



A Global, Values-Based, R&D-Driven Biopharmaceutical Leader



January 7, 2019

Christophe Weber

President & CEO

Takeda Pharmaceutical Company Limited

Better Health, Brighter Future

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Important Notice



Certain Non-IFRS Financial Measures

This presentation includes certain non-IFRS financial measures and targets. Takeda's management evaluates results and makes operating and investment decisions using both IFRS and non-IFRS measures included in this presentation. Non-IFRS results exclude certain income and cost items which are included in IFRS results. By including these non-IFRS measures, management intends to provide investors with additional information to further analyze Takeda's performance, core results and underlying trends. Non-IFRS results are not prepared in accordance with IFRS and non-IFRS information should be considered a supplement to, and not a substitute for, financial statements prepared in accordance with IFRS. Investors are encouraged to review the reconciliation of non-IFRS financial measures to their most directly comparable IFRS measures, which are on slides 27-28.

Medical information

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Financial information

Takeda's financial statements are prepared in accordance with International Financial Reporting Standards ("IFRS"). The financial statements of Shire plc ("Shire") are presented in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). Therefore, the respective financial information of Takeda and Shire are not directly comparable.

Furthermore, this presentation refers to Takeda's Adjusted EBITDA and Shire's Non-GAAP EBITDA. Takeda's Adjusted EBITDA is not a measure presented in accordance with IFRS, and Shire's Non-GAAP EBITDA is not a measure presented in accordance with U.S. GAAP. The most closely comparable measure presented in accordance with IFRS (for Takeda) is net profit for the year and in accordance with U.S. GAAP (for Shire) is net income. Please see slides 25-28 for a further description of Takeda's Adjusted EBITDA and Shire's Non-GAAP EBITDA and a reconciliation to the respective most closely comparable measures presented in accordance with IFRS and U.S. GAAP.

The information in this presentation describes the Takeda group following completion of the acquisition of Shire on January 8, 2019.

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Transaction Value & Multiples

- Equity Value: \$61bn¹
- Enterprise Value: \$79bn^{1,2}

5.2x	12.1x	17.8x
LTM Shire Revenue ³	LTM Shire Non GAAP EBITDA ³	LTM Shire Net Income ³

Pro Forma Financials

Revenue	\$31.3bn⁴
Adjusted EBITDA	\$10.1bn^{4,5}



**A GLOBAL, VALUES-BASED,
R&D-DRIVEN
BIOPHARMACEUTICAL
LEADER**

Financial Benefits

- At least \$1.4bn of run-rate synergies
- Significantly accretive to underlying EPS⁶
- Attractive ROIC
- Strong cash flow to maintain dividend

Preserving Balance Sheet Strength

- Maintain investment grade
- Attractive interest rate
- Plan to de-lever to 2x net debt to Adjusted EBITDA within 3 to 5 years

¹ Based on the closing price of ¥ 4,535 per Takeda Share and converted using the E:¥ exchange rate of 1:147.61 and E:\$ of 1:1.3546 on May 4, 2018 (being the latest practicable date prior to 2.7 announcement on May 8, 2018);

² Not pro forma for the divestiture of Shire's oncology business to Servier for \$2.4bn completed on August 31, 2018; ³ LTM (Last Twelve Months) ended March 31, 2018, includes Oncology contribution; ⁴ LTM ended September 30, 2018 and an exchange rate of \$:¥ of 1:113.6 as at September 30, 2018; ⁵ The sum of Takeda's Adjusted EBITDA and Shire's Non-GAAP EBITDA. Please see slides 25-28 for more details; ⁶ EPS on an underlying basis is the per-share amount of underlying core net profit. Please see slides 26 for more details.

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Closing of the Shire acquisition: January 8th, 2019



8 months from deal announcement to deal close

- **Regulatory approvals obtained ahead of plan**
- **Financing completed** at highly competitive interest rates against a challenging market backdrop
- **Strong shareholder support** with high approval rates for both Takeda (89.1%) & Shire (99.8%)
- **Listing of Takeda ADSs on the New York Stock Exchange** on December 24, 2018

