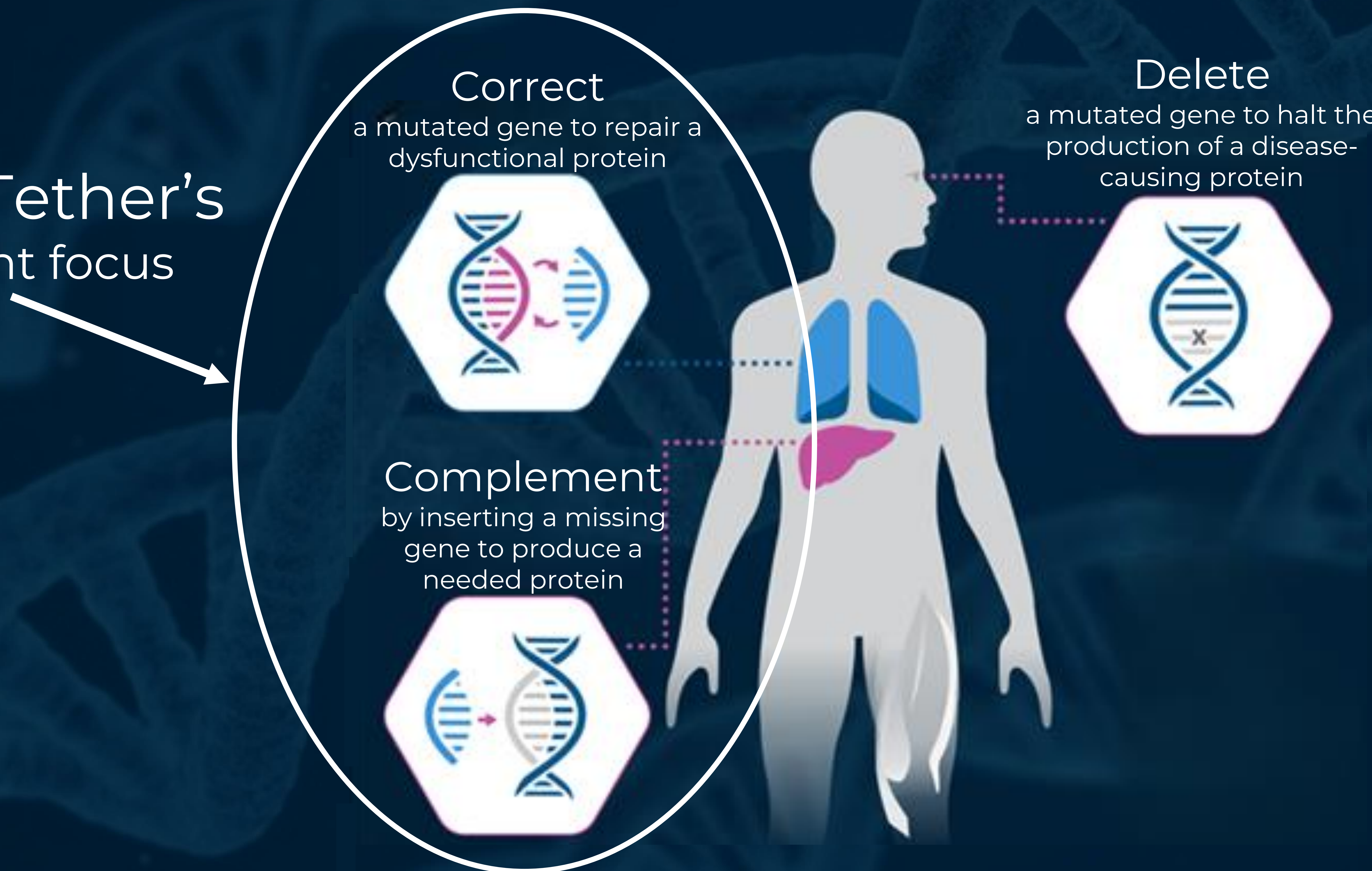
Repair via HDR is like a biological “find and replace” function.



# The Gene Editing Ecosystem

## Altering a DNA Sequence in an Endogenous Gene

GeneTether's  
current focus





# The Problem

Current technologies for correcting or complementing aberrant genes are inherently inefficient



**Efficiency:** The ratio of gene edits actually made versus the maximum number that *could* have been made through the insertion of donor DNA templates.

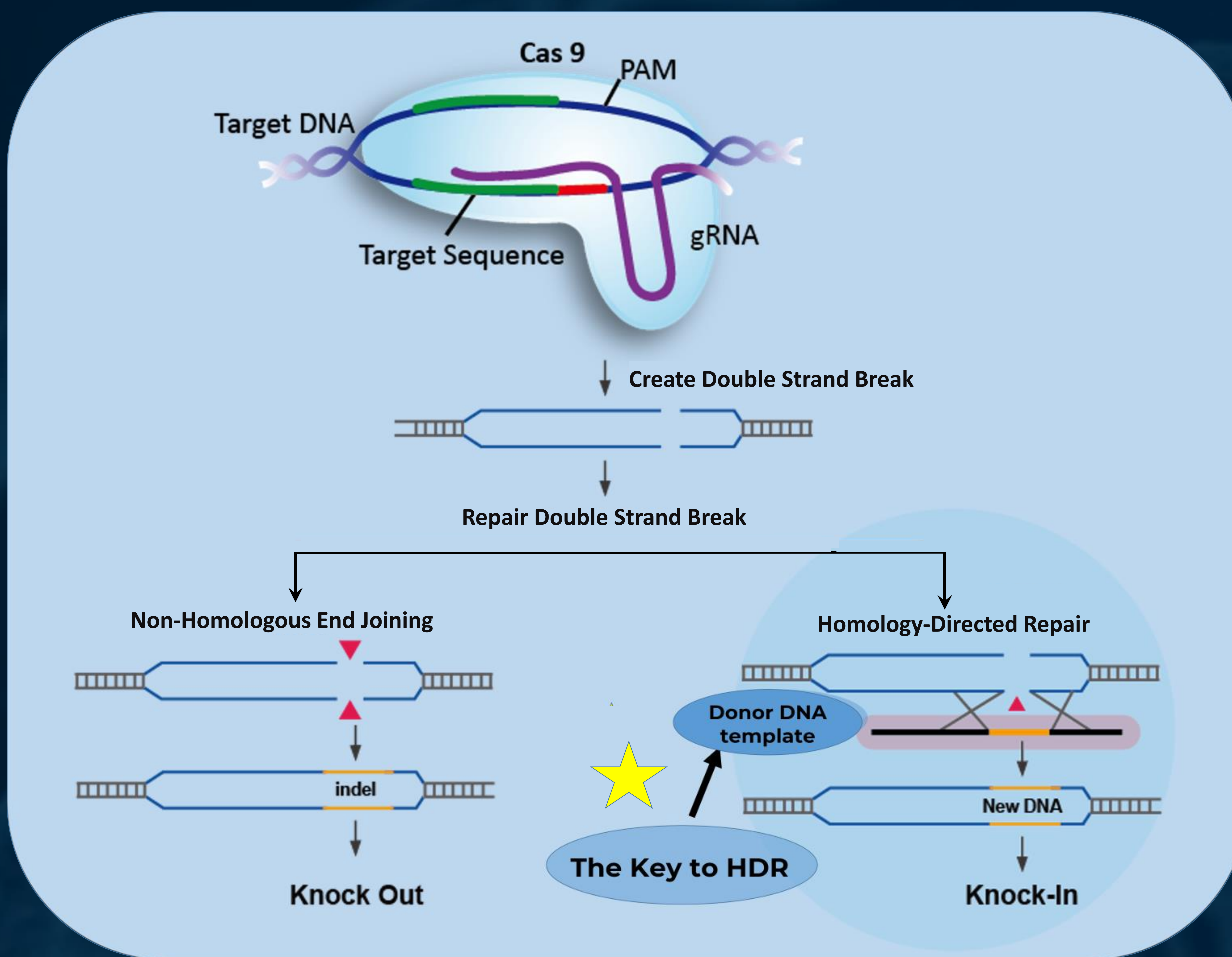
Correcting or complementing with a donor DNA template requires that a strand break be repaired via HDR. HDR requires a donor DNA template in the immediate vicinity of a break.

