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

January 8, 2019

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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.

Transaction Value & Multiples

- Equity Value: $57bn[1]
- Enterprise Value: $73bn[1,2]

4.6x	11.1x	15.1x
LTM Shire Revenue[3]	LTM Shire Non GAAP EBITDA[3]	LTM Shire Net Income[3]

Takeda + Shire

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

Acquisition price
6.2tn JPY

Pro Forma Financials

Revenue	$31.3bn[4]
Adjusted EBITDA	$10.1bn[4,5]

Financial Benefits

- At least $1.4bn of run-rate synergies
- Significantly accretive to underlying EPS[6]
- 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 ¥ 3,995 per Takeda Share and converted using the £:¥ exchange rate of 1:138.40 and £:$ of 1:1.276 on January 7, 2019 (at 16.30 GMT); [2] Net debt figure of $15,154mm used as of September 30, 2018; [3] LTM (Last Twelve Months) ended September30, 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.

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

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

FEB
Takeda FY2018 Q3 results
- Takeda Apr-Dec 2018 financial results

MAR/APR
Takeda FY2018 revised full year guidance
- To be announced after completion of Purchase Price Allocation

MAY
Takeda FY2018 results
- Guidance for FY2019 on combined basis
- Integration update
- Longer term aspiration

JUL/AUG
Takeda FY2019 Q1 results

OCT/NOV
Takeda FY2019 Q2 results

2019
JAN FEB MAR APR MAY JUN JUL AUG SEP OCT

JAN
J.P. Morgan Healthcare Conference
- Announce deal close and strategic intent of combined company

FEB
Shire FY2018 results
- Shire Jan-Dec 2018 financial results

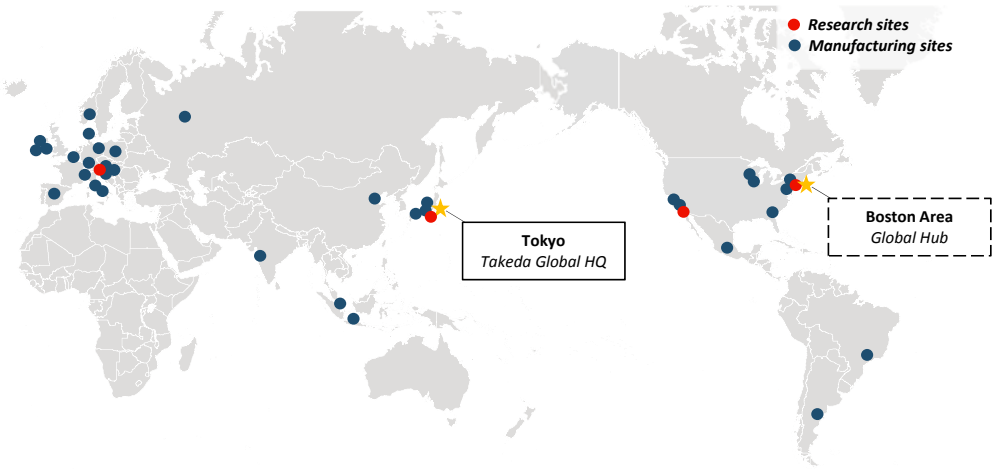
JUN
Takeda Annual General Meeting of Shareholders
- General update on integration and delivery to date

LATE 2019
Takeda R&D Day 2019
- Update on integrated R&D strategy and pipeline progress

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

$31.3bn[1]
Revenue

$10.1bn[1,2]
Adjusted EBITDA



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.

VALUES-BASED

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

VALUES

誠実 Integrity

公正 Fairness

正直 Honesty

不屈 Perseverance

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

1 Putting the patient at the center

2 Building trust with society

3 Reinforcing our reputation

4 Developing the business

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

1 R&D Engine

- 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**

2 Business Area Focus

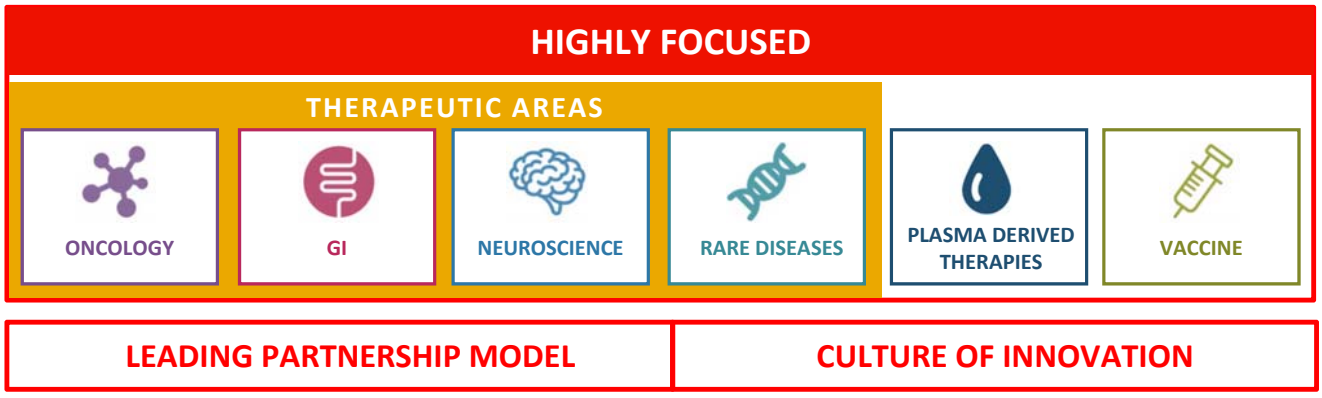
- Focus on **5 key business areas** of oncology, GI, neuroscience, rare diseases and plasma derived therapies
- **Lean & focused organization** making the right investments to fuel future growth of our **robust and innovative product portfolio**, and able to respond with agility to changing market conditions