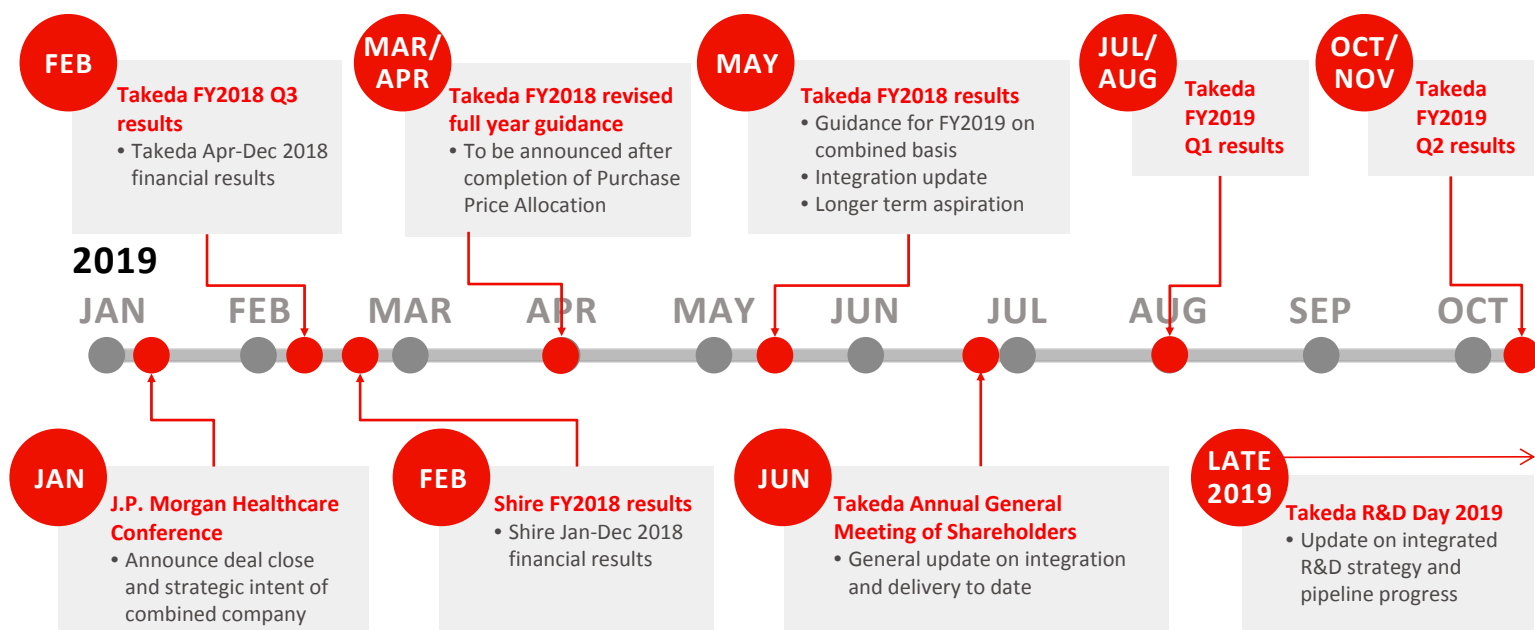


Integration planning well underway

- **A new operating model** to leverage Takeda and Shire know-how
- **Announcement of New Takeda Executive Team** and top 200 leaders
- **Excited to formally welcome our new colleagues** after months of close cooperation

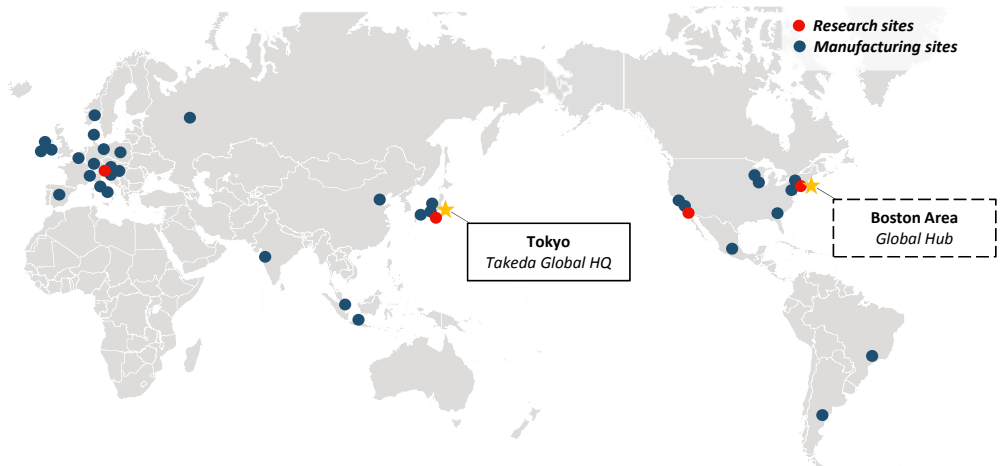
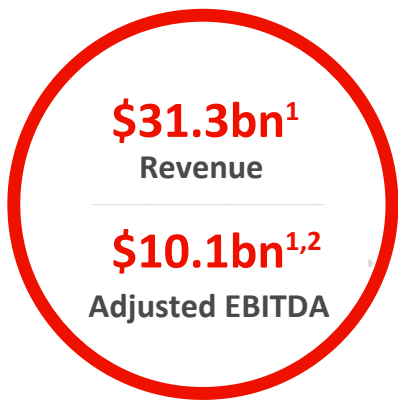
4

Timeline of key upcoming IR events for further business updates (excluding IR roadshows, etc.)



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A global, values-based, R&D-driven biopharmaceutical leader with an attractive geographic footprint and scale to drive future development



Approx. breakdown by region ³	Japan	US	Europe & Canada	Emerging Markets
Revenue	18%	49%	19%	14%
Employees	12%	33%	16%	39%

¹ LTM ended September 30, 2018 and an exchange rate of \$:¥ of 1:113.6 as at September 30, 2018; ² The sum of Takeda's Adjusted EBITDA and Shire's Non-GAAP EBITDA. Please see slides 25-28 for more details;
³ Percentages calculated using (a) the revenue by geography for the 12 month period ending on March 31, 2018 (in the case of Takeda) and (b) the approximate revenue by geography for the 12 month period ending on December 31, 2017 (in the case of Shire) and converted using the \$:¥ of 1:112.65 as of that date. Percentages for the combined group are calculated by aggregating the revenue by geography for Takeda and Shire.

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VALUES-BASED

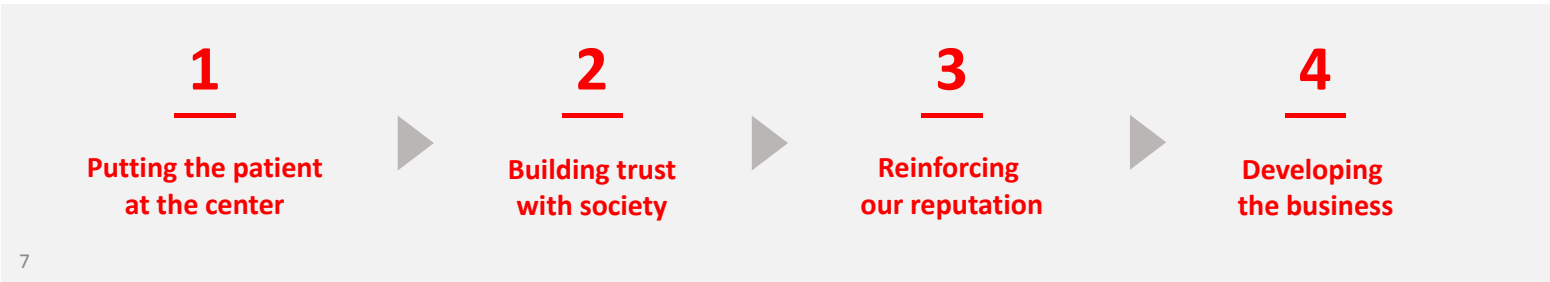
Our long history since 1781 has shaped the values that are fundamental to the success of Takeda in the long term



VALUES



We take action and make decisions by focusing on our four priorities, in order of:



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Takeda's long-term profitable growth will be driven by our R&D Engine, Business Area Focus, and Financial Strength



