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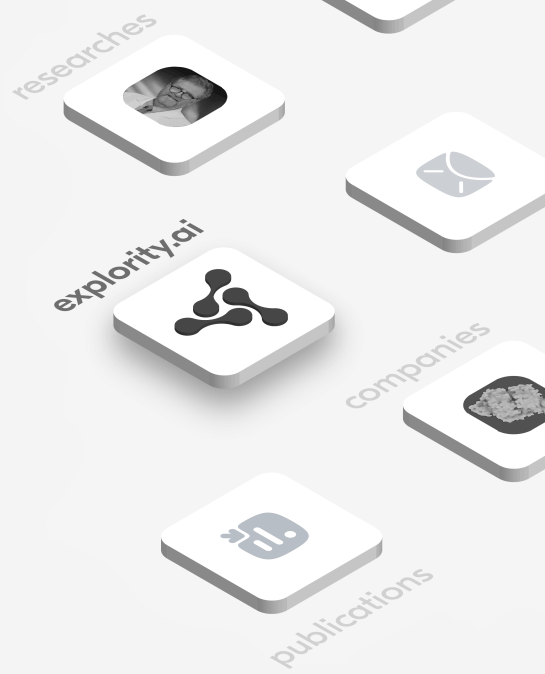
Investment memorandum

11 Jun 2026



First-generation therapy forecast:

Xeroderma pigmentosum

Categories: rare developmental anomalies during embryogenesis, rare genetic diseases, rare neoplastic diseases +3

Gene therapies

Forecast for the first gene therapies based drug for the disease.

Disease landscape:

Orphan designations: **4**

Approved drugs: **0**

De-risked by AI:

Top 2.9%
of research

Highest probability of becoming an approved therapy from the research stage.

Disease overview

AI-generated summary. Verify critical details against original sources.

Xeroderma pigmentosum

Xeroderma pigmentosum (XP) is a rare autosomal recessive disorder characterized by defective DNA repair mechanisms, leading to extreme photosensitivity, UV-induced skin cancers (10,000× higher risk), ocular damage, and progressive neurodegeneration in 20-30% of cases. Symptoms manifest in infancy with severe sunburns, freckling, and premature skin aging. Diagnosis relies on clinical features and genetic testing. Management focuses on rigorous UV avoidance, frequent cancer surveillance, and prompt lesion treatment. Median survival is 32 years, with metastatic skin cancer as the leading cause of death [1] [4] [11].

Population

Affects 1 in 1 million in the US/Europe, with higher prevalence in Japan (1:20,000), North Africa, and consanguineous communities. Carrier rates reach 1:113 in Japanese populations (XPA-related) [1] [7] [12].

Current Therapeutic Strategies

- Strict UV avoidance: Protective clothing, UV-blocking films, and sunscreen [5] [11].
- Early cancer intervention: Surgical excision, photodynamic therapy, and topical 5-fluorouracil/imiquimod [3] [5] [10].
- Investigational approaches: Oral retinoids, nicotinamide, and gene therapy (preclinical) [5] [13].

Burden of the Disease

- 60% mortality before age 20; median lifespan 32 years [4] [11].
- Neurological decline (ataxia, dementia) affects 25-30%, worsening prognosis [1] [12].
- 95% develop skin cancer by age 14 without protection, with 50-fold increased CNS cancer risk [4] [14].

Literature overview

Most influential articles for LLM-classifier prediction.

20.7% influence 14 Oct 2016

Understanding photodermatoses associated with defective DNA repair: Syndromes with cancer predisposition.

Open article

Cerrene N. Giordano · Yik Weng Yew 169 · Graciela Spivak 41 · Henry W. Lim 575

Hereditary photodermatoses are a spectrum of rare photosensitive disorders that are often caused by genetic deficiency or malfunction of various components of the DNA repair pathway. This results clinically in extreme photosensitivity, with many syndromes exhibiting an increased risk of cutaneous malignancies. This review will focus specifically on the syndromes with malignant potential, including xeroderma pigmentosum, Bloom syndrome, and Rothmund-Thomson syndrome. The typical phenotypic findings of each disorder will be examined and contrasted, including noncutaneous identifiers to aid in diagnosis. The management of these patients will also be discussed. At this time, the mainstay of therapy remains strict photoprotection; however, genetic therapies are under investigation.

12.9% influence 13 Nov 2025

Impact du xeroderma pigmentosum sur la santé mentale des patients : une étude basée sur le questionnaire DAAS-21

Open article

M. Jones 185 · S. Bacha · S. Gara · M. Akid · M. Karoui · Faten Zéglaoui

nan

11.6% influence 21 Nov 2024

Open article

Co-infection of HSV-1 amplicons containing the XPC gene and a human artificial chromosome vector into primary XPC deficient fibroblast cells.

Daniela Moralli 99 · Avi Smith · Jonathan A. Garlick 149 · Kenneth H. Kraemer 289 · Zoia L. Monaco

Gene therapy for xeroderma pigmentosum (XP), a rare, recessive DNA repair disease, has been considered since defects in XP genes result in severe and debilitating symptoms. Mutations in the XPC DNA repair gene result in a more that 1000-fold increased sensitivity to sunlight-induced skin cancer. The XPC gene is large (33 Kb) and the entire genomic locus is a difficult candidate for many gene therapy vectors to incorporate into their system by conventional cloning. Artificial chromosome vectors were developed to accommodate large genes and their regulatory sequences to allow full gene expression in cells. The HSV-1 human artificial chromosome (HAC) vectors we previously generated incorporated genes up to 100 Kb in a single vector. Subsequently, we modified the system to allow larger (>100 Kb) DNA gene sequences to be introduced by simultaneously infecting cells with two separate HSV-1 vector particles, one containing DNA required for HAC formation and the other with the desired gene. Following transduction, recombination of DNA formed a gene expressing HAC in vitro. The dual transduction system was successful for introduction and expression of the HPRT gene in human 3D engineered tissues and stem cells. In this study, we report the XPC gene delivery and transient gene expression via the dual transduction system in human cultured fibrosarcoma (HT1080) and primary XPC deficient patient cells.

