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ADISINSIGHT REPORT

Vimseltinib: First Approval

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Abstract
Vimseltinib (ROMVIMZA™) is an orally administered kinase inhibitor that targets colony-stimulating factor 1 receptor (CSF1R), which is being developed by Deciphera Pharmaceuticals. As CSF1R activity has been identified as a contributing factor for tenosynovial giant cell tumour (TGCT), treatments targeting CSF1R have been investigated. Vimseltinib received its first approval in February 2025 in the USA for the treatment of TGCT and is under development for the treatment of chronic graft versus host disease. This article summarizes the milestones in the development of vimseltinib leading to this first approval for the treatment of adult patients with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity.

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Vimseltinib (ROMVIMZA™): Key Points

A small molecule CSF1R inhibitor being developed by Deciphera Pharmaceuticals for the treatment of TGCT and graft versus host disease

Received its first approval on 14 Feb 2025 in the USA

Approved for use in the treatment of adult patients with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity

1 Introduction

Tenosynovial giant cell tumour (TGCT) is a rare neoplasm affecting synovial joints, which can be associated with significant morbidity, but typically is not associated with mortality (except for malignant disease) [1]. Although surgery is the standard of treatment for TGCT, the benefits of resection must be weighed against the risk of overtreatment that may result in unacceptable morbidity. In patients with symptomatic disease where surgery is associated with significant morbidity, colony-stimulating factor 1 receptor (CSF1R) inhibitors are the standard of treatment [1]. Pexidartinib was the first approved systemic therapy in the USA with CSF1R inhibitor activity [2]. However, it is associated with a boxed warning regarding potentially life-threatening hepatoxicity reactions and requires a Risk Evaluation Management System program to manage this risk [2].

Vimseltinib (ROMVIMZA™) is a small molecule, orally administered CSF1R inhibitor being developed by Deciphera Pharmaceuticals for the treatment of TGCT. Vimseltinib received its first approval in February 2025 in the USA for the treatment of adult patients with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity [3]. It is also being evaluated for the treatment of chronic graft versus host disease [4].

The recommended dosage of vimseltinib is 30 mg taken orally twice weekly, with a minimum of 72 h between doses [5]. Vimseltinib may be taken with or without food.

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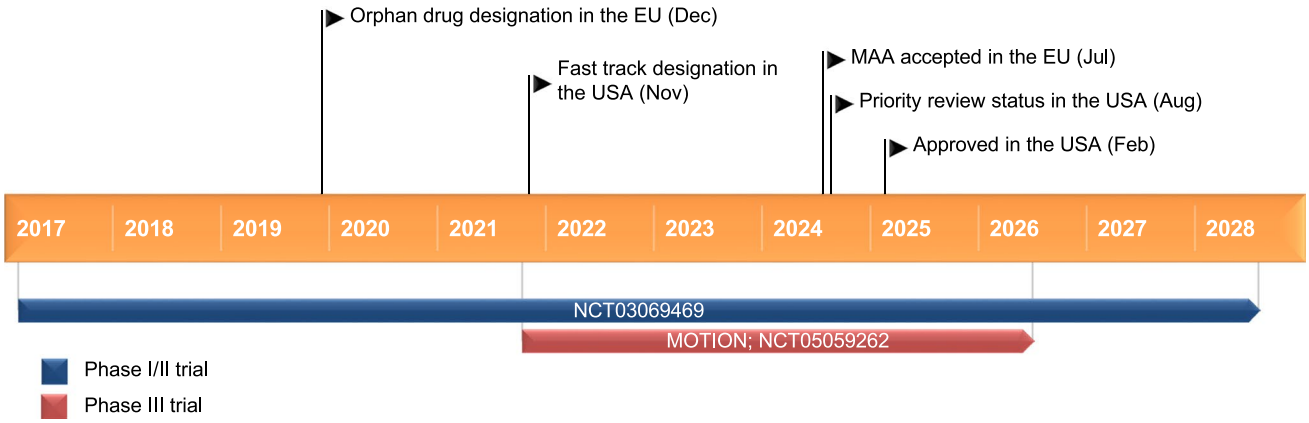


Key milestones in the development of vimseltinib for treatment of tenosynovial giant cell tumour. *MAA* marketing authorization application

Consult local prescribing information regarding dosage modification for the management of adverse reactions or for recommendations regarding concomitant use of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), or organic cation transporter 2 (OCT2) substrates. Serious and fatal liver injury have not been observed with vimseltinib. Vimseltinib capsules containing FD&C Yellow No. 5 (tartrazine) or No. 6 (Sunset Yellow FCF) may cause allergic reactions in sensitive patients. Alternative measures to assess renal function that are not based on serum creatinine may be required, as an increase in serum creatinine without affecting renal function may occur [5].