1 R&D Engine



2 Business Area Focus



3 Financial Strength

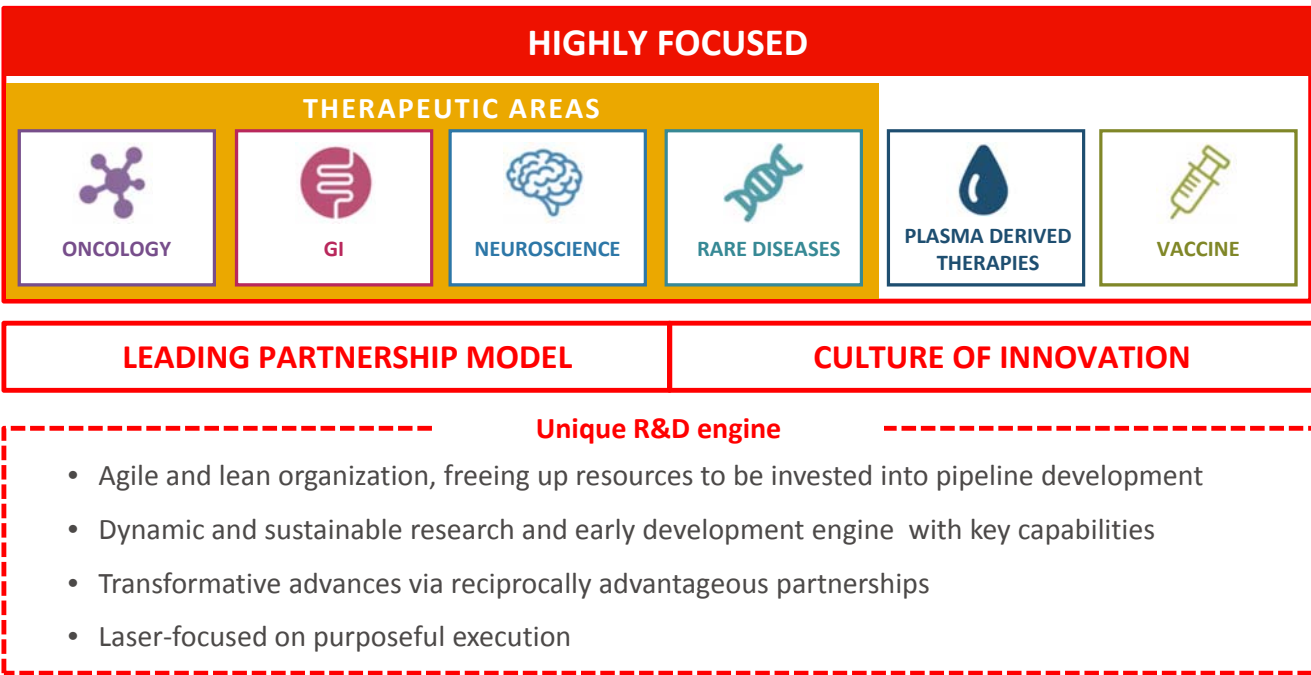


- A unique R&D engine based on **Therapeutic Area focus**, leading **partnership model**, and patient-centric, science-driven **culture of innovation**
 - Focus on **highly innovative medicines** to progress a pipeline that can deliver significant value in areas of **high unmet medical need**
- Focus on **5 key business areas** of oncology, GI, neuroscience, rare diseases and plasma derived therapies
 - Lean & focused organization** making the right investments to fuel future growth of our **robust and innovative product portfolio**, and able to respond with agility to changing market conditions
- Substantial cash flow generation** to invest in R&D, de-leverage rapidly, and maintain 180 yen dividend
 - Continued **focus on further boosting profitability** through delivering on synergies and improving OPEX discipline
 - Committed to **solid investment grade credit rating**

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R&D ENGINE

Takeda has a unique R&D engine driving innovation



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Highly focused pipeline concentrated on 4 therapeutic areas + Plasma Derived Therapies & Vaccines