Efficiency rates vary from gene to gene and from cell type to cell type, but all are currently below rates that make large scale, cost-effective commercialization feasible.



# Gene Editing Efficiency

## Homology-Directed Repair vs Non-Homologous End Joining



Correcting and complementing genes requires delivery of a donor DNA template to the site of a DNA double strand break.

If a donor DNA template is not located near a double strand break, repair will not incorporate the donor DNA template via HDR.

The result is error-prone repair via NHEJ, leading to low gene editing efficiency, DNA mutation and rearrangements, and cell death.



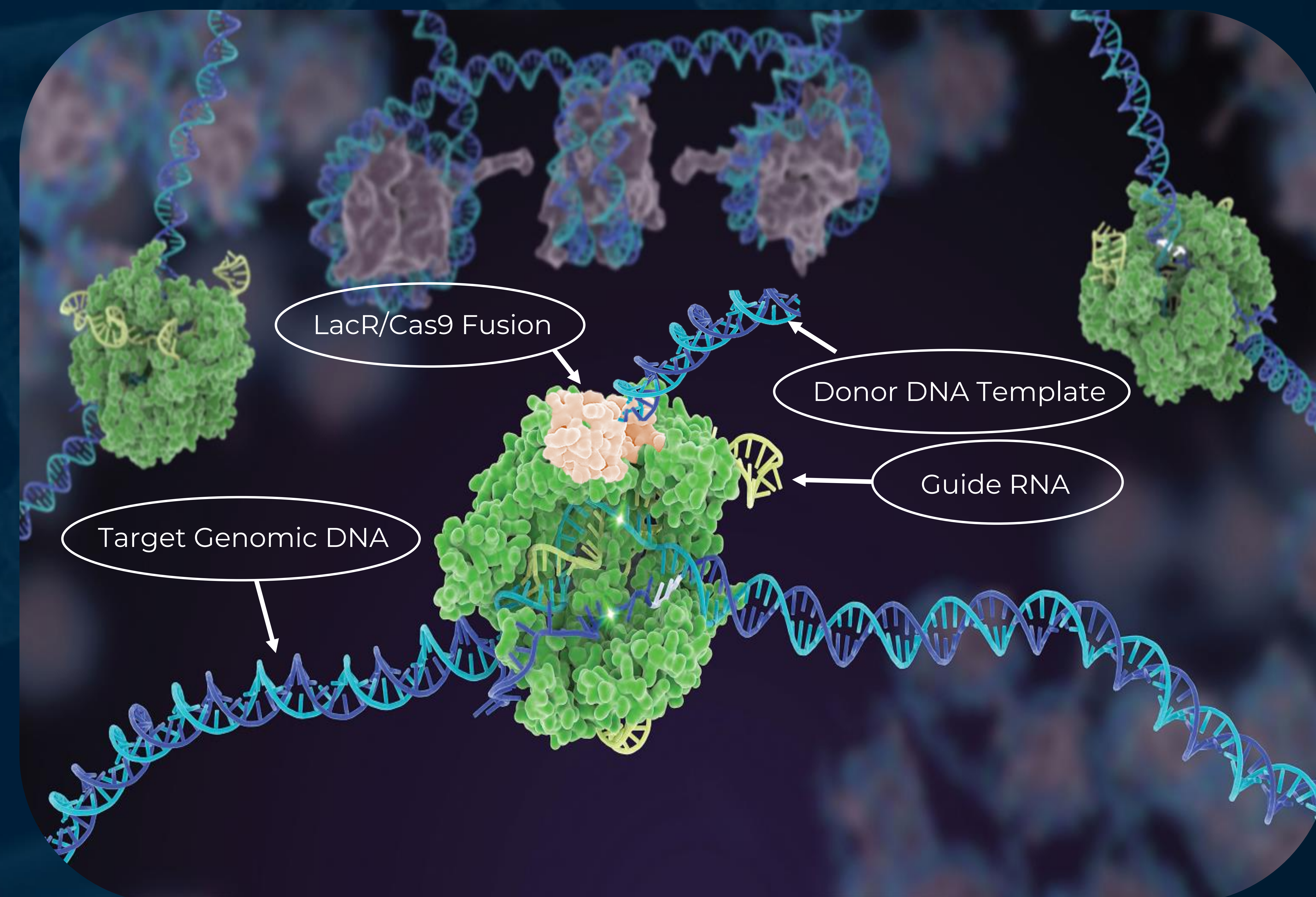
# The GeneTether Solution

## Proximity Matters

GeneTether has developed a proprietary method to attach, or "tether," donor DNA templates to gene editing nucleases.

The result is that the donor DNA template is nearby at the time a strand break is induced.

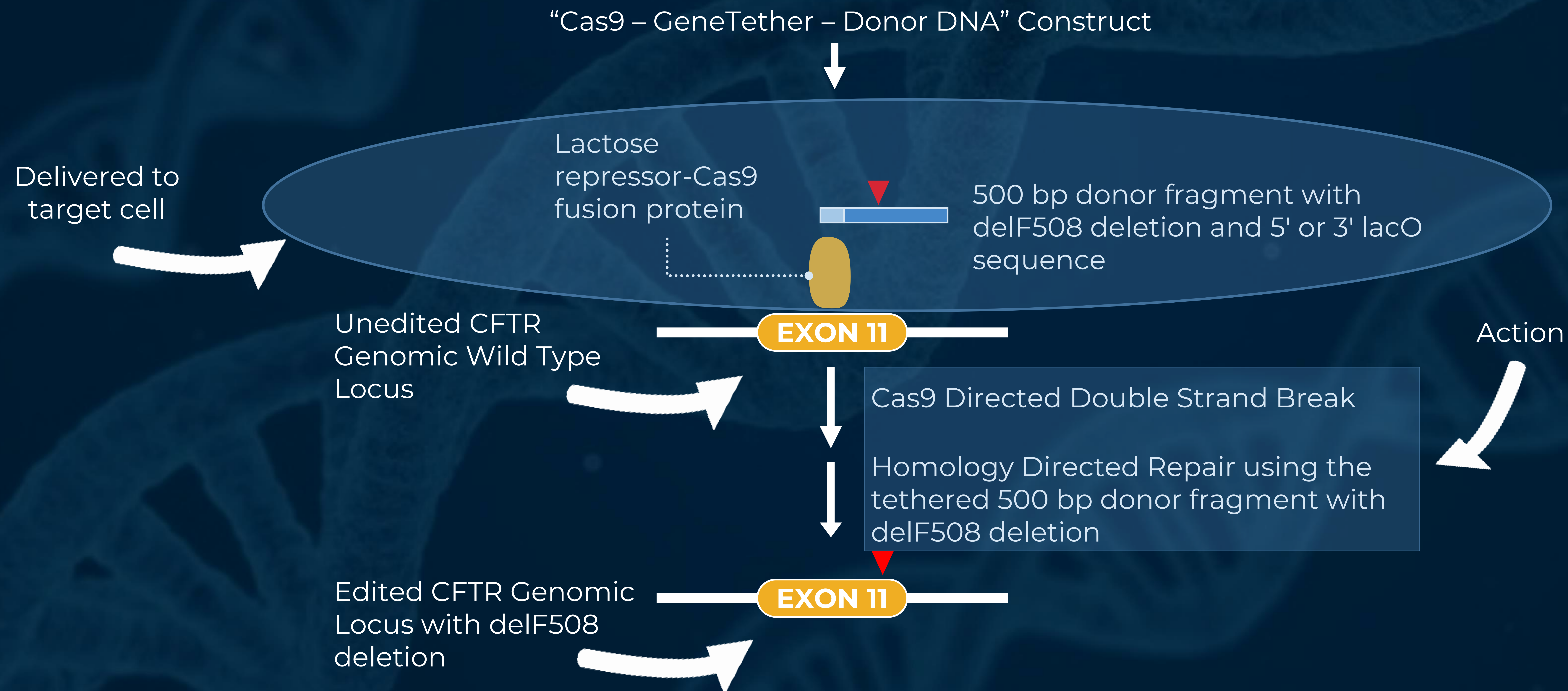
Correspondingly, there is an enhanced likelihood that **repair of the break will take place via HDR**, thereby allowing a far **greater number of gene edits** per payload delivery and **reducing the risk of mutagenesis or off-target gene edits**.