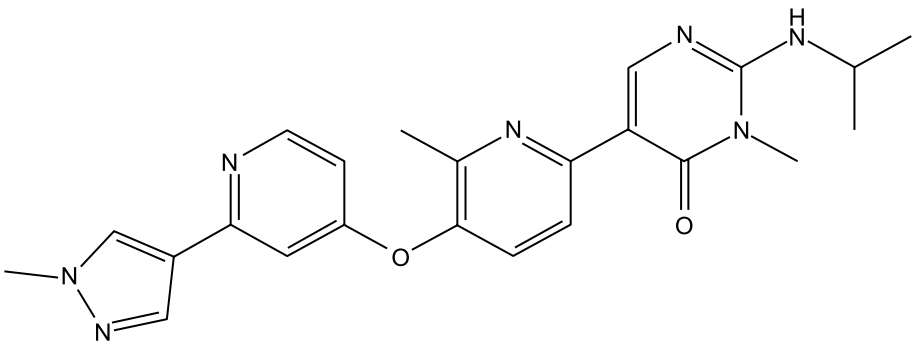
1.1 Company Agreements and Patent Information

In June 2024, Deciphera Pharmaceuticals was acquired by Ono Pharmaceutical, and continues to operate as Deciphera Pharmaceuticals as a wholly owned subsidiary of Ono Pharmaceutical [6]. Deciphera Pharmaceuticals holds three issued patents and one pending patent in the USA relating to vimseltinib, which are expected to expire between 2034 and 2040 [7]. Issued and pending patents in Australia, Canada, Asia, Europe and South America relating to vimseltinib are expected to expire between 2034 and 2039 [7].

2 Scientific Summary

2.1 Pharmacodynamics

Vimseltinib binds to CSF1R and stabilizes its inactive 'off' state [8, 9]. In vitro, vimseltinib selectively inhibits CSF1R (IC_{50} 2.8–3.7 nM [8, 9]) in contrast to other kinases (>500-fold selectivity for CSF1R) and inhibits the growth of cells that are driven by CSF1R phosphorylation (IC_{50} 19 nM) [8]. Vimseltinib also prevents the differentiation of human osteoclasts (IC_{50} 9.3 nM), which is a process driven by CSF1R activity and is associated with bone resorption [9].



Chemical structure of vimseltinib

Features and properties of vimseltinib

Alternative names	ROMVIMZA™, DCC 3014, DP-6865
Class	Antineoplastics, pyrazoles, pyridines, pyrimidinones, small molecules
Mechanism of action	Macrophage colony-stimulating factor receptor antagonists
Route of administration	Oral
Pharmacodynamics	Binds to CSF1R stabilizing the inactive 'off' state; selectively inhibits CSF1R (IC_{50} 2.8–3.7 nM) and growth of cells that are driven by CSF1R phosphorylation (IC_{50} 19 nM), blocks differentiation of human osteoclasts (IC_{50} 9.3 nM)
Pharmacokinetics	Steady state C_{max} and AUC 747 ng/mL and 13,400 ng·h/mL; T_{max} 1 h; V/F 90 L; plasma protein binding 96.5%; predominantly metabolised by oxidation, N-demethylation, and N-dealkylation; 43% and 38% of a single dose was recovered in faeces and urine (9.1% and 5.1% unchanged); P-gp substrate and inhibits transporters (e.g., P-gp, BCRP and OCT2)
Most common adverse reactions	Periorbital oedema, fatigue, rash, peripheral oedema, face oedema, pruritus
ATC codes	
WHO ATC code	L01X-E (protein kinase inhibitors), L01EX15 (L01 (antineoplastic), L01EX (other protein kinase inhibitors))
EphMRA ATC code	L1H (protein kinase inhibitor antineoplastics)
Chemical name	3-methyl-5-[6-methyl-5-[2-(1-methylpyrazol-4-yl)pyridin-4-yl]oxypyridin-2-yl]-2-(propan-2-ylamino)pyrimidin-4-one

2.2 Pharmacokinetics

The pharmacokinetics of vimseltinib are dose proportional [5]. Following a single oral dose of vimseltinib 30 mg, the maximum plasma concentration (C_{max}) and area under the plasma-time curve (AUC) are 283 ng/mL and 46,900 ng·h/mL. At steady state, the C_{max} and AUC are 747 ng/mL and 13,400 ng·h/mL. The median time to C_{max} (T_{max}) is 1 h. The volume of distribution (V/F) of vimseltinib is 90 L, and it is highly bound to plasma proteins (96.5%) [5].

Vimseltinib is predominantly metabolised by oxidation, N-demethylation, and N-dealkylation, and is unlikely to be metabolised by CYP450 enzymes [5]. After a single radiolabelled dose of vimseltinib, 43 and 38% of the dose was recovered in faeces and urine (9.1 and 5.1% unchanged). Vimseltinib is a P-gp substrate and inhibits transporters including P-gp, BCRP and OCT2 [5].