~40% of pipeline is **partnered**

~50% of pipeline with Orphan Drug Designation

~50% non small molecule modalities

10 Note: Pipeline as of January 4, 2019 for Takeda and September 30, 2018 for Shire

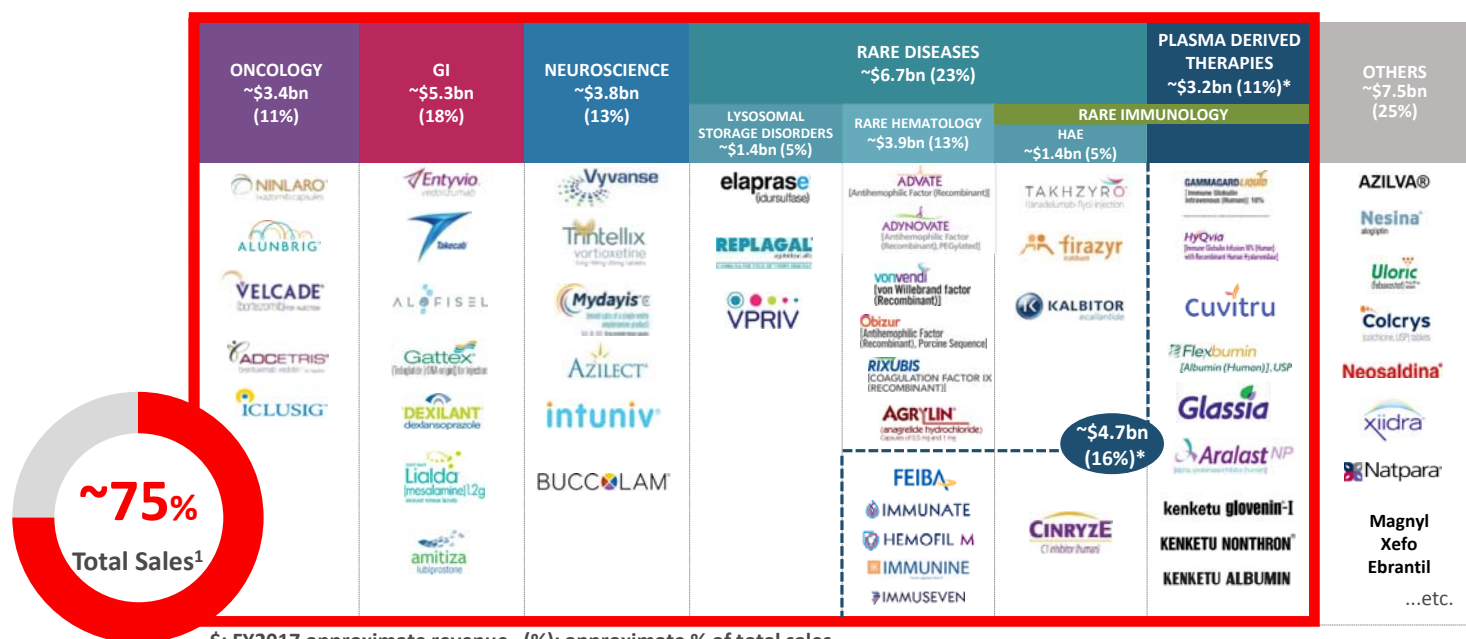
	PHASE 1	PHASE 2	PHASE 3/FILED	APPROVED*
ONCOLOGY	TAK-981 CD40 inhibitor Multiple cancers TAK-164 ImmuGen CSG-101 ADG GI cancer TAK-573 Tevd Anti-CD38-antennae A/R MM TAK-079 Anti-CD38 mAb A/R MM, SLE TAK-788 EGFR/HER2 inhibitor NSCC	TAK-228 (Sapanisertib) mTORC1/2 inhibitor Endometrial cancer TAK-931 COC7 inhibitor mCRC, ESCC, sqNSCLC TAK-659 SWI/SNF-1 inhibitor DLBCs, Solid Tumors	relugolix Mvotact PR/AR/ER inhibitor Prostate Cancer (JP) (Phase 1 in CN) TAK-924 (pionvestin) NAE inhibitor HR-MDS/CMML/LB AML	NINLARO[®] Zincfinger Nuclease FL MDS/CMML FL MDS/CMML ALUNBRIG[®] ALK inhibitor 2L ALK+ NSCLC 1L ALK+ NSCLC ACDETRIS[®] Scatterin Genetics CD34-ADG FL MDS/CMML, A/R MDS, ALL cabozantinib Exelixis VEGFR/RET inhibitor 2nd-line RCC, HCC (JP) Niraparib Tesaro PARP-1/2 inhibitor Multiple cancer (JP) ICLUSIG[®] BCL-2 inhibitor 2L Chronic Phase CML Phr ALL
GASTRO-ENTEROLOGY	TAK-671 Sansung Biopis Protease inhibitor Acute Pancreatitis TAK-018 Enterome Small Intestine Crohn's Disease Kumab062 PYP Biologics Glucozyme Celiac Disease TIMP-Gliadin Gour Imm ToI Induction Celiac Disease	TAK-906 DJ-006 antagonist Gastroparesis TAK-954 Thyroglobulin diuretic 5-HTAR agonist Enteral Feeding Intolerance	TAK-721 (SHP621) BOS Fof TAK-647 (SHP647) MAQCAM-1 mAb IBD	ENTYVIO[®] UCR-001 Intestine mAb SC, UC, CD Quality Improvement Vonoprazan Pfizer GERD PPI partial resp. ad ALOFISEL Intestine mAb Perianal Fistulas in CD
NEUROSCIENCE	TAK-653 AMPAK agonist TRO MEDI-1341 Alzeta Zentac Alpha-syn mAb Parkinson's Disease TAK-418 USJ1 inhibitor Kabuki Syndrome TAK-041 GPCR39 agonist CIAAS NS TAK-925 Orxent A agonist Narcolepsy TAK-580 Foundation Neurological Conditions WVE-120101 Wve mHTT SNP1 ASO Huntington's Disease WVE-120102 Wve mHTT SNP2 ASO Huntington's Disease	TAK-935 Ovid Therapeutics CD44 inhibitor Rare Pediatric Epilepsies TAK-831 DAAG inhibitor Ataxia, CIAAS NS		TRINTELIX[™] Lumefex Multimodal anti-depressant MDD (JP) BUCCOLAM Seizures (US, JP) VYVANSE ADHD (JP) MYDAYIS ADHD
RARE DISEASES	TAK-611 (SHP611) LEI MLO TAK-754 (SHP654) Gene therapy Hema TAK-531 (SHP631) ERT Hunter CNS	TAK-607 (SHP607) GF-1/AGR19 Chronic Lung Disease TAK-609 (SHP609) Hunter (IT) TAK-752 (SHP652) SE	TAK-755 (SHP655) ERT ADAMTS-13 CTP TAK-620 (SHP620) CMV infection in transplant patients	FIRAZYR HAE (JP) VONVENDI vWf TAKHZYRO Anti haemolysis mAb HAE prophylaxis (EU) OBIZUR CHAWI Surgery NATPARA Hypoparathyroidism (JP)
PLASMA-DERIVED THERAPIES				
VACCINES	TAK-021 EV71 Vaccine TAK-426 BIARDA Zika Vaccine	TAK-195 Gates Foundation Inactivated Polio Vaccine TAK-214 Norovirus Vaccine	TAK-003 Dengue Vaccine	
OPHTHALMOLOGY	TAK-639 (SHP639) Glaucoma	TAK-759 (SHP659) DED	TAK-640 (SHP640) Infectious conjunctivitis	XIIDRA DED (EU)

11 *With ongoing significant clinical development activities. Pipeline as of January 4, 2019 for Takeda and September 30, 2018 for Shire
As announced on October 27, 2018, Takeda has proposed a remedy to the European Commission of a potential divestment of SHP647 and certain associated rights

Orphan Drug Designation

BUSINESS AREA FOCUS

A distinctive focus on 5 key business areas representing ~75% of sales



\$: FY2017 approximate revenue (%): approximate % of total sales

* \$3.2bn (11%) excludes Plasma Derived Therapies in HAE and Rare Hematology (Cinryze, Feiba, Immunate, Hemofil M, Immune and Immuseven). \$4.7bn (16%) includes these products.

Source: Shire plc Annual Report 2017, Takeda Consolidated Financial statements for the Fiscal Year Ended March 31, 2018

Notes: Percentages calculated using (a) the amount for the 12 month period ending on March 31, 2018 and converted using the \$:¥ of 1:110 (in the case of Takeda) and (b) the amount for the 12 month period ending on March 31, 2018 (in the case of Shire).

