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Investment memorandum

12 Feb 2026

First-generation therapy forecast:

Rhabdoid tumor

Categories: rare neoplastic diseases

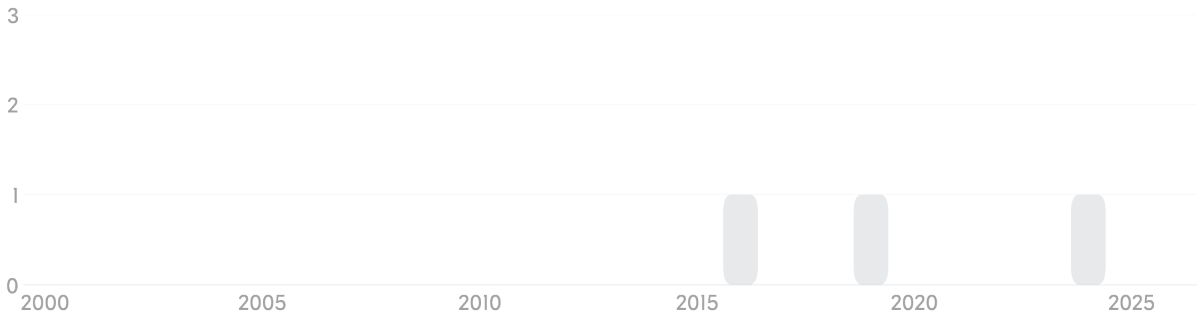
Gene therapies

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

Disease landscape:

Orphan designations: **3**

Approved drugs: **0**



De-risked by AI:

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

Top 1.1%
of research

Disease overview

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

Rhabdoid tumor

Synonyms: Malignant rhabdoid tumor.

Rhabdoid tumor is a rare, highly aggressive malignancy primarily affecting infants and young children, with peak incidence under age 4 [1] [4] [12]. These tumors most commonly arise in the CNS (atypical teratoid rhabdoid tumors, ATRT), kidneys (malignant rhabdoid tumors, MRT), or soft tissues [1] [6] [17]. Over 90% involve biallelic SMARCB1 inactivation, disrupting chromatin remodeling and driving epigenetic dysregulation [1] [8] [19]. Prognosis remains poor despite multimodal therapy, with survival rates heavily influenced by age and primary site [4] [12] [16].

Population

- Primarily infants/toddlers (median diagnosis at 15 months); second incidence peak >70 years [4] [12]
- Annual incidence: ~1-2/million children <15 years [6] [14] [19]
- ~50% of CNS tumors in infants <1 year; 20-25% of pediatric renal malignancies [1] [17] [19]

Current Therapeutic Strategies

- **Multimodal approach**: Maximal safe resection + intensive chemotherapy (vincristine, cyclophosphamide, cisplatin/etoposide) + age-adjusted radiotherapy [1] [3] [13]
- **High-dose chemotherapy** with autologous stem cell rescue for consolidation [1] [3] [5]
- **Protocols**: COG ACNS0333 (surgery → chemo → HDCT) vs. Eu-Rhab (anthracycline-based regimens + early RT) [1] [3] [5]

Burden of the Disease

- **Mortality**: 5-year OS 20-25% for renal MRT vs. 32-50% for ATRT [1] [6] [16]
- **Metastasis**: >50% present with disseminated disease; CNS involvement predicts worst outcomes [4] [12] [17]
- **Toxicity**: Intensive therapies cause significant neurocognitive, renal, and growth impairments in survivors [3] [13] [18]

Literature overview

Most influential articles for LLM-classifier prediction.

15.4% influence 19 May 2025

A novel conditionally replicative oncolytic adenovirus under the control of the SALL4 promoter inhibits the growth of rhabdoid tumors.

Open article

Satoru Oya 6 Hideki Yoshida 336 Akimasa Tomida 13 Mitsuru Miyachi 113 Shigeki Yagyu 118 Yoshiki Katsumi 74 Ken Kikuchi 76 Kunihiko Tsuchiya Eiichi Konishi 385 Subbaya Subramanian 284 Masato Yamamoto 412 Tomoko Iehara