# Proof of Concept Study Design

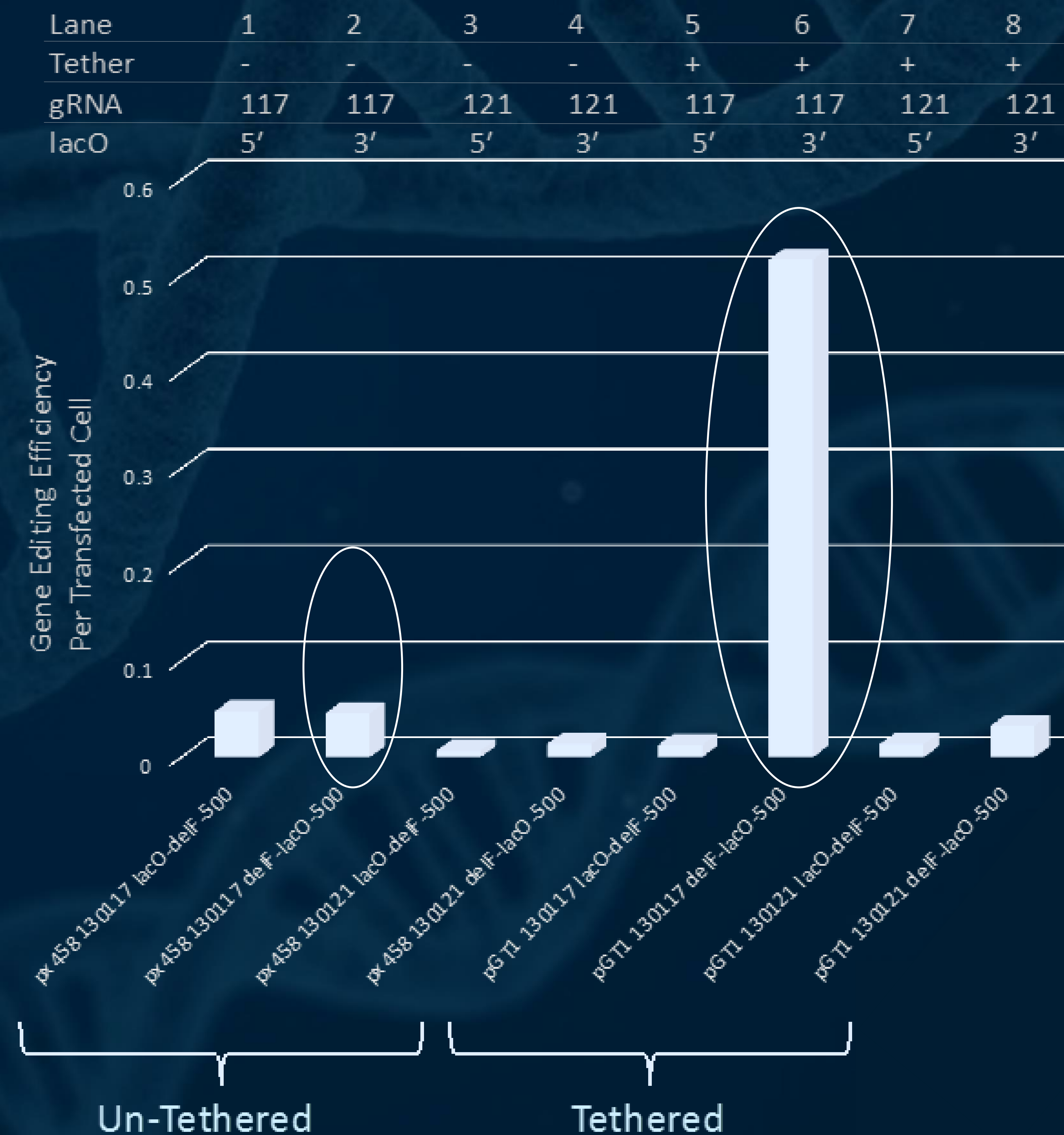
Introducing the delF508 mutation with GeneTether platform + CRISPR/Cas9 versus untethered CRISPR/Cas9





# Proof of Concept Study Results

As shown, the lactose repressor-Cas9/GeneTether plasmid (pGT1) with the 130117 guide (lane 6) demonstrated a robust editing efficiency, resulting in **~7x more edits** than the px458 vector with unmodified Cas9 and the same donor DNA fragment (lane 2).





# Our Research Pipeline

## Therapeutic Programs

	Disease	Gene	Target Discovery <sup>1</sup>	Lead Target Selection	Lead Optimization <sup>2</sup>	IND-Enabling
Nephrology	ADTKD-UMOD	<i>UMOD</i>	→			
	ADPKD	<i>PKD1</i>	→			
	Alport	<i>COL4A5</i>	→			
	Cell Delivery		→			
Dermatology	RDEB	<i>COL7A1</i>	→			
	Netherton	<i>SPINK5</i>	→			
	Cell Delivery		→			

## Platform & Intellectual Property Expansion

	Initiated	Target Completion	Study Site
Large animal cell lines	✓	Q1 2022	<b>UCDAVIS</b>
Zebrafish	✓	Q2 2022	<b>ZeClinics</b> <small>Powering discovery with Zebrafish</small>
<i>In vitro</i> editing in human cell lines		Ongoing	

<sup>1</sup> Target discovery includes identifying and/or developing cell line and animal models, conducting proof-of-concept studies, and identifying and/or developing tissue selective delivery vehicles.

<sup>2</sup> Lead optimization includes refinement of GeneTether construct and delivery formulation, and demonstrating efficacy and tolerability in animal models.