¹ Management Data

BUSINESS AREA FOCUS

Robust and innovative portfolios in focus business areas to drive growth



ONCOLOGY



Aspiration to become global top 10 oncology player

- Growing leadership position in hematologic malignancies with NINLARO, ADCETRIS and ICLUSIG, and exciting pipeline in Multiple Myeloma, Acute Myeloid Leukemia & Myelodysplastic Syndromes
- Building presence in lung cancer with ALUNBRIG and pipeline assets
- Pursuing novel Immuno-Oncology targets and next-generation platforms with external partners as well as exploring innovative cell therapies

GI



A global leader in IBD & other GI diseases

- Maximizing the potential of our Inflammatory Bowel Disease franchise around flagship product ENTYVIO, including ALOFISEL in complex perianal fistulas
- Expanding position in specialty GI with GATTEX
- Progressing a pipeline built through partnerships exploring opportunities in motility disorders, celiac disease, liver disease, and the microbiome

NEUROSCIENCE



A leading force in alleviating patient need in neuroscience

- Expanding presence in psychiatric diseases such as Major Depressive Disorder and Attention Deficit Hyperactivity Disorder with VYVANSE, TRINTELLIX, and MYDAYIS
- Building pipeline in neurology and rare diseases through combination of in-house expertise and collaboration with world class partners

Robust and innovative portfolios in focus business areas to drive growth

RARE DISEASES



A global leader in rare diseases

- Area of **significant market growth** (~11% over next five years¹) with **high unmet medical need** and **focused patient groups**
- **R&D incentives** available such as Orphan Drug Designation, Breakthrough Therapy Designation, Fast Track Approvals, PRIME designation
- Takeda focused on **strong portfolio of multiple leading brands** across LSD, HAE, Primary/Secondary immunodeficiency diseases, and Hematology
- **Innovative pipeline** of 8 clinical-stage assets

1

Rare Immunology, e.g., Hereditary Angioedema (HAE)

- Potential for **TAKHZYRO** to **transform the treatment paradigm**; launched in the US in 2018, received European approval, and global regulatory progress on track

2

Rare Hematology

- **Deep expertise** and established leadership in Hematology
- **Broadest portfolio** across its competitors in Hematology and offers **differentiated personalised treatment** through ADYNOVATE or ADVATE plus myPKFit

3

Lysosomal Storage Disorders (LSD)

- **Market leading LSD franchise** supported by steady demand growth and high barriers to entry against biosimilar competition
- **Strong portfolio** focused on addressing Fabry Disease, Hunter Syndrome and Gaucher Disease

Source: Shire plc Corporate Presentation August 2018, Shire plc Investor Presentation November 2018

14 ¹ 2017-2022E, EvaluatePharma, Rare Diseases market includes all orphan drugs. Limited to drugs where the FDA Orphan designation is for primary indication; Excludes sales in Oncology and multiple sclerosis

Robust and innovative portfolios in focus business areas to drive growth

PLASMA DERIVED THERAPIES



Leading position in PDT

- **IG is highly attractive market segment** with ~8% growth expected over the medium term¹ and **strong & stable cash flow**
- Takeda is a leading player in a **large market with only three global competitors**
- Takeda has a **broad, differentiated portfolio** with **significant opportunity for global expansion**
- **Newly created global end-to-end business unit**

Covington Manufacturing Facility approved in 2018

- **World-class manufacturing facility** with \$1.5bn+ investment to increase capacity for Plasma Derived Therapies
- **Ramp up to full production expected in 2020**, with a focus on manufacturing **the IG portfolio** and **albumin**
- **Fully integrated end-to-end production site**
Plasma testing – Fractionation – Purification – Filling – Packaging
- **Manufacturing campus covering 1 million+ ft²** with the opportunity for further expansion over time to meet demand



Covington, Georgia

Source: Shire plc Investor Presentation November 2018, Shire plc Covington Day Presentation from November 7, 2018 and management information

15 ¹ Market share by value, 2016 WW MRB Report, 2017 US MRB Report

Profitability and cash flow will support R&D investment, deleveraging and cash returns to shareholders

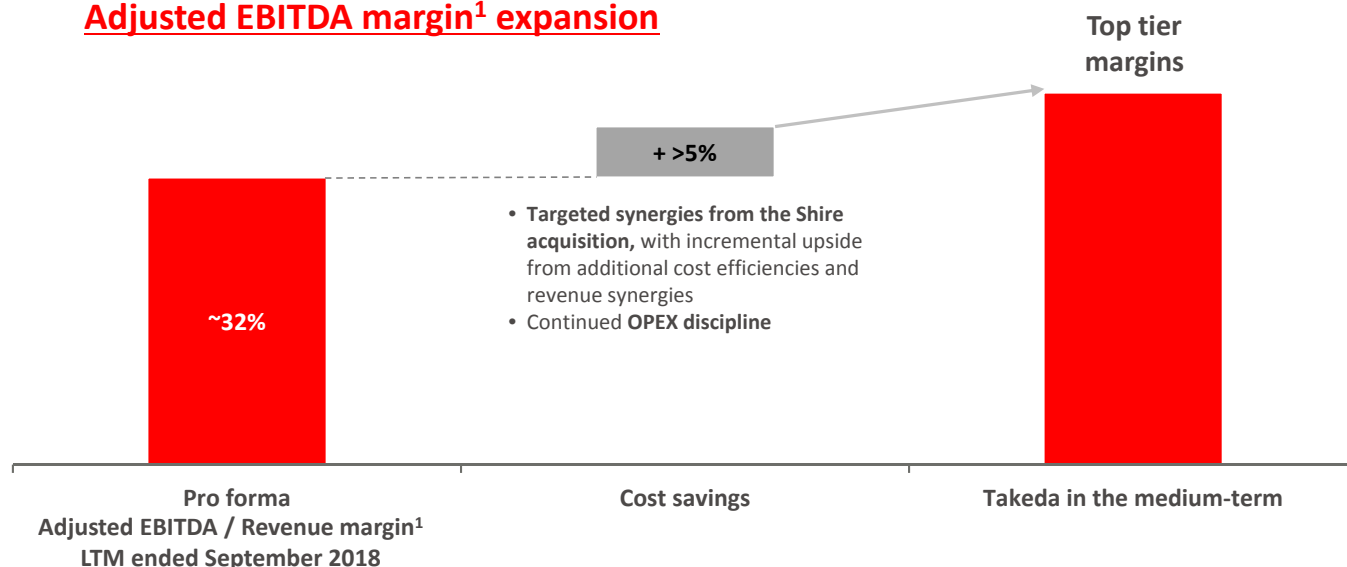
- Significantly EPS accretive on underlying basis¹ from the first full fiscal year, and reported basis from fiscal year 2021
- Recurring pre-tax cost synergies expected to reach a run-rate of at least \$1.4bn per annum by the end of fiscal year 2021
- Return on Invested Capital (ROIC) is expected to exceed Takeda's weighted average cost of capital (WACC) within the first full fiscal year
- Committed to solid investment grade credit rating
- Intend to maintain well-established dividend policy with 180 JPY dividend per share

¹ EPS on an underlying basis is the per-share amount of underlying core net profit. Please see slides 26 for more details.