Rhabdoid tumors (RTs) are highly aggressive pediatric malignancies with limited treatment options. SALL4, a gene essential for embryonic stem cell pluripotency and self-renewal, is frequently overexpressed in RTs. To exploit this, we developed a conditionally replicating oncolytic adenovirus (pSALL4-OAd) by placing the E1 region under the control of the SALL4 promoter, restricting viral replication to SALL4-positive cells. SALL4 protein expression was analyzed in 10 clinical RT specimens via immunohistochemistry, while SALL4 mRNA levels and promoter activity were assessed in eight RT cell lines using quantitative PCR and dual-luciferase assays. The replication selectivity and cytopathic effects of pSALL4-OAd were tested in vitro at doses of 0-1000 viral particles (vp)/cell. In vivo, 1.0 × 10^7 G401 cells were implanted subcutaneously into immunodeficient mice, followed by intratumoral administration of pSALL4-OAd (3 × 10^10 vp) or phosphate-buffered saline. Tumor growth was monitored over the treatment period. SALL4 protein was detected in 40% of clinical RT specimens, and RT cell lines exhibited 4- to 400-fold higher SALL4 mRNA levels compared with normal tissues. Elevated SALL4 promoter activity was confirmed in three of five RT cell lines. pSALL4-OAd selectively replicated in SALL4-positive cells and induced significant cytopathic effects proportional to promoter activity in vitro. In vivo, pSALL4-OAd administration caused tumor necrosis, reduced SALL4-positive cells, and suppressed tumor proliferation. These results demonstrate the potential of pSALL4-OAd as a targeted and effective therapeutic strategy for SALL4-expressing RTs.

13.3% influence 16 Apr 2025

Open article

Multi-omics analysis reveals key immunogenic signatures induced by oncolytic Zika virus infection of paediatric brain tumour cells.

Matt Sherwood 17 · Thiago Mitsugi 21 · Carolini Kaid 48 · Brandon Coke 13 · Mayana Zatz 877 · Kevin Maringer 55 · Oswaldo Keith Okamoto 199 · Rob M. Ewing 133

Brain tumours disproportionately affect children and are the largest cause of paediatric cancer-related death. Novel therapies that engage the immune system, such as oncolytic viruses (OVs), hold great promise and are desperately needed. Zika virus (ZIKV) infects and destroys aggressive cells from multiple paediatric central nervous system (CNS) tumours. Despite this, the molecular mechanisms underpinning this response are largely unknown. We comprehensively investigate the transcriptomic response of paediatric medulloblastoma and atypical teratoid rhabdoid tumour (ATRT) cells to ZIKV infection. We observe conserved TNF signalling and cytokine signalling-related signatures and show that the TNF-alpha signalling pathway is implicated in oncolysis by reducing the viability of ZIKV-infected brain tumour cells. Our findings highlight TNF-alpha as a potential prognostic marker for oncolytic ZIKV (oZIKV) therapy. Complementing our analysis with a 49-plex ELISA, we demonstrate that ZIKV infection induces a clinically relevant and diverse pro-inflammatory brain tumour cell secretome, including TNF-alpha. We assess publicly available scRNA-Seq data to model how ZIKV-induced secretome paracrine and endocrine signalling may orchestrate the anti-tumoural immune response during oZIKV infection of brain tumours. Our findings significantly contribute to understanding the molecular mechanisms governing oZIKV infection and will help pave the way towards oZIKV therapy.

9.8% influence · 1 Apr 2019

Open article

ATRT-03. EFFICACY OF THE ONCOLYTIC ADENOVIRUS DELTA-24-RGD AS A THERAPEUTIC AGENT FOR THE TREATMENT OF PEDIATRIC EMBRYONAL BRAIN TUMORS

Marc García-Moure 88 · Marisol Gonzalez-Húarriz 109 · Lucía Marrodán 61 · Montse Puigdelloses 62 · Ana Patiño-García 346 · Marta M. Alonso 407

Atypical teratoid/rhabdoid tumors (ATRTs) and primitive neuroectodermal tumors (PNETs) are two rare primary embryonal brain tumors, which are among the most frequent solid brain tumors in infants under one year old. The outcome for these children remains dismal, especially in ATRTs which have a 2-year overall survival below 20%. Therefore, we need to find out new efficient and safe therapeutic options for these children. Delta-24-RGD (DNX-2401 in the clinic) is an oncolytic adenovirus that has already been tested in Phase I/II clinical trials in patients affected by recurrent glioblastoma (NCT00805376; NCT01956734), demonstrating anti-tumor effect without any evidence of severe side effect associated with viral administration. Of interest for pediatric brain tumors, an ongoing Phase I trial using Delta-24-

RGD for the treatment of diffuse intrinsic pontine gliomas (NCT03178032) has also demonstrated a safe profile in these children. For these reasons, we propose to evaluate the anti-tumor effect of Delta-24-RGD in preclinical models of ATRT and PNET. The virus was able to infect and replicate in tumor cell cultures (three models of ATRT and four of PNET), inducing a potent cytotoxic effect. In addition, this cytotoxicity resulted in the released the immunogenic cell death markers Hsp70, Hsp90, HMGB1 and ATP, as well as an increased calreticulin exposure in the outer cell surface. Although not conclusive, the presence of these markers suggest the triggering of an anti-tumor immune response. Intratumoral administration of the virus extended significantly the overall survival of mice bearing ATRT or PNET xenografts, leading to up to 40% of long-term survivors. We are currently setting up an intraventricular model of disseminated disease, since most of patients with ATRT actually die due to the presence of metastases. In conclusion, these results demonstrate that Delta-24-RGD could be a feasible therapeutic option for chi ...

