

A Real Revolution in Osteoarthritis of the Knee (OAK) Treatment



Pacira is redefining innovation in gene therapy to bring its benefits to the population at large. PCRX-201 is a gene therapy that mimics the body's response to inflammation.

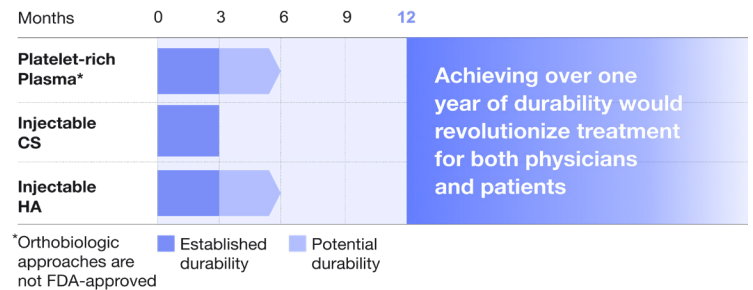
Pacira BioSciences' PCRX-201 is an investigational gene therapy product candidate for the treatment of osteoarthritis of the knee. As an investigational therapy, PCRX-201 has not been approved by the U.S. Food and Drug Administration (FDA) for any use.

Significant Unmet Need in OAK

Why are we focusing on osteoarthritis of the knee (OAK)?

- Patients aren't satisfied with current treatment options, which only provide 3-6 months of relief.
- Millions of patients per year are receiving total knee replacements as a last resort, which are expensive, can have complications, and aren't guaranteed solutions.
- Highly prevalent degenerative disease that limits mobility and engagement in activities of daily living.
- Patients state their condition results in loss of independence and isolation.

The durability gap: Seeking transformative OAK treatments



Enekinragene Inzadenovec (PCRX-201): Redefining Innovation in Gene Therapy to Bring Its Benefit to the Population at Large

PCRX-201's innovative design, manufacturing process, and local administration solve many of the challenges that have made gene therapy inaccessible for common diseases



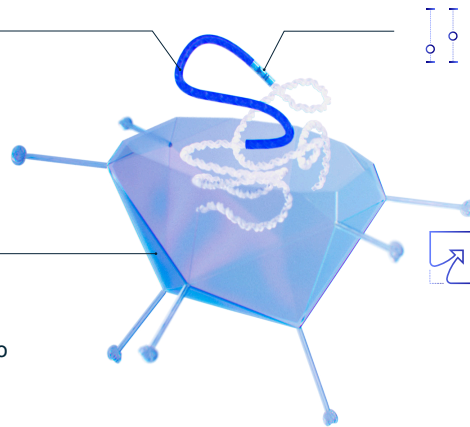
Medicine where it matters

PCRX-201 is injected locally into the knee joint to boost cellular IL-1Ra production and block IL-1 pathway activation, significantly reducing chronic inflammation.



Overcomes gene therapy pitfalls

PCRX-201's innovative HCAAd vector is more efficient at delivering genes into cells than other vectors, which means less medication to achieve the desired effect.



Protein production only when needed

PCRX-201 uses an inflammation-responsive promoter to only produce IL-1Ra when needed, mimicking the body's natural response to inflammation.



Attractive cost of goods profile

Smaller doses, localized administration, and scalable manufacturing processes result in an attractive cost of goods profile because we can make many thousands of doses in a single batch.

IL-1's Role in Inflammation

The IL-1 pathway: A well-validated driver of chronic inflammation

It's been known for years that chronic IL-1 activation is an underlying driver of knee inflammation, joint degeneration, and pain. By targeting it, we're able to target a root cause of disease rather than just alleviating only the symptoms of OA.

Several FDA-approved drugs, such as anakinra and canakinumab, have successfully targeted the IL-1 pathway in other joint inflammatory conditions, proving that blocking its activation is a well-validated, de-risked strategy for reducing inflammation.

Existing drugs that target IL-1 are not practical for OAK because they would require very high doses or daily injections directly into the knee.

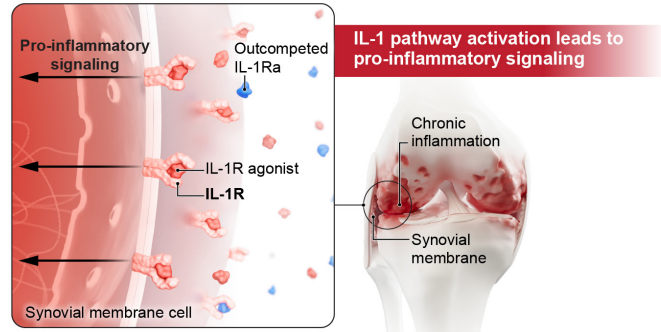
Abbreviations: CS, Corticosteroids; HA, hyaluronic acids; HCAAd, high-capacity adenovirus; IL-1, interleukin-1; IL-1R, IL-1 receptor; IL-1Ra, IL-1 receptor antagonist; OA, osteoarthritis; OAK, osteoarthritis of the knee.

PCRX-201: Medicine Where it matters

Mechanism of Disease

What is the IL-1 pathway?

