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

December 14th, 2022
IMPORTANT NOTICE

For the purposes of this notice, “presentation” means this document, any oral presentation, any question and answer session and any written or oral material discussed or distributed by Takeda Pharmaceutical Company Limited ("Takeda") regarding this presentation. This presentation (including any oral briefing and any question-and-answer in connection with it) is not intended to, and does not constitute, represent or form part of any offer, invitation or solicitation of any offer to purchase, otherwise acquire, subscribe for, exchange, sell or otherwise dispose of, any securities or the solicitation of any vote or approval in any jurisdiction. No shares or other securities are being offered to the public by means of this presentation. No offering of securities shall be made in the United States except pursuant to registration under the U.S. Securities Act of 1933, as amended, or an exemption therefrom. This presentation is being given (together with any further information which may be provided to the recipient) on the condition that it is for use by the recipient for information purposes only (and not for the evaluation of any investment, acquisition, disposal or any other transaction). Any failure to comply with these restrictions may constitute a violation of applicable securities laws.

The companies in which Takeda directly and indirectly owns investments are separate entities. In this presentation, “Takeda” is sometimes used for convenience where references are made to Takeda and its subsidiaries in general. Likewise, the words “we”, “us” and “our” are also used to refer to subsidiaries in general or to those who work for them. These expressions are also used where no useful purpose is served by identifying the particular company or companies.

The product names appearing in this document are trademarks or registered trademarks owned by Takeda, or their respective owners.

Forward-Looking Statements

This presentation and any materials distributed in connection with this presentation may contain forward-looking statements, beliefs or opinions regarding Takeda’s future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as “targets”, “plans”, “believes”, “hopes”, “continues”, “expects”, “aims”, “intends”, “ensures”, “will”, “may”, “should”, “would”, “could”, “anticipates”, “estimates”, “projects” or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda’s global business, including general economic conditions in Japan and the United States; competitive pressures and developments; changes to applicable laws and regulations, including global health care reforms; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic, on Takeda and its customers and suppliers, including foreign governments in countries in which Takeda operates, or on other facets of its business; the timing and impact of post-merger integration efforts with acquired companies; the ability to divest assets that are not core to Takeda’s operations and the timing of any such divestment(s); the extent to which our internal energy conservation measures and future advancements in renewable energy or low carbon energy technology will enable us to reduce our greenhouse gas emissions; and other factors identified in Takeda’s most recent Annual Report on Form 20-F and Takeda’s other reports filed with the U.S. Securities and Exchange Commission, available on Takeda’s website at: https://www.takeda.com/investors/sec-filings/ or at www.sec.gov. Takeda does not undertake to update any of the forward-looking statements contained in this presentation or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this presentation may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda’s future results.

Medical Information

This presentation contains information about products that may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different strengths. Nothing contained herein should be considered a solicitation, promotion or advertisement for any prescription drugs including the ones under development.
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

<table>
<thead>
<tr>
<th></th>
<th>NDI-034858</th>
<th>Deucravacitinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>TYK2 –JH2 binding $K_D$</td>
<td>0.0034 nM</td>
<td>0.0045 nM</td>
</tr>
<tr>
<td>JAK1 –JH2 binding $K_D$</td>
<td>5000 nM</td>
<td>0.49 nM</td>
</tr>
<tr>
<td>Biochemical Selectivity (Fold)</td>
<td>$1.5 \times 10^6$</td>
<td>109</td>
</tr>
<tr>
<td>Fold Selectivity (vs. deucravacitinib)</td>
<td>$1.3 \times 10^4$</td>
<td></td>
</tr>
</tbody>
</table>

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

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

**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

**Active Psoriatic Arthritis**
- Phase 2b study ongoing

**Inflammatory Bowel Disease**

**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