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Takeda has a clear path to realize top tier margins in the medium-term

Adjusted EBITDA margin¹ expansion



Note: does not include potential divestitures

¹ Adjusted EBITDA margin represents the ratio of (1) the sum of Takeda's Adjusted EBITDA for the LTM ended September 30, 2018, of ¥405bn and Shire's Non-GAAP EBITDA for the LTM ended September 30, 2018, of \$6,552mm and (2) the sum of Takeda's revenue of ¥1,770bn for the LTM ended September 30, 2018, and Shire's revenue of \$15,702mm for the LTM, based on an exchange rate of \$:¥ of 1:113.6 as at September 30, 2018. Please see slides 25-28 for more details.

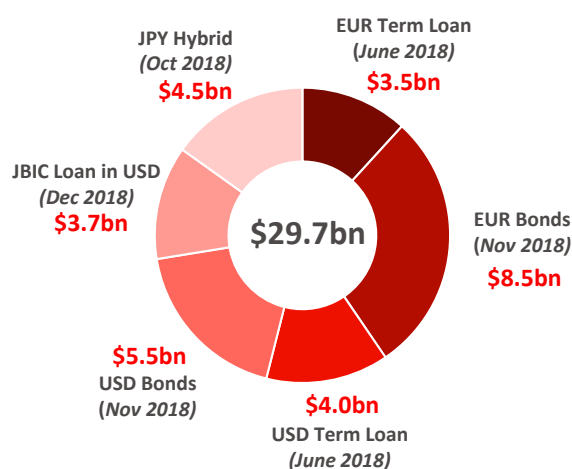
17

FINANCIAL STRENGTH

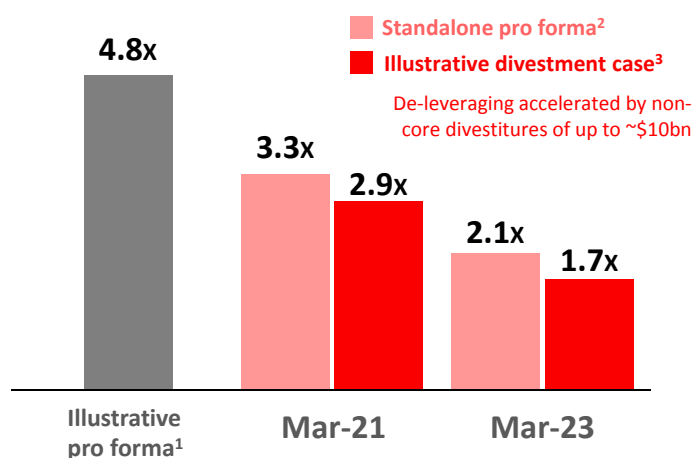
Committed to solid investment grade credit rating, with rapid deleveraging to 2.0x Net Debt/Adjusted EBITDA in the medium term, supported by divestitures



Acquisition financing split by type



Illustrative Net Debt⁵ / Adjusted EBITDA⁶ Ratio



Blended interest rate for new debt approx. 2.5%⁴

Blended interest rate for Takeda total debt of approx. 2.3%⁴

¹ Illustrative pro forma net debt / Adjusted EBITDA of 4.8x calculated using the illustrative pro forma net debt of ~\$48.0bn. Adjusted EBITDA is calculated by adding: i) Takeda's Adjusted EBITDA for the LTM ended September 30, 2018, of ¥405bn, based on an exchange rate of ¥:¥ of 1:113.6 as at September 30, 2018; and ii) Shire's Non-GAAP EBITDA for the LTM ended September 30, 2018, of \$6,552mm. Please see slides 25-28 for more details; ² Based on forecast net debt taking into account the expected cash balance, annual cash generation and forecast FY EBITDA; ³ Based on forecast net debt taking into account the expected cash balance, annual cash generation, an illustrative \$10bn of divestitures (post-tax) and forecast FY EBITDA (adjusted for divestitures); ⁴ Interest calculated based on weighted average interest rate on EUR, USD, JPY bonds and loans issued as at November 19, 2018; ⁵ Gross debt (incl. all Senior and Hybrid Bonds and Senior Term Loans) less cash and cash equivalents; ⁶ The sum of Takeda's Adjusted EBITDA and Shire's Non-GAAP EBITDA. Please see slides 25-28 for more details.

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INTEGRATION

A new operating model to leverage Takeda and Shire know-how



PRINCIPLES

Patient-centric

- Developing more innovative medicines through a leading R&D engine
- Getting closer to patients and meeting their unique needs in each market

Agile & Simple

- Continuing to be LOC-centric¹, empowering General Managers to make local decisions
- Minimizing complexity

Lean & Focused

- Focusing on five business areas
- Leveraging global scale while keeping the right balance of country resources
- Resilience to deal with demanding healthcare environments

4 Regional Business Units

3 Global Specialty Business Units



¹ Local Operating Company; ² Plasma Derived Therapies

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INTEGRATION



An experienced and diverse executive team with a strong track record



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GOVERNANCE



Board composition for best-in-class governance

INTERNAL DIRECTORS



Christophe Weber
Representative Director,
President & CEO



Masato Iwasaki
Director, President,
Japan Pharma Business Unit



Andrew Plump
Director, President,
Research & Development

CC

Compensation Committee

NC

Nomination Committee

Independent External Director

EXTERNAL DIRECTORS



Masahiro Sakane
Independent Director
Chair of the Board meeting
Chair of Nomination Committee