2.3 Therapeutic Trials

The objective response rate (ORR) determined by independent radiological review (IRR) at week 25 was 40% (complete or partial response [CR or PR] in 5 and 35% of patients) in 83 vimseltinib recipients and 0% in 40 placebo recipients (intergroup difference 40%; $p < 0.0001$) during the MOTION phase III trial (NCT05059262) in patients with symptomatic TGCT not amenable to surgery (primary endpoint) [10]. During this global, double-blind trial, patients were randomised to receive vimseltinib 30 mg or placebo twice weekly taken orally in 28-day cycles over 24 weeks. At the data cutoff date, the median duration of response (DOR) was not yet reached in vimseltinib recipients (range 0.03+ to 11.7+ months). The ORR per tumour volume score was 67% (including 5% CR) in vimseltinib recipients versus 0% in placebo recipients. Significant ($p < 0.05$) and clinically meaningful improvements in symptom-related and function-related endpoints (presented as LS mean change from baseline unless noted as response rate) were reported for vimseltinib over placebo, including active range of motion (18.4 vs 3.8% for vimseltinib and placebo, respectively), physical function (PROMIS-PF scores 4.6 vs 1.3), worst stiffness (NRS −2.1 vs −0.3) and worst pain (BPI response rate 48 vs 23%) [10]. In an updated analysis, the median DOR was not yet reached in vimseltinib recipients (range 2.5+ to 19.4+ months) [11].

The ORR determined by IRR was 72% (3% CR, 69% PR) in 32 patients with TGCT not amenable to surgery across three cohorts during the phase I/II NCT03069469 trial (exploratory endpoint, primary endpoints were related to safety and pharmacokinetics) [12]. During this global, open-label, dose escalation trial, patients received 3-day or 5-day loading doses of vimseltinib once daily and subsequently received vimseltinib 30 mg twice weekly or vimseltinib 6 mg or 10 mg once daily, depending on their assigned cohort. The patients in these cohorts (cohorts 5, 8 and 9) had a confirmed diagnosis of TGCT which was not amenable to surgery, other cohorts included patients who had advanced malignant solid tumours [12].

Key clinical trials of vimseltinib

Drug(s)	Indication	Phase	Sponsor	Status	Location(s)	Identifier
Vimseltinib, placebo	Tenosynovial giant cell tumour	III	Deciphera Pharmaceuticals	Ongoing	Global	NCT05059262, MOTION
Vimseltinib	Advanced tumors and tenosynovial giant cell tumour	I/II	Deciphera Pharmaceuticals	Ongoing	Global	NCT03069469
Vimseltinib, avelumab	Advanced or metastatic sarcomas	I	Memorial Sloan Kettering Cancer Center	Ongoing	USA	NCT04242238
Vimseltinib	Chronic graft-versus-host disease	II	Deciphera Pharmaceuticals	Enrolling	USA	NCT06619561

2.4 Adverse Reactions

During the MOTION trial, the most common (all-grade incidence ≥ 25%) adverse reactions that occurred at an incidence > 5% higher in vimseltinib recipients ($n = 83$) than placebo recipients ($n = 39$) were periorbital oedema (all-grade incidence in vimseltinib vs placebo recipients 60% vs 21%; grade 3 or 4 incidence 3.6 vs 0%), fatigue (59 vs 38%; 1.2 vs 2.6%), rash (47 vs 5%; 3.6 vs 0%), peripheral oedema (33 vs 8%; 1.2 vs 0%), face oedema (31 vs 8%; 1.2 vs 0%) and pruritus (29 vs 8%; 2.4 vs 0%) [5]. Serious adverse reactions occurred in 2.4% of vimseltinib recipients and permanent discontinuation of vimseltinib due to an adverse reaction occurred in 4.8% of patients [5].

The most common (incidence ≥ 25%) laboratory anomalies worsening from baseline in vimseltinib recipients with a difference in incidence between arms of > 5% compared to placebo were AST increased (all-grade incidence in vimseltinib vs placebo recipients 92 vs 11%; no grade 3 or 4 reactions were reported), cholesterol increased (43 vs 16%; no grade 3 or 4 reactions), neutrophils decreased (31 vs 2.6%; 1.2 vs 0%) and leukocytes decreased (29 vs 8%; no grade 3 or 4 reactions) [5]. Creatinine increase occurred in 17 versus 2.6% of patients in the respective groups; however, these increases may not be due to renal damage [5].

2.5 Ongoing Clinical Trials

There are four ongoing clinical trials investigating vimseltinib that have completed enrolment. Ongoing trials in cancer indications include the MOTION phase III trial in patients with TGCT (NCT05059262, vimseltinib monotherapy vs placebo), the NCT03069469 phase I/II trial in patients with malignant solid tumours or TGCT (vimseltinib monotherapy) and the NCT04242238 phase I trial in patients with advanced or metastatic sarcomas (vimseltinib in combination with avelumab). In non-cancer indications, the NCT06619561 phase II trial is evaluating vimseltinib in patients with active moderate to severe chronic graft versus host disease (vimseltinib monotherapy).

3 Current Status

Vimseltinib received its first approval on 14 Feb 2025 in the USA for the treatment of adult patients with symptomatic TGCT for which surgical resection will potentially cause worsening functional limitation or severe morbidity [3]. The marketing authorization application was accepted in the EU in July 2024 [13].

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40265-025-02191-z.

Declarations

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Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability Not applicable.

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