8.7% influence · 1 Mar 2026

Open article

301P Early access program of birabresib in NUT carcinoma patients

M.V. Sanchez Becerra · Maxime Annereau 70 · I. Yoldjan · F-X. Legrand · D. Chauvey · Thomas Fleury · P. Guinot · L. Zullo · L. Millier · M. Ngo Camus · C. Nicotra · A. Italiano · Bernard Do 100 · Benjamin Besse 1839

Background: Rare malignancies arising in genetic cancer syndromes, chronic inflammatory states, congenital anomalies, therapy-related settings, and those with unusual paraneoplastic or metastatic patterns represent a distinct, under-reported subgroup Here we are presenting 37 such rare malignancies due to the rarity and for documentation.Methods: This retrospective observational study included 37 patients treated between January 1998 and August 2025 at a tertiary cancer center in Eastern India.Eighteen cases had been previously published and 19 new cases were added.Patients were categorized into: (1) common malignancies arising in rare genetic or acquired predisposing conditions, and (2) common malignancies with rare clinical, biological, paraneoplastic, or metastatic manifestations.Results: Patients with xeroderma pigmentosum (n=6) had squamous, basal cell and malignant melanomas with tongue and ovarian carcinoma, Tuberous sclerosis (n=4) had SEGA and bilateral renal angiomyolipomas.Neurofibromatosis (n=7) had malignant peripheral nerve sheath tumors and intracranial tumors, hereditary multiple exostoses (n=1) had chondrosarcomaa nd Klinefelter

syndrome (n=1) had CML.Malignancies arising in chronic states were SCC over burn scars (n=3), filarial scrotum (n=1), tropical ulcer (n=1), adenocarcinoma in ectopia vesicae (n=1).Therapy-related second cancer were meningioma 12 years after childhood ALL and AML 63 months after CTRT for cancer cervix. 2 patients had primary granulocytic sarcoma of meninges and mediastinum.Paraneoplastic syndromes included carcinoma larynx with pemphigus, bronchial carcinoid with ectopic cushing's syndrome and solitary fibrous tumor with hypoglycemia.Rare associations included vanishing bone disease, ectopic male breast cancer on the upper chest wall, synchronous GIST with papillary RCC, synchronous Lobular carcinoma of breast with clear cell carcinoma of right kidney and colonic metastasis fr ...

6.8% influence 3 Sep 2025

Unraveling the Anesthesia Enigma in Xeroderma Pigmentosum: A Case Report

Xeroderma pigmentosum (XP) is a rare autosomal recessive disorder.It was first described by Kaposi in the 1870s.Its incidence ranges from 1 per 20,000 in Japan to 2.3 per 1 million live births in the United States, 1,2 with more cases in North Africa and the Middle East. 3 However, data about the incidence in India remains limited.It affects all races and both sexes, with a higher incidence in areas with consanguinity. 4 Xeroderma pigmentosum is marked by an extreme sensitivity to ultraviolet (UV) radiation and progressive neurological complications stemming from a deoxyribonucleic acid (DNA) repair defect.It manifests in early childhood, and approximately 60% die before the age of 20 years. 5,6The most common presentations include cutaneous (100%), ophthalmic (75%), and neurological symptoms (25%). 6eroderma pigmentosum may present with sunburn reactions, freckle-like pigmentation, cutaneous and noncutaneous tumors, ocular pathologies (photophobia, conjunctivitis, corneal drying and ulcer,

Open article

Ankita Kaasat 9 Sakshi Thakore 11 Madhavi Unmesh Santpur Mamatha Achampeta Suman Kaushik Nirdesh Thakore 6

Related companies

AI-generated summary of companies related to the forecast. Verify critical details against original sources.

Company	Lead candidate	Stage
Protheragen (USA & Denmark)	Autologous stem-cell gene therapy — lentiviral delivery of functional DNA repair genes (example cited: XPC). Protheragen describes preclinical gene-therapy and gene-editing programs for Xeroderma pigmentosum and lists lentiviral delivery of functional DNA-repair genes (e.g., XPC) to hematopoietic stem cells as a therapeutic approach; the work is presented as preclinical research and service/therapeutic development.	Preclinical [1]
Cellectis (Paris, France)	Engineered nuclease (meganuclease / TALEN)-based gene editing to correct XPC mutations (research constructs; no public clinical candidate name). Cellectis researchers published preclinical/in vitro work demonstrating meganuclease- and TALEN-mediated correction of an XPC founder mutation leading to re-expression of full-length XPC protein and restoration of nucleotide excision repair capacity in patient cells. This represents company-associated preclinical gene-editing research rather than an identified clinical candidate.	Preclinical / in vitro research [1] [2]

Drug discovery timeline

Orphan designations and approvals related to the disease.

Drug	Therapy type		Orphan designation	Approval	Sponsor
Afamelanotide	peptides	EMA	2024-05-24	nan	Clinuvel Europe Limited
Pro-Pro-Thr-Val-Pro-Thr-Arg	peptides	FDA	2017-07-27	nan	ProGeLife S.A.S
PRO-PRO-THR-VAL-PRO-THR-ARG [INHOX]	peptides	EMA	2014-11-19	nan	ProGeLife S.A.S.
T4 endonuclease V, liposome encapsulated	proteins	FDA	1989-06-27	nan	AGI Dermatics