# Genetic Kidney Diseases & CKD

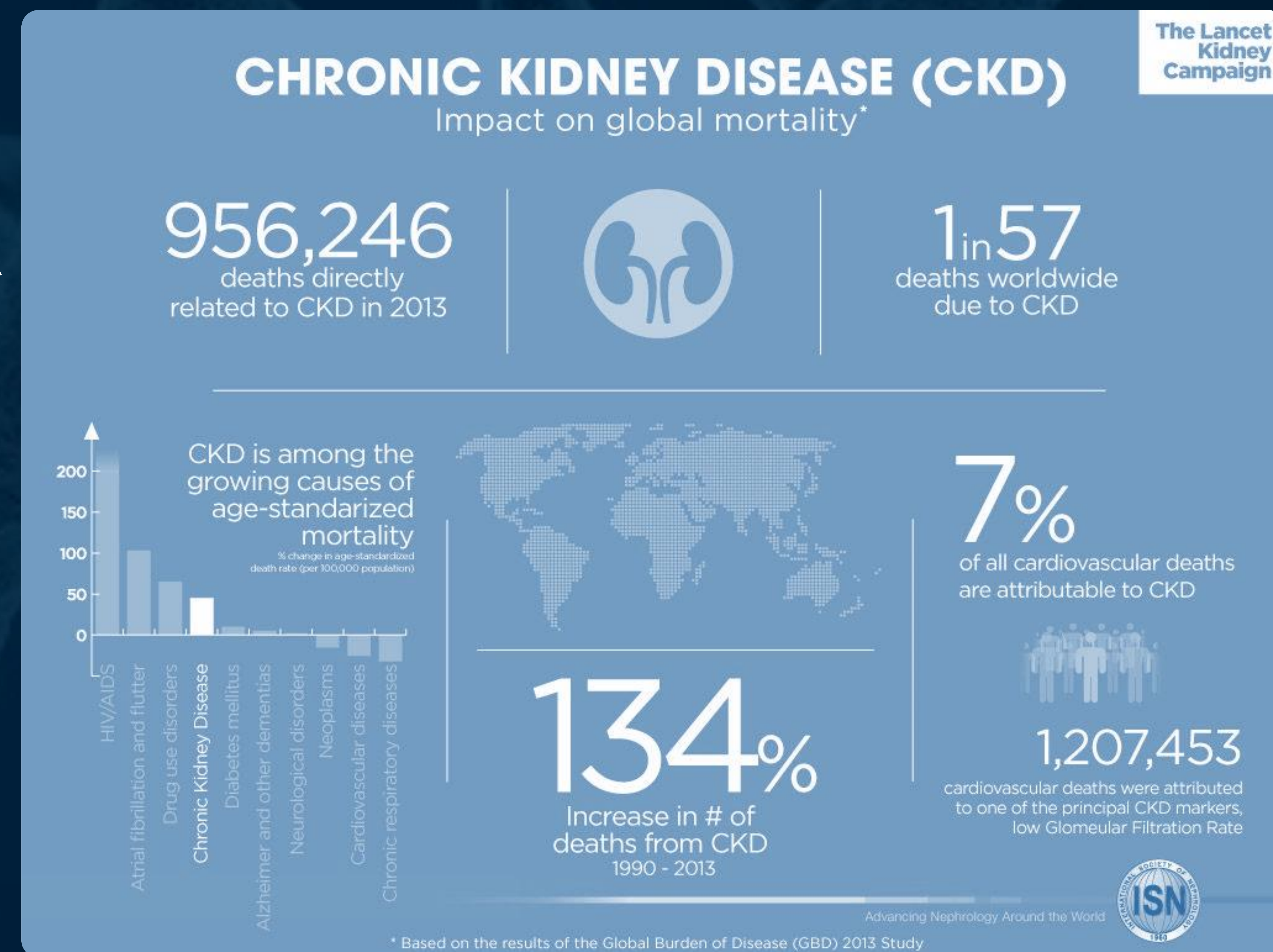
We are developing gene correction and complementation therapies for the treatment of patients with rare, monogenic kidney diseases that lead to chronic kidney disease (CKD).

625 monogenic disorders associated with kidney and urological traits have been identified.

CKD treatment strategies only address symptom management and prolonging time to end-stage kidney disease (ESKD) and kidney transplant.



Gene editing offers the possibility of a permanent curative therapy.