8.8% influence 29 Dec 2020

Delta-24-RGD, an Oncolytic Adenovirus, Increases Survival and Promotes Proinflammatory Immune Landscape Remodeling in Models of AT/RT and CNS-PNET

Abstract Purpose: Atypical teratoid/rhabdoid tumors (AT/RT) and central nervous system primitive neuroectodermal tumors (CNS-PNET) are pediatric brain tumors with poor survival and life-long negative side effects. Here, the aim was to characterize the efficacy and safety of the oncolytic adenovirus, Delta-24-RGD, which selectively replicates in and kills tumor cells. Experimental Design: Delta-24-RGD determinants for infection and replication were evaluated in patient expression datasets. Viral replication and cytotoxicity were assessed in vitro in a battery of CNS-PNET and AT/RT cell lines. In vivo, efficacy was determined in different orthotopic mouse models, including early and established tumor models, a disseminated AT/RT lesion model, and immunocompetent humanized mouse models (hCD34+-NSG-SGM3). Results: Delta-24-RGD infected and replicated efficiently in all the cell lines tested. In addition, the virus induced dose-dependent cytotoxicity [IC50 value below 1 plaque-forming unit (PFU)/cell] and the release of immunogenic markers. In vivo, a single intratumoral Delta-24-RGD injection (10^7 or 10^8 PFU) significantly increased survival and led to long-term survival in AT/RT and PNET models. Delta-24-RGD hindered the dissemination of AT/RTs and increased survival, leading to 70% of long-term survivors. Of relevance, viral administration to established tumor masses (30 days after engraftment) showed therapeutic benefit. In humanized immunocompetent models, Delta-24-RGD significantly extended the

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survival of mice bearing AT/RTs or PNETs (ranging from 11 to 27 days) and did not display any toxicity associated with inflammation. Immunophenotyping of Delta-24-RGD—treated tumors revealed increased CD8+ T-cell infiltration. Conclusions: Delta-24-RGD is a feasible therapeutic option for AT/RTs and CNS-PNETs. This work constitutes the basis for potential translation to the clinical setting.

8.1% influence 6 Jun 2018

Poliovirus Receptor (CD155) Expression in Pediatric Brain Tumors Mediates Oncolysis of Medulloblastoma and Pleomorphic Xanthoastrocytoma

Poliovirus oncolytic immunotherapy is a putatively novel approach to treat pediatric brain tumors. This work sought to determine expression of the poliovirus receptor (PVR), CD155, in low-grade and malignant pediatric brain tumors and its ability to infect, propagate, and inhibit cell proliferation. CD155 expression in pleomorphic xanthoastrocytoma (PXA), medulloblastoma, atypical teratoid rhabdoid tumor, primitive neuroectodermal tumor, and anaplastic ependymoma specimens was assessed. The ability of the polio: rhinovirus recombinant, PVSRIPO, to infect PXA (645 [BRAF V600E mutation], 2363) and medulloblastoma (D283, D341) cells were determined by viral propagation measurement and cell proliferation. PVR mRNA expression was evaluated in 763 medulloblastoma and 1231 normal brain samples. CD155 was expressed in all 12 patient specimens and in PXA and medulloblastoma cell lines. One-step growth curves at a multiplicity of infection of 10 demonstrated productive infection and peak plaque formation units at 5—10 hours. PVSRIPO infection significantly decreased cellular proliferation in 2363, 645, and D341 cell lines at 48 hours ($p < 0.05$) and resulted in cell death. PVR expression was highest in medulloblastoma subtypes Group 3γ, WNTα, and WNTβ ($p < 0.001$). This proof-of-concept in vitro study demonstrates that PVSRIPO is capable of infecting, propagating, prohibiting cell proliferation, and killing PXA and Group 3 medulloblastoma.

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Related companies

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

Company	Lead candidate	Stage
SynerGene Therapeutics, Inc. (Potomac, MD, USA)	scL-SMARCB1 nanocomplex A systemically administered immuno-lipid nanoparticle (termed scL-SMARCB1) delivering wild-type SMARCB1 transgene across the blood–brain barrier via transferrin receptor-mediated transcytosis, restoring SMARCB1 expression in SMARCB1-deficient ATRT cells to induce senescence, apoptosis, and tumor growth inhibition.	Preclinical [1] [2]

Drug discovery timeline

Orphan designations and approvals related to the disease.

Drug	Therapy type		Orphan designation	Approval	Sponsor
N-hydroxy-N-(methylacylfulvene)urea	small molecules	FDA	2024-10-28	nan	Lantern Pharma Inc.
O-18F-fluoroethyl-L-tyrosine	small molecules	FDA	2019-05-08	nan	Advanced Imaging Projects, LLC
tazemetostat	small molecules	FDA	2016-02-04	nan	Epizyme Inc.