GLPG3667 (TYK2)

Mechanism: As a Tyrosine Kinase-2-targeting (TYK2) drug, GLPG3667 targets a receptor of the JAK family, implicated in IFN-a, IL-6, IL-10 and IL-12 signaling.

Key trials and catalysts: P1b in psoriasis was initiated in November 2020, with results possibly available in 2021 (**PCD: May 2021; NCT04594928**). The endpoints in this study include frequency and severity of TEAEs, Psoriasis Area and Severity Index (PASI) change and plasma trough concentrations.

Summary of competitive landscape in TYK2: The current TYK2 landscape consists of multiple players including BMS, Pfizer, JNJ as well as smaller players such as Theravance, Sareum, Innocare and Nimbus Therapeutics. We note the collaboration of JNJ with Theravance and BMS with Nimbus. As the most advanced TYK2 asset in this space, BMS-986165/deucravacitinib is a selective TYK2 inhibitor with positive P3 data in psoriasis and positive P2 data in psoriatic arthritis (further detail below), whilst additional data in psoriasis is expected in Q1'21 from the P3 POETYK PSO-2 trial with additional data expected at AAD in April (23-25 April). We note that BMY's TYK2 data will serve as the benchmark for efficacy; we summarise key details so far below.

Key TYK2 inhibitors in development

Company	Product	Mechanism of Action	Phase	Key Indications
Bristol-Myers Squibb	BMS-986165 (deucravacitinib)	TYK2	3	Psoriasis, Psoriatic arthritis, Lupus nephritis, Systemic Lupus Erythematosus, Crohn's, Ulcerative colitis
Pfizer	PF-06826647	TYK2	2	Plaque psoriasis, Hidradenitis suppurativa, Ulcerative colitis
Pfizer	PF-06700841 (brepocitinib)	TYK2 / JAK1	2	Plaque psoriasis, Ulcerative colitis, Crohn's, Vitiligo, Atopic dermatitis, Psoriasis, Alopecia areata, Lupus, Hiddradenitis suppurativa
Johnson & Johnson	TD-1473	TYK2 / JAK1,2,3	3	Ulcerative colitis
Oncostellae	OST-122	ARK5 / JAK1,2,3 / TYK2	2	Ulcerative colitis
Theravance Biopharma	TD-8236	TYK2 / JAK1,2,3	2	Inflammatory lung diseases (asthma)
Theravance Biopharma	TD-0903	TYK2 / JAK1,2,3	2	COVID-19 Acute Lung Injusry
Pfizer	PF-06700841 (brepocitinib)Topical	TYK2 / JAK1	2	Atopic dermatitis, Plaque psoriasis
Bristol-Myers Squibb/Nimbus	Tyk2 Allosteric Inhibitor Research Program	TYK2	1	N/A
Galapagos	GLPG3667	TYK2	1b	Psoriatic arthritis
Sareum	SDC-1802	TYK2 / JAK1	Pre-clinical	N/A
Sareum	SAR-20347	TYK2 / JAK1	Pre-clinical	N/A
InnoCare	ICP-332	TYK2	Pre-clinical	N/A
Nimbus Therapeutics	Tyk2 Catalytic Inhibitor Research Program	TYK2	Pre-clinical	N/A

Details so far for BMY's deucravacitinib

- **P2 data in psoriatic arthritis**: In September 2020, BMS announced positive P2 data in psoriatic arthritis, in which both 6mg (n=70) and 12mg (n=67) deucravacitinib once daily showed at least a 20% improvement vs placebo in signs and symptoms of disease at Week 16. There were also improvements from baseline in the Health Assessment QuestionnaireDisability Index (HAQ-DI) and in the Physical Component Summary (PCS) Score of the Short Form Health Survey-36 Item (SF-36) Questionnaire. There were no serious AEs in deucravacitinib patients, with most common AEs including nasopharyngitis (17.9% vs 7.6% in placebo), rash (6.0% vs 0% in placebo) and headache (1.5% vs 4.5% in placebo).
- **P3 data in psoriasis: Both of BMY's P3 pivotal trials have read out positive.** Positive data from POETYK PSO-1 were announced in March 2020, whilst topline results from POETYK-PSO-2, evaluating deucravacitinib in moderate-severe plaque psoriasis were announced in February 2021. POETYK PSO-2 trial (plaque psoriasis) met the same primary and secondary endpoints and demonstrated a safety profile in line with POETYK PSO-1, with full data expected to be presented at a future meeting (AAD 23-25 April 2021; a BMY analyst meeting is scheduled on 23rd April).

Details so far for PFE's topical TYK2/JAK1 brepocitinib/PF-06700841

P2 data in moderate-severe atopic dermatitis: Presented at EADV October 2020, topical brepocitinib demonstrated a reduction in eczema area and severity index (EASI) total score and improvement in investigator's global assessment (IGA). In terms of safety, 37% of patients had TEAEs with more reported in the vehicle arm vs brepocitinib arms. The majority of TEAEs were mild and did not increase with dose in the brepocitinib arms.

26 April 2021

https://www.evaluate.com/vantage/articles/news/trial-results/bristols-tyk2-ticks-boxes