3 Financial Strength

- **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**

R&D ENGINE

Takeda has a unique R&D engine driving innovation

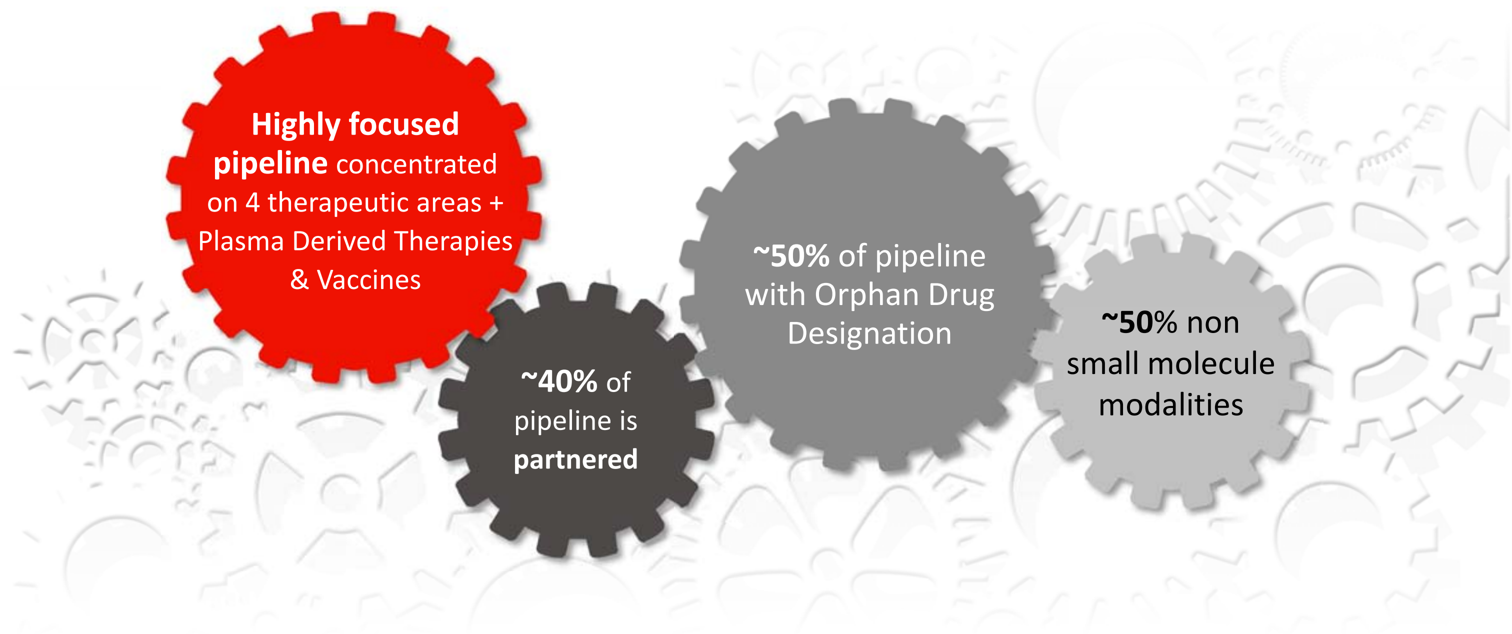


Unique R&D engine

- Agile and lean organization, freeing up resources to be invested into pipeline development
- Dynamic and sustainable research and early development engine with key capabilities
- Transformative advances via reciprocally advantageous partnerships
- Laser-focused on purposeful execution