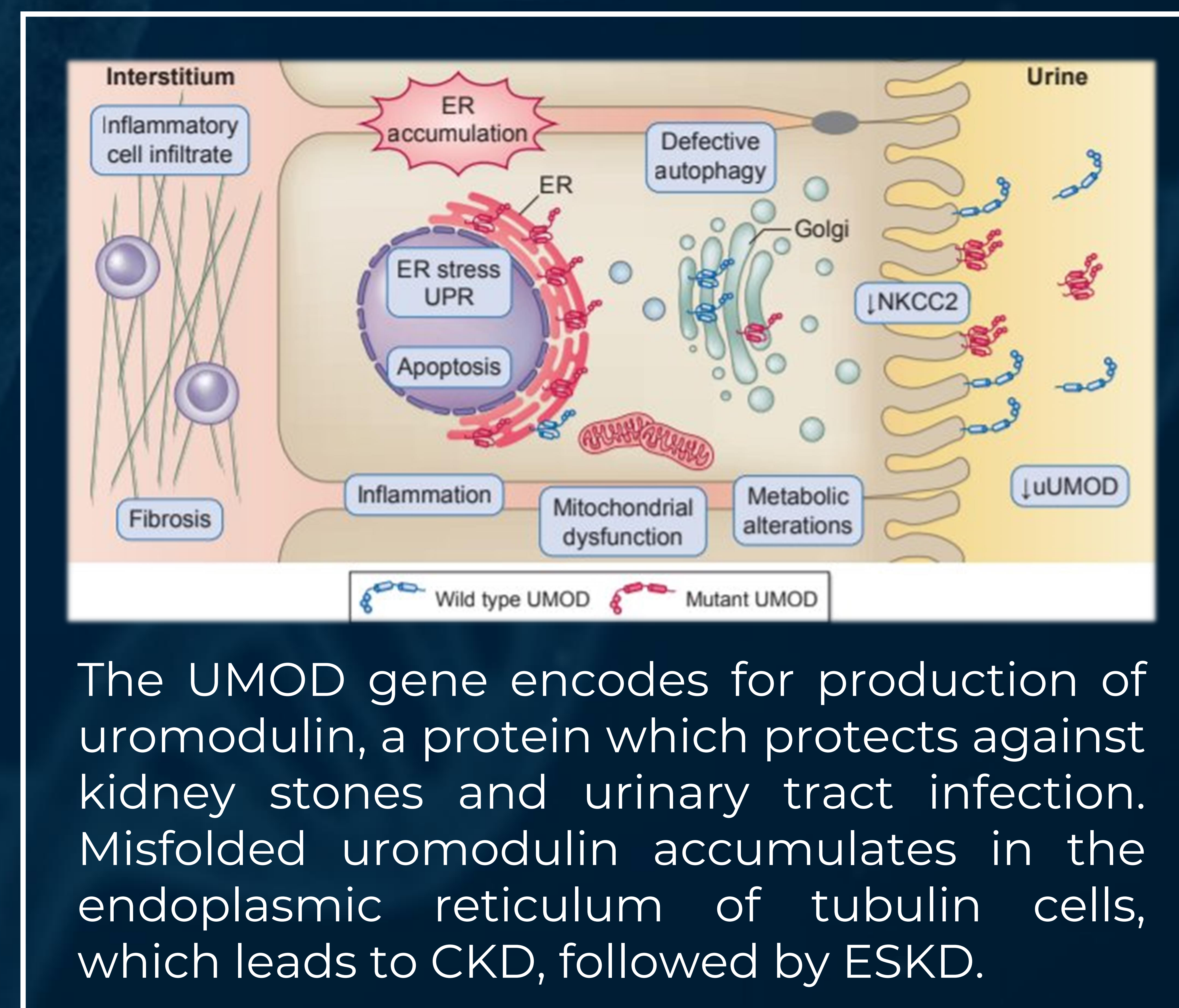
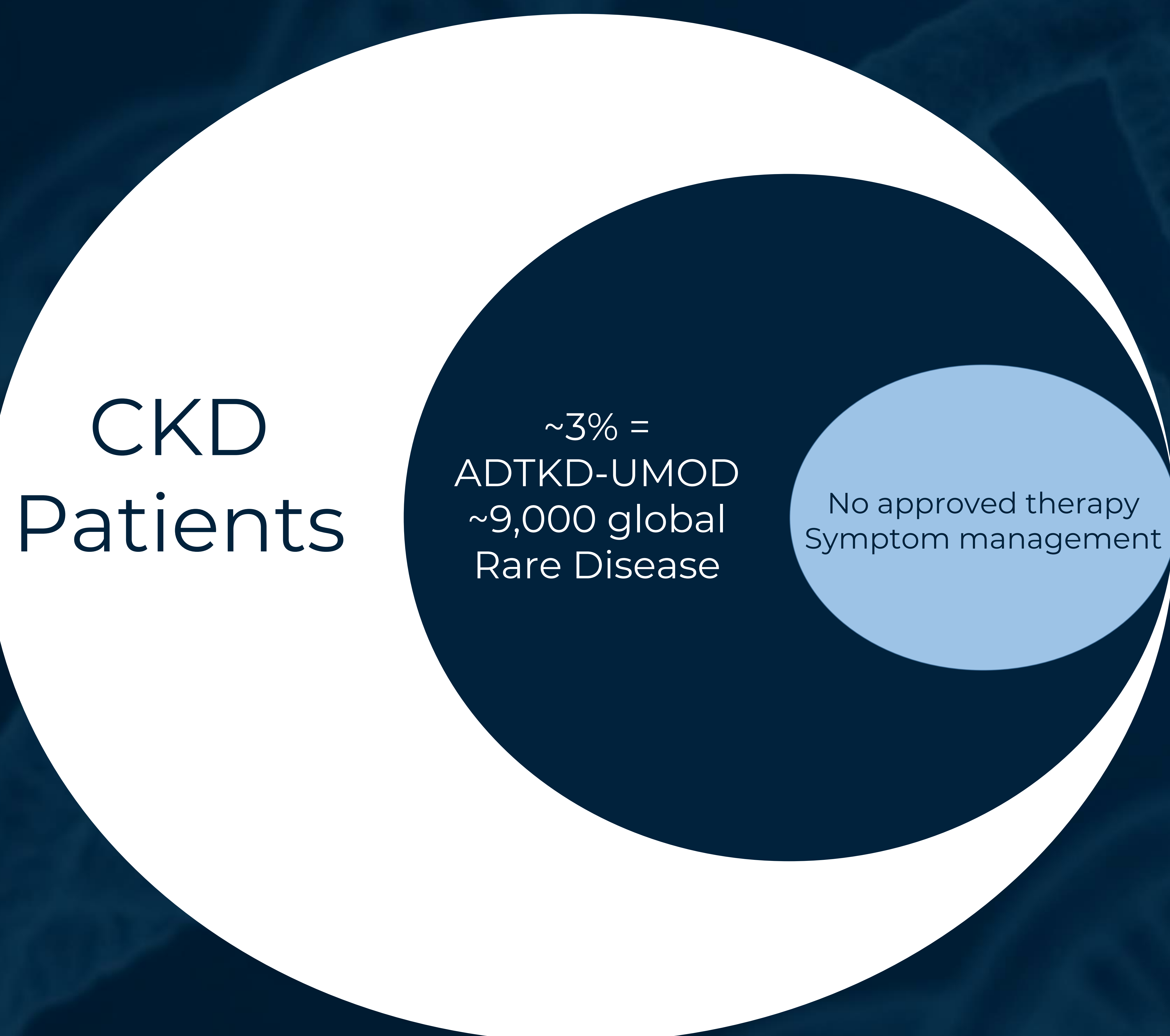




# Genetic Kidney Diseases

## Autosomal Dominant Tubulo-Interstitial Kidney Disease

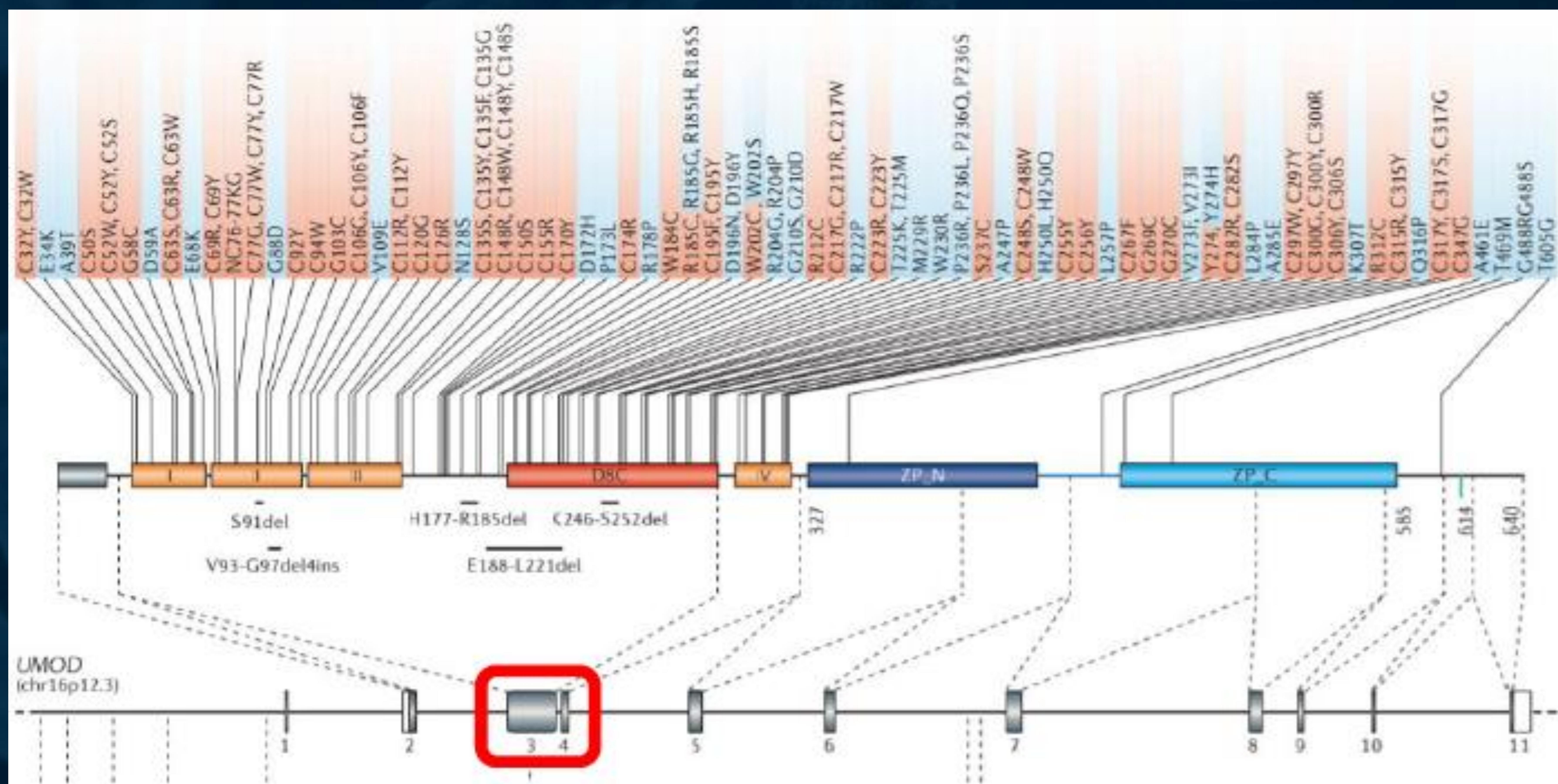
Autosomal dominant tubulo-interstitial kidney disease (ADTKD) is a group of rare genetic diseases that affect the tubules of the kidney. The most common form is ADTKD-UMOD.