Michel Orsinger
Independent Director



Toshiyuki Shiga
Independent Director
Chair of Compensation Committee



Emiko Higashi
Independent Director



Yoshiaki Fujimori
Independent Director



Ian Clark
Independent Director



Olivier Bohuon
Independent Director



Steven Gillis
Independent Director

DIRECTORS ON THE AUDIT & SUPERVISORY COMMITTEE (A&SC)



Yasuhiko Yamanaka
Director,
A&SC member



Shiro Kuniya
Independent Director,
Chair A&SC



Koji Hatsukawa
Independent Director,
A&SC member



Jean-Luc Butel
Independent Director,
A&SC member

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In 2019: Flawless execution of the new business model



- 1** Sustain the impressive momentum of the underlying business
- 2** Continue to drive pipeline with minimal R&D disruption
- 3** Integration - one company, one team
- 4** Dispose non-core assets to accelerate deleveraging and simplify portfolio

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Appendix

Definition of Takeda's EBITDA / Adjusted EBITDA



We present EBITDA and Adjusted EBITDA because we believe that these measures are useful to investors as they are frequently used by securities analysts, investors and other interested parties in the evaluation of companies in our industry. We further believe that Adjusted EBITDA is helpful to investors in identifying trends in its business that could otherwise be obscured by certain items unrelated to ongoing operations because they are highly variable, difficult to predict, may substantially impact our results of operations and may limit the ability to evaluate our performance from one period to another on a consistent basis.

EBITDA and Adjusted EBITDA should not be considered in isolation or construed as alternatives to operating income, net profit for the year or any other measure of performance presented in accordance with IFRS. These non-IFRS measures may not be comparable to similarly-titled measures presented by other companies.

The usefulness of EBITDA and Adjusted EBITDA to investors has limitations including, but not limited to, (i) they may not be comparable to similarly titled measures used by other companies, including those in our industry, (ii) they exclude financial information and events, such as the effects of an acquisition or amortization of intangible assets, that some may consider important in evaluating our performance, value or prospects for the future, (iii) they exclude items or types of items that may continue to occur from period to period in the future and (iv) they may not exclude all items which investors may consider to be unrelated to our long-term operations, such as the results of businesses divested during a periods. These non-IFRS measures are not, and should not be viewed as, substitutes for IFRS reported net income (loss). We encourage investors to review our historical financial statements in their entirety and caution investors to use IFRS measures as the primary means of evaluating our performance, value and prospects for the future, and EBITDA and Adjusted EBITDA as supplemental measures.

EBITDA and Adjusted EBITDA

We define EBITDA as net profit before income tax expenses, depreciation and amortization and net interest expense. We define Adjusted EBITDA as EBITDA further adjusted to exclude impairment losses, other operating expenses and income (excluding depreciation and amortization), finance expenses and income (excluding net interest expense), our share of loss from investments accounted for under the equity method and other items that management believes are unrelated to our core operations such as purchase accounting effects and transaction related costs.

Use of Takeda's Adjusted EBITDA and Shire's Non-GAAP EBITDA in pro forma financials



Takeda's Adjusted EBITDA and Shire's Non-GAAP EBITDA are not directly comparable due to differences in definition and accounting standards. Adjusted EBITDA and Non-GAAP EBITDA adjust for items not core to Takeda and Shire's ongoing operations such as the effect of taxes, profit / loss attributable to equity method affiliates, impairment losses, certain restructuring and transaction costs, financing income and loss and certain other cash and non-cash items. The most closely comparable measure presented in accordance with IFRS (for Takeda) are net profit for the year and in accordance with U.S. GAAP (for Shire) is net income. Please see slides 27-28 for a further description of Takeda's Adjusted EBITDA and Shire's Non-GAAP EBITDA and a reconciliation to the respective most closely comparable measures presented in accordance with IFRS and U.S. GAAP.

Definition of EPS on an underlying basis

EPS on an underlying basis is the per-share amount of underlying core net profit, which is not a measure presented in accordance with IFRS. The closest comparable measure to underlying core net profit presented in accordance with IFRS is net profit. Takeda defines underlying core net profit as net profit adjusted for amortization and impairment of intangibles, other income and expenses (including integration costs relating to the Shire acquisition), costs and financial expenses related to the Shire acquisition, other exceptional gains and losses, the effect of foreign exchange fluctuations and divestitures. A reconciliation of EPS on an underlying basis for the first full fiscal year following the completion of the Shire acquisition has not been presented, as Takeda is unable to forecast without unreasonable efforts the amounts of its expected net profit or of the adjustments to net profit necessary to calculate underlying core net profit for such fiscal year.

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Reconciliation from net profit to EBITDA / Adjusted EBITDA of Takeda



(Bn JPY)	Full year ended Mar 31			6 months ended Sep 30	
	2016	2017	2018	2017	2018
Net profit for the year	83.5	115.5	186.7	172.7	126.5
Income tax expenses	37.1	27.8	30.5	60.3	126.5
Depreciation and amortization	182.2	171.4	182.1	93.4	78.0
Interest expense, net	3.0	5.5	6.8	3.3	3.4
EBITDA	305.8	320.2	406.1	329.7	242.2
Impairment losses	15.2	51.4	13.5	(9.2)	0.7
Other operating expense (income), net, excluding depreciation and amortization	17.0	(78.3)	(61.1)	(105.5)	(17.5)
Finance expense (income), net, excluding interest income and expense, net	7.3	5.4	(14.4)	(1.4)	11.8
Share of loss on investments accounted for under the equity method	0.0	1.5	32.2	(0.5)	(4.0)
Other adjustments:					
Loss on deconsolidation	6.3	—	—	—	—
Transaction costs related to the acquisition of ARIAD	—	3.2	—	—	—
Impact on profit related to fair value step up of inventory in ARIAD acquisition	—	—	1.4	0.8	—
Acquisition costs related to Shire	—	—	—	—	7.9
Adjusted EBITDA	351.6	303.4	377.7	213.8	241.0

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Reconciliation from U.S. GAAP Net income to Non GAAP EBITDA of Shire



This presentation contains the Non GAAP EBITDA of Shire, which is a financial measure not prepared in accordance with U.S. GAAP. Non GAAP measures exclude the effect of certain cash and non-cash items, which Shire's management believes are not related to the core performance of Shire's business. Shire's Remuneration Committee uses these Non GAAP measures when assessing the performance and compensation of employees, including Shire's Executive Directors. The most directly comparable measure under U.S. GAAP for Non GAAP EBITDA is U.S. GAAP Net income.