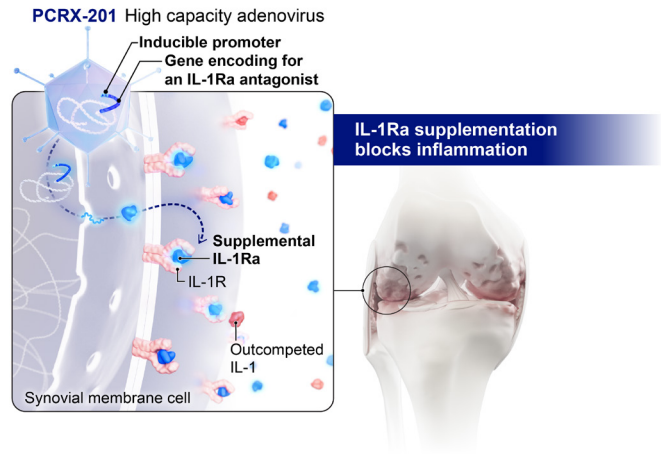
- The IL-1 pathway triggers inflammation in response to pathogens and cellular stress.
- IL-1Ra is a core regulator of this pathway and helps keep inflammation in balance by turning off the IL-1 pathway when it's not needed.
- As we get older, our bodies have a more challenging time maintaining that balance. As a result, we develop chronic IL-1-driven inflammation that eventually causes joint damage and pain.



PCRX-201 Mechanism of Action

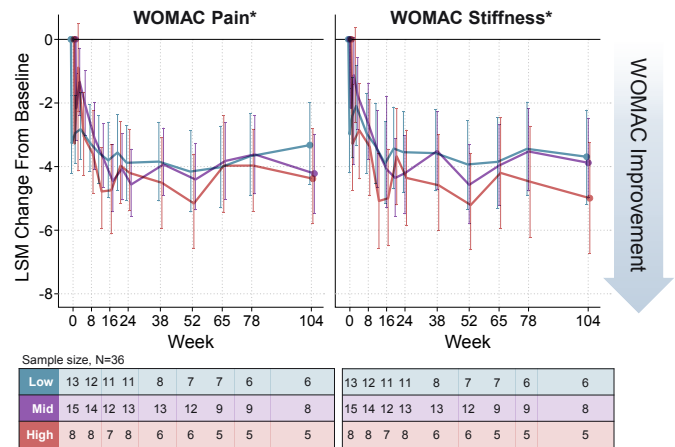
What is PCRX-201? How does it work?

- PCRX-201 is a gene therapy that boosts cellular IL-1Ra (IL-1 receptor antagonist) production, which blocks IL-1 pathway activation and dampens down chronic inflammation in the knee.
- It uses an inflammation-responsive promoter to only produce IL-1Ra when needed, mimicking how the body naturally responds to inflammation.
- Similar to how a smart thermostat works – if it detects a room is too hot, it starts producing cold air. The thermostat turns off once the temperature is returned to a more comfortable setting.
- It's delivered directly into the knee joint capsule providing durable pain relief where it matters most and with no to minimal systemic exposure.



PCRX-201 Safety and Efficacy¹

- PCRX-201 already exceeded expectations in an early-stage clinical trial.
- PCRX-201 has been studied in a large Phase 1 trial of 72 OAK patients and demonstrated unprecedented pain relief and durability across all levels of disease severity (KL2-KL4) for at least 3 years from a single injection.
- In all 3 doses >70% of patients saw a >50% improvement in pain vs. baseline at week 16 and 78.
- 2 years of clinically meaningful improvement observed across all severity subgroups, including the most severe group with KL4 OAK; the greatest improvement was observed among individuals with KL2.
- Preliminary data suggests clinical immunogenicity may not reduce sustained improvements in knee pain, stiffness and function; initial data support potential for redosing in future trials.
- PCRX-201 was well-tolerated with no serious treatment-emergent AEs related to the treatment or procedure reported regardless of steroid pretreatment or dose level administered.
- While other therapies typically provide relief for 3-6 months, PCRX-201 has shown the potential to set a new standard with pain relief lasting 3 years from a single injection.
- PCRX-201 is the first gene therapy to achieve these results and is the only OA gene therapy to earn the FDA RMAT designation—a testament to its promise and potential.
- We believe PCRX-201 has the potential to revolutionize the treatment of OAK.



PCRX-201 is the first gene therapy to achieve these results and is the only OA gene therapy to earn the FDA RMAT designation



¹Data from steroid pretreated cohort.

¹3-year data presented at the European Alliance of Associations for Rheumatology (EULAR) Congress in 2025 (Conaghan et. al.), 2-year data presented at ACR Convergence in 2024 (Cohen et. al.), severity subgroup analysis presented at 2025 OARSI World Congress (Mobasheri et. al.) and immunogenicity subgroup analysis presented at 2025 ASGCT Annual Meeting (Kim et. al.).

Abbreviations: AE, adverse event; HCAAd, high-capacity adenovirus; IL-1, interleukin-1; IL-1R, IL-1 receptor; KL2, Kellgren-Lawrence mild knee OA; KL4, Kellgren-Lawrence severe knee OA;

LSM, least square mean; OA, osteoarthritis; OAK, osteoarthritis of the knee; RMAT, Regenerative Medicine Advanced Therapy; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.