# GeneTether for ADTKD-UMOD

Over 95% of known UMOD mutations underlying ADTKD are reported in a small segment of the UMOD gene known as exon 3 and exon 4 (highlighted in red below). Our GeneTether technology may allow the development of a single treatment for ADTKD-UMOD resulting from mutations in this region by correcting a locus that fully encompasses exons 3 and 4.





# Genetic Kidney Diseases

## Autosomal Dominant Polycystic Kidney Disease

Autosomal dominant polycystic kidney disease (ADPKD) is a rare genetic disorder characterized by the growth of numerous cysts in the kidneys.

Affects  
**~140,000\* people**  
in the U.S. and  
**~12.5 million people**  
worldwide

**No cure**  
approved  
**Treatment limited**  
to symptom management

Responsible  
**for up to 10%**  
of all cases of  
**ESKD**

\*Qualifies as a rare disease

### What are the causes of ADPKD?

- 85% of cases: mutations in PKD1
- 15% of cases: mutations in PKD2



### Manifestations of ADPKD include

- | Renal                    | Extrarenal   |
|--------------------------|--|
| Cyst formation           | Cysts in the liver, pancreas, spleen, and central nervous system |
| Increased kidney volume  | Cerebral aneurysms   |
| Kidney stones            | Polycystic liver disease   |
| Urinary tract infection  | Diverticular disease and mitral valve prolapse                   |
| Abdominal pain           |  |
| End-stage kidney disease |  |



# GeneTether for ADPKD-PKD1

Because mutations of the PKD1 gene account for ~85% of ADPKD cases, we intend to investigate the use of our GeneTether technology to correct or complement PKD1 gene function. We believe this may enable the restoration of functional polycystin 1 protein with an objective of developing a potentially permanent cure.



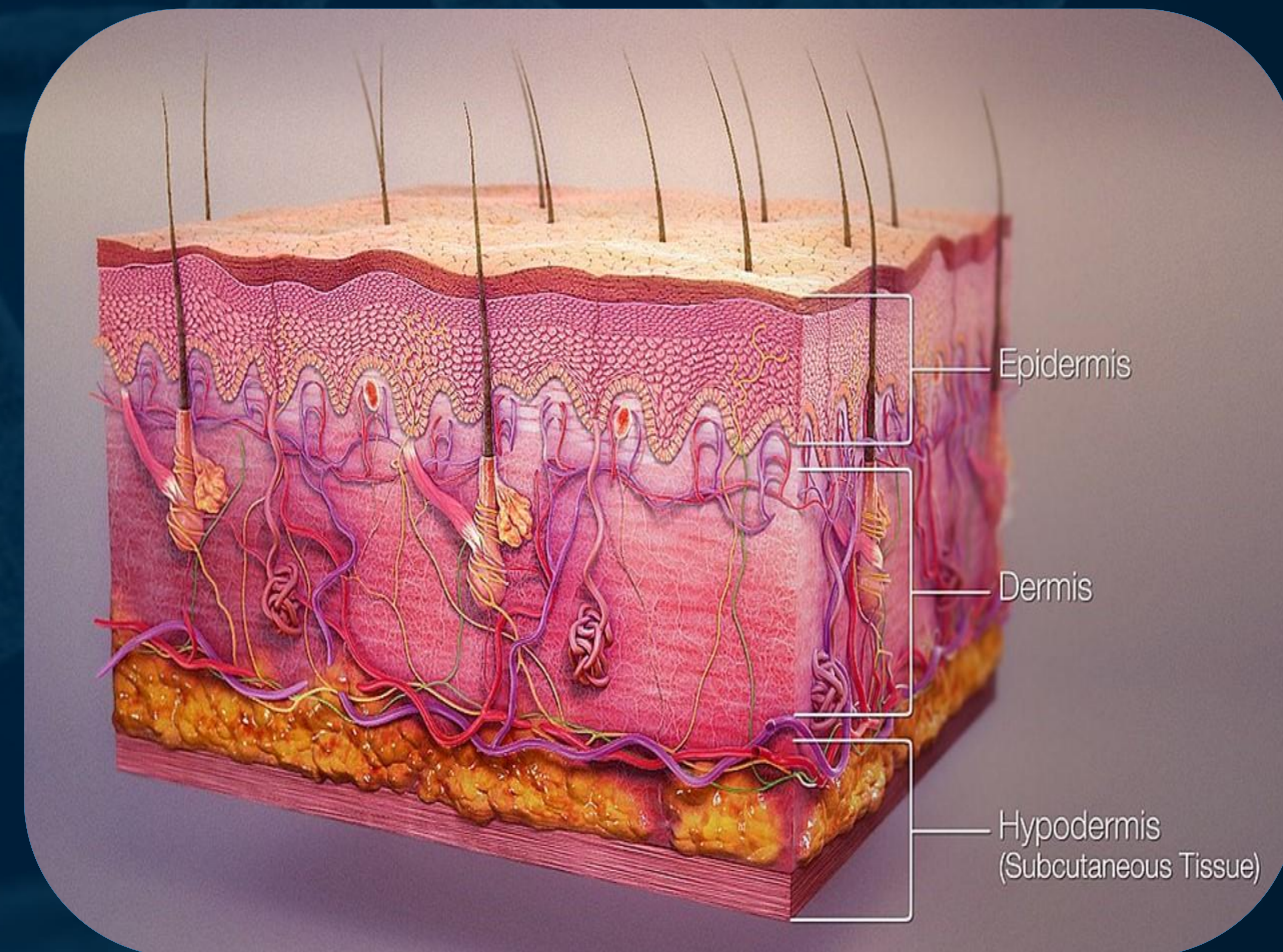


# Genetic Skin Diseases

Genetic skin diseases represent a broad class of rare diseases with confluent and overlapping phenotypes.

We have identified genetic skin diseases as one of our initial discovery targets due to:

- the **well-characterized** underlying genetic mutations of certain diseases,
- the **significant unmet need** for curative treatments, and
- the potential for **topical delivery** of our therapies.