(USDmm)	Full year ended Dec 31			9 months ended Sep 30	
	2015	2016	2017	2017	2018
U.S. GAAP Net income	1,303.4	327.4	4,271.5	1,166.1	1,703.3
(Deduct) / add back:					
Loss / (gain) from discontinued operations net of tax	34.1	276.1	(18.0)	(18.6)	—
Equity in losses / (earnings) of equity method investees, net of taxes	2.2	8.7	(2.5)	(0.1)	(11.2)
Income taxes	46.1	(126.1)	(2,357.6)	44.6	371.0
Other expense/(income), net	33.7	476.8	561.8	412.9	417.2
U.S. GAAP Operating income from continuing operations	1,419.5	962.9	2,455.2	1,604.9	2,480.3
Revenue from upfront license fee	—	—	(74.6)	—	—
Expense related to the unwind of inventory fair value adjustments	31.1	1,118.0	747.8	688.7	40.9
Inventory write down related to the closure of a facility	—	18.9	—	—	—
One-time employee related costs	—	20.0	(4.0)	—	—
Impairment of acquired intangible assets	643.7	8.9	20.0	20.0	10.0
Costs relating to license arrangements	—	110.0	131.2	123.7	10.0
Legal and litigation costs	9.5	16.3	10.6	8.6	—
Amortization of acquired intangible assets	498.7	1,173.4	1,768.4	1,280.5	1,375.3
Integration and acquisition costs	39.8	883.9	894.5	696.7	512.0
Reorganization costs	97.9	121.4	47.9	24.5	268.9
Gain on sale of product rights	(14.7)	(16.5)	(0.4)	0.4	267.2
Depreciation	138.5	292.9	495.8	363.5	432.8
Costs related to AbbVie's terminated offer	60.1	—	—	—	—
Non GAAP EBITDA	2,924.1	4,710.1	6,492.4	4,806.7	4,866.3

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Glossary of Abbreviations



AD	Alzheimer's disease	EE H	erosive esophagitis healing	LCM	lifecycle management	RCC	renal cell cancer
ADC	antibody drug conjugate	EE M	erosive esophagitis maintenance	mAb	monoclonal antibody	RTK	receptor tyrosine kinase
ADHD	attention deficit hyperactivity disorder	EFI	enteral feeding intolerance	MAOB	monoamine oxidase B	sALCL	systemic anaplastic large cell lymphoma
ALK	anaplastic lymphoma kinase	EGFR	epidermal growth factor receptor	MLD	metachromatic leukodystrophy	SBS	short bowel syndrome
ALS	amyotrophic lateral sclerosis	EOE	eosinophilic esophagitis	NAE	NEDD8 activating enzyme	SC	subcutaneous formulation
AML	acute myeloid leukemia	ESCC	esophageal squamous-cell carcinoma	NASH	non-alcoholic steatohepatitis	SCt	stem cell transplant
AMR	antibody mediated rejection	FL	front line	ND	newly diagnosed	SCZ	schizophrenia
ASCT	autologous stem cell transplant	FLT-3	FMS-like tyrosine kinase 3	NDA	new drug application	SLE	systemic lupus erythematosus
ARD	acid-related diseases	FSI	first subject in	Neg	negative	sq	squamous
BTK	Bruton's tyrosine kinase	GCC	guanylyl cyclase C	NERD	non-erosive reflux disease	SR	steroid refractory
BBB	blood brain barrier	GERD	gastroesophageal reflux disease	NF	new formulation	SR-GvHD	steroid refractory acute graft vs host disease
BOS	budesonide oral suspension	GI	gastrointestinal	NK	natural killer	STING	stimulator of interferon genes
CAR-T	Chimeric antigen receptor-T	GnRH	gonadotropin-releasing hormone	NME	new molecular entity	SUMO	small ubiquitin-related modifier
CD	Crohn's disease	GU	gastric ulcer	NSCLC	non-small cell lung cancer	SYK	spleen tyrosine kinase
CHAWI	congenital hemophilia A with inhibitors	GvHD	graft versus host disease	NSCT	non stem cell transplant	TESD	treatment emergent sexual dysfunction
CIA5	cognitive impairment associated with schizophrenia	HAE	hereditary angioedema	NS	negative symptoms		
CIC	chronic idiopathic constipation	H2H	head to head	OIC	opioid induced constipation		
CIDP	chronic inflammatory demyelinating polyneuropathy	HCC	hepatocellular carcinoma	ORR	overall response rate		
CML	chronic myeloid leukemia	HemA	hemophilia A	PARP	poly (ADP-ribose) polymerase		
CMML	chronic myelomonocytic leukemia	HER2	human epidermal growth factor receptor 2	PBS	phosphate buffered saline		
CSF	cerebrospinal fluid	HL	Hodgkin's lymphoma	PCAB	potassium competitive acid blocker		
CNS	central nervous system	HR MDS	high-risk myelodysplastic syndromes	PFIC	progressive familial intrahepatic cholestasis		
CRL	complete response letter	IBD	inflammatory bowel disease	Ph+ ALL	Philadelphia chromosome-positive acute lymphoblastic leukemia		
CTCL	cutaneous T-cell lymphoma	IBS-C	irritable bowel syndrome with constipation	PID	primary immunodeficiency		
CTTP	congenital thrombotic thrombocytopenic purpura	IND	investigational new drug	PPI	proton pump inhibitor		
DAAO	D-amino acid oxidase	I/O	immuno-oncology	PK	pharmacokinetics		
DED	dry eye disease	IV	intravenous	POC	proof of concept		
DLBCL	diffuse large B-cell lymphoma	iPSC	induced pluripotent stem cells	POI	post-operative ileus		
DM	diabetes mellitus	LBD	Lewy body dementia	PTCL	peripheral T-cell lymphoma		
DU	duodenal ulcer	LB AML	low-blast acute myeloid leukemia	R/R	relapsed/refractory		
Dx	diagnosis	LSD1	Lysine specific demethylase 1	RA	rheumatoid arthritis		

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