R&D ENGINE

Our innovative pipeline has the potential to deliver significant value



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

R&D ENGINE

We have an innovative and maturing pipeline

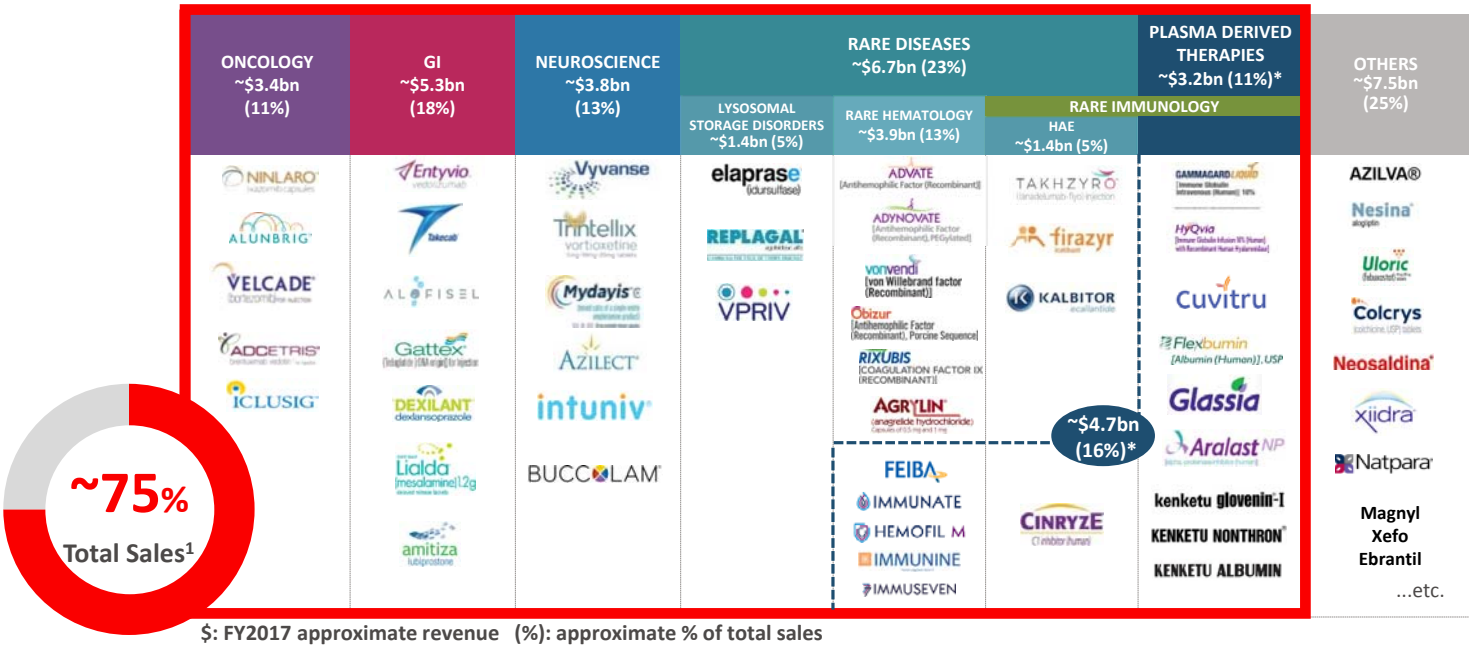
	PHASE 1	PHASE 2	PHASE 3/FILED	APPROVED*
ONCOLOGY	TAK-981 SUMO inhibitor Multiple cancers TAK-573 *Teva* Anti-CD38-attenukine R/R MM TAK-788 EGFR/HER2 inhibitor NSCLC TAK-164 *ImmunoGen* GCC IGN ADC GI cancer TAK-079 Anti-CD38 mAb R/R MM, SLE	TAK-228 (sapanisertib) mTORC 1/2 inhibitor Endometrial cancer TAK-659 (OD) SYK/FLT-3 inhibitor DLBCL, Solid Tumors TAK-931 CDC7 inhibitor mCRC, ESCC, sqNSCLC	relugolix *Myovant* GnRH antagonist Prostate Cancer (JP) (Phase 1 in CN) TAK-924 (OD) (pevonedistat) NAE inhibitor HR-MDS/CMML/LB AML	NINLARO® (OD) Proteasome inhibitor Amyloidosis, ND MM, R/R MM dara combo, R/R MM Ninlaro/dex, Maint. MM post-SCT Maint. MM non-SCT ADCETRIS® (OD) *Seattle Genetics* CD30 ADC FL HL, FL PTCL, R/R HL, sALCL ICLUSIG® (OD) BCR-ABL inhibitor 2L Chronic Phase CML, Ph+ ALL ALUNBRIG® (OD) ALK inhibitor 2L ALK+ NSCLC, 1L ALK+ NSCLC cabozantinib *Exelixis* VEGFR/RTK inhibitor 2nd line RCC, HCC (JP) Niraparib (OD) *Tesaro* PARP 1/2 inhibitor Multiple cancer (JP)
GASTRO-ENTEROLOGY	TAK-671 *Samsung Bioepis* Protease inhibitor Acute Pancreatitis Kuma062 *PvP Biologics* Glutenase Celiac Disease TIMP-Gliadin *Cour