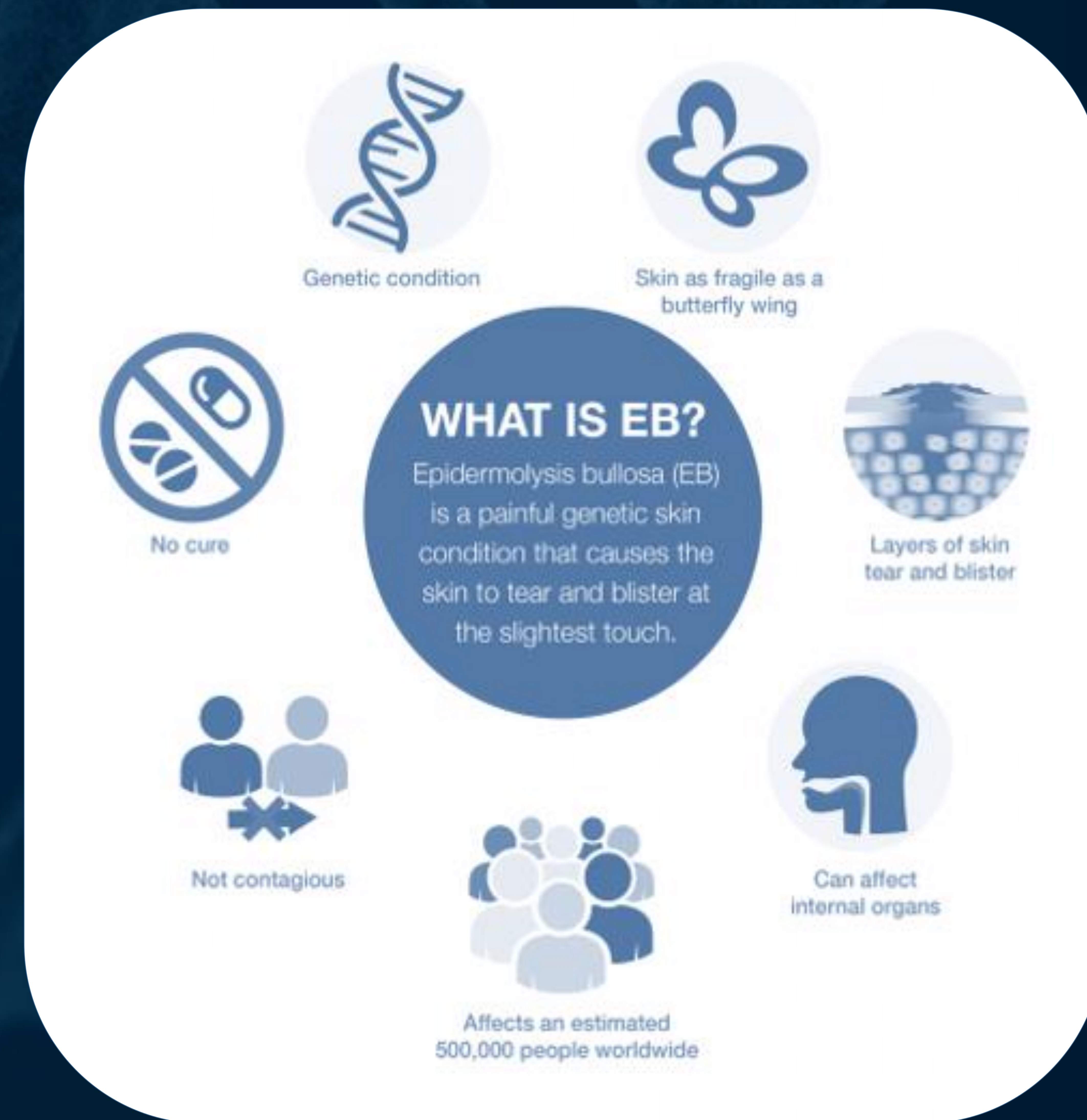
# Genetic Skin Diseases

## Recessive Dystrophic Epidermolysis Bullosa

Recessive Dystrophic Epidermolysis Bullosa (RDEB) is a rare, often fatal, genetic skin condition caused by a mutation in the *COL7A1* gene.

Lack of collagen protein makes the skin incredibly fragile, leading to blistering or skin loss at the slightest friction.

There is currently no cure for RDEB. The standard-of-care includes wound care, pain management, prevention of skin trauma, and early detection and treatment of **squamous cell carcinoma**.





# GeneTether for RDEB

Skin grafts engineered to include normal copies of the *COL7A1* gene complimentary DNA has shown promise for improved wound healing.

As with other non-integrating gene therapies, the effects were not long lasting, as cell division reduces expression of the *COL7A1* gene over time.

We believe that RDEB is a candidate for *in vivo* gene correction, as a single donor DNA template inserted via HDR may permanently restore *COL7A1* functionality across multiple mutations.



