Takeda to Acquire Late-Stage, Potential Best-in-Class, Oral Allosteric TYK2 Inhibitor NDI-034858 From Nimbus Therapeutics

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Better Health, Brighter Future

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Takeda to acquire late-stage, potential best-in-class, oral allosteric TYK2 inhibitor NDI-034858 from Nimbus Therapeutics

- Potential to demonstrate best-in-class efficacy and safety in psoriasis as well as multiple other immune-mediated diseases, including Inflammatory Bowel Disease (IBD), psoriatic arthritis and Systemic Lupus Erythematosus

- Phase 3 psoriasis study expected to start in 2023; potential for regulatory filing in FY25-27 timeframe

- Acquisition strengthens Takeda's growing late-stage pipeline, in alignment with the company's therapeutic area strategy and expertise in immune-mediated diseases

- Under the terms of the agreement, Takeda will pay Nimbus USD $4B upfront, and two milestone payments of $1B each upon achieving annual net sales of $4B and $5B. The upfront payment will be primarily funded by cash on hand

- The transaction is expected to close before the end of FY2022, contingent on completion of review under antitrust laws

NDI-034858, a selective allosteric tyrosine kinase 2 (TYK2) inhibitor

High Selectivity Allows for Greater Inhibition of TYK2

- NDI-034858 is a novel, investigational, oral, allosteric inhibitor of tyrosine kinase 2 (TYK2) with high specificity for TYK2 over JAK1, JAK2, JAK3 kinases
  - NDI-034858 has 1,500,000-fold selectivity for TYK2 over JAK1

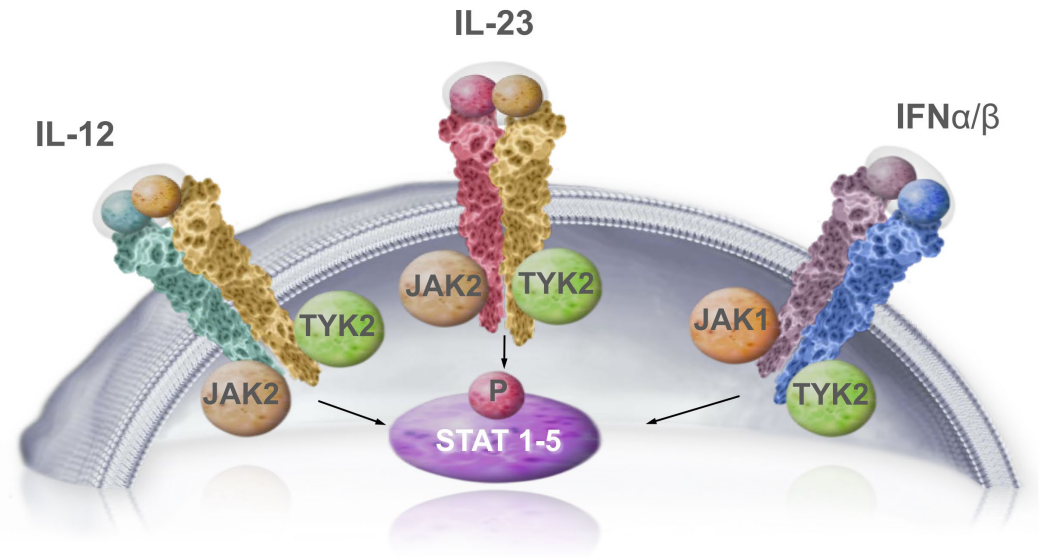
	NDI-034858	Deucravacitinib
TYK-2 –JH2 binding K_D	0.0034 nM	0.0045 nM
JAK1 –JH2 binding K_D	5000 nM	0.49 nM
Biochemical Selectivity (Fold)	1.5×10^6	109
Fold Selectivity (vs. deucravacitinib)	1.3×10^4	

Source: Nimbus proprietary structure based computational modeling; side-by-side evaluation of biochemical potency of NDI-034858 and deucravacitinib (synthesized by Nimbus for nonclinical research purposes only).

Potential for enhanced efficacy without introducing JAK-related toxicities

Tyrosine Kinase 2 (TYK2)

- Obligate signal transducer of receptors for interleukin (IL)-12, IL-23 and Type I interferon
- Heterodimer with JAK1 or JAK2; inhibition of either dimer moiety impedes signal transduction



Source: Gangolli, et al. 2022. Characterization of pharmacokinetics, pharmacodynamics, tolerability and clinical activity in Phase 1 studies of the novel allosteric tyrosine kinase 2 (TYK2) inhibitor NDI-034858.

Potential best-in-class efficacy & safety in multiple immune-mediated diseases

- Mechanism of action could lead to activity in broad range of indications representing a multi-billion dollar revenue opportunity
- Aligned with Takeda's therapeutic area strategy and expertise in immune-mediated diseases

~$30B market*

Psoriasis

- In a Phase 2b study, once-daily, oral dosing with NDI-034858 achieved statistical significance in the number of moderate-to-severe psoriasis patients achieving PASI-75 compared to placebo. Data from the trial to be disclosed early in 2023
- Phase 3 study expected to start in 2023
- Potential regulatory submission in FY25-27 timeframe

~$7B market*

Active Psoriatic Arthritis

- Phase 2b study ongoing

~$30B market*

Inflammatory Bowel Disease

>$50B market*

Other immune-mediated diseases (e.g. SLE, RA, MS, atopic dermatitis)

*Estimated market size in 2028. Source: Evaluate Pharma
PASI: Psoriasis area and severity index
SLE: Systemic Lupus Erythematosus; RA: Rheumatoid Arthritis; MS: Multiple Sclerosis

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