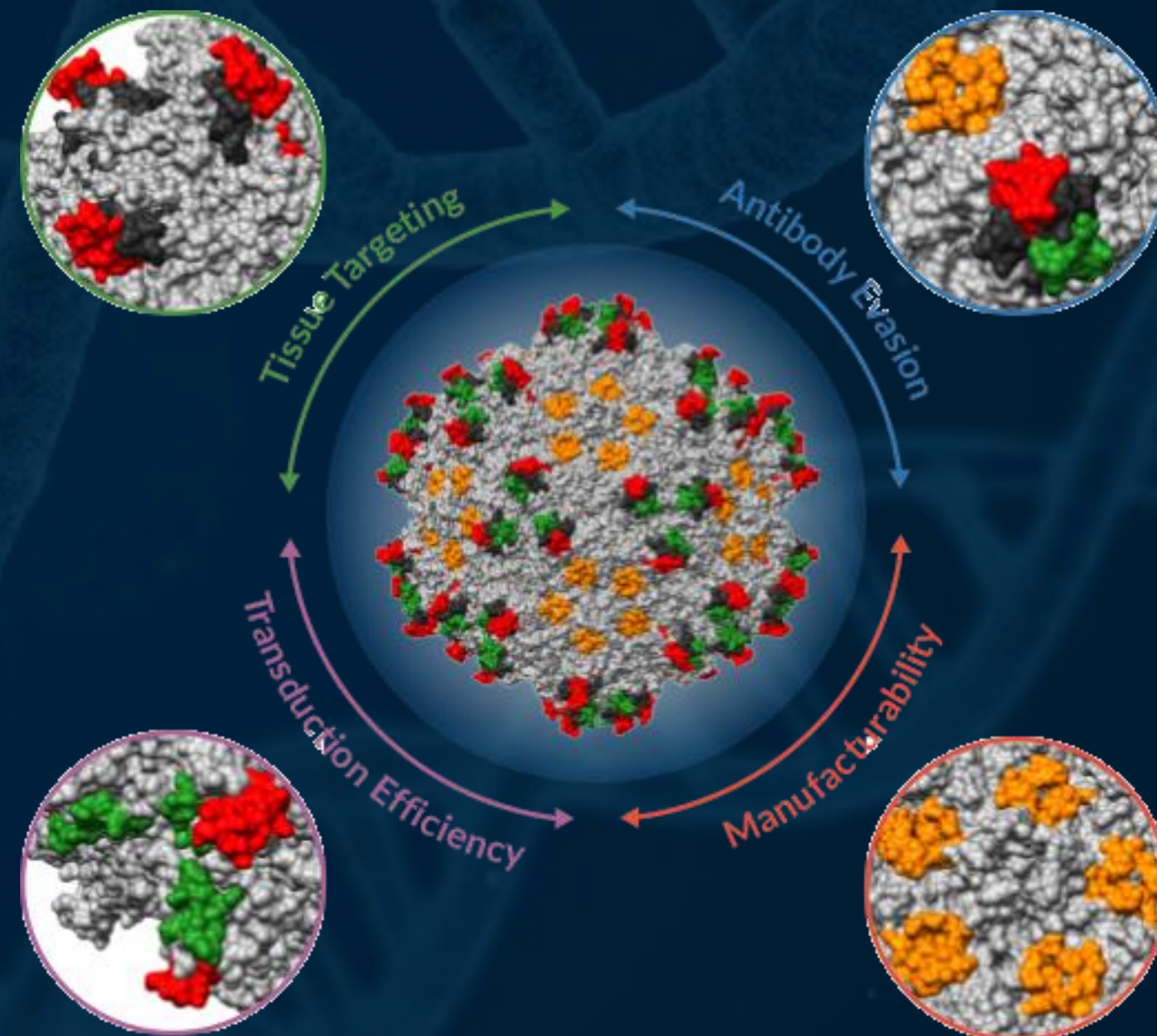


# Cell Delivery

Cellular delivery of gene editing payloads is an important and difficult component of a viable therapeutic.

We are currently evaluating multiple viral and non-viral delivery technologies that have enhanced kidney and skin tropism, high levels of functional transduction, and improved manufacturability.

Technologies we are evaluating include next generations of lipid nanoparticles, helper-dependent adenoviruses, and adeno-associated viruses.





# Intellectual Property

## Patents and Pending Applications<sup>1</sup>

Wholly-owned patent portfolio; no 3<sup>rd</sup> party financial obligations

We will seek to continue to innovate and strategically protect our innovations in the following three main areas:

- Composition of matter claims combining components of our GeneTether platform with other components of various gene editing systems;
- Uses in monogenic kidney disorders, monogenic skin disorders, and other non-kidney and non-skin disease targets; and
- Cell delivery into tissues and cells of interest.

<sup>1</sup>There is no guarantee that new patents will issue or effectively protect the commercial prospects of GeneTether's assets if they do. GeneTether has not received any written legal opinion in relation to patentability of the subject matter disclosed and claimed in its patent applications.

<sup>2</sup>On October 13, 2021 the USPTO issued an Office Action indicating likely allowance of claims covering current embodiment of GeneTether technology

### Granted

Australia



### Office Action Indicating Allowance of Claims<sup>2</sup>

USA



### Pending

Canada



China



Japan



Korea



Israel



EU



Singapore





# Development Timeline/Catalysts

Objective	Activities	Estimated Initial Completion <sup>1</sup>			
		H1 2022	H2 2022	H1 2023	H2 2023
Continued validation of GeneTether platform technology and expansion of IP portfolio	Identify and engage qualified contract research organizations	█			
	Non-cGMP manufacturing of key components of our GeneTether-based gene editing system	█			
	Identify and engage qualified contract manufacturing organizations for cGMP components			█	
	Editing in: <ul style="list-style-type: none"> <li>- large animal cell lines</li> <li>- zebrafish</li> <li>- human cell lines</li> </ul>	█			
Identification of lead development program(s)	Identify and engage key opinion leaders in the areas of our potential disease targets	█			
	Complete <i>in vitro</i> cell line editing in potential rare, genetic disease targets as described in the prospectus under: <ul style="list-style-type: none"> <li>- “Our GeneTether Platform for Rare, Monogenic Kidney Diseases”</li> <li>- “Our GeneTether Platform for Rare, Monogenic Skin Diseases”</li> </ul>			█	

<sup>1</sup>Dates generally represent anticipated completion of activities and are subject to factors that may be beyond our control, including the availability of third-party collaborators and contractors. The activities included are summaries only and are subject to change at management’s discretion. Many of the activities listed above will be ongoing for the duration of our development programs.



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		H1 2022	H2 2022	H1 2023	H2 2023
Optimization of GeneTether-based gene editing system for lead program(s)	Complete disease-specific <i>in vitro</i> cell line editing to optimize among other things, gRNAs, cell delivery vehicles, and donor DNA templates			█	
	Develop and/or optimize selective tissue delivery vehicle			█	
Functional rescue of animal model in lead program(s)	Identify and/or develop clinically-relevant animal model(s)			█	
	Identify and engage qualified contract research organizations		█		
	Complete gene correction and/or gene complementation studies in validated animal models of our disease target(s) using the GeneTether platform technology				█

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# Peer Group Comparables

In accordance with Section 13.7(4) of National Instrument 41-01 – General Prospectus Requirements, all the information relating to GeneTether’s comparables and any disclosure relating to the comparables, which is contained in the presentation to be provided to potential investors, has been removed from this template version for purposes of its filing on the System for Electronic Document Analysis and Retrieval (SEDAR).



# Capital Structure | Sources & Uses of Funds

Pre-Offering Shares Outstanding <sup>1</sup>		Source of Funds	Amount
Common Stock	41.7M	Working Capital as at September 30, 2020	C\$[.]
Options to Purchase Common Stock	14.2M	Estimated Net Proceeds from the Offering <sup>2</sup>	C\$[.]
Pre-Offering FD Shares	<hr/> 55.9M	<hr/> Total Available Funds <sup>4</sup>	<hr/> C\$[.]
Owned by Insiders	~81%		
Shares Offered <sup>2,3</sup>		Use of Available Funds	Amount
Post-Offering FDITM Shares	<hr/> [.]	GeneTether technology R&D	C\$[.]
Post-Offering Market Cap at C\$[.]	<hr/> C\$[.]	General and Administrative Expenses	C\$[.]
		Unallocated Working Capital <sup>5</sup>	C\$[.]
		<hr/> Total Available Funds <sup>4</sup>	<hr/> C\$[.]

<sup>1</sup>On a post-split basis following GeneTether's reorganization event

<sup>2</sup>Assuming no exercise of Agent's overallotment option.

<sup>3</sup>[.] Units are being offered. Each Unit is comprised of one common share and [.] common share purchase warrant. Each warrant is exercisable to purchase one common share at a price of C\$[.] per share. Warrant shares are not included in "Post-Offering Fully Diluted In-the-Money (FDITM) Shares" above.

<sup>4</sup>Unaudited

<sup>5</sup>Unallocated working capital is to provide additional contingency for overhead and general and administrative expense overrun



# Terms of the Offering

Company	GeneTether Therapeutics Inc.
Offering	Prospectus offering of [.] Units to raise up to C\$[.] <sup>1</sup> on a commercially reasonable efforts basis
Issue Price	C\$[.] per Unit
Units	Each Unit is comprised of one Common Share and one common share purchase warrant
Warrant	Each warrant is exercisable to purchase one Common Share at a price of C\$[.] per share for a period of [.] months following the closing of the offering
Agent's Option	The Agent shall have the option to increase the size of the offering by up to [.] Units (C\$[.] <sup>1</sup> )
Use of Proceeds	To conduct certain R&D activities related to the GeneTether platform technology and for general and administrative purposes
Eligibility	The Units will be eligible for registered plans <sup>1</sup>
Offering Jurisdictions	British Columbia, Alberta, and Ontario
Closing Date	On or about December [.] , 2021
Lead Agent	Research Capital Corporation

<sup>1</sup>Gross proceeds before deducting Agent's commission and expenses of the Offering

<sup>2</sup>See prospectus for full disclosure regarding holding Offering securities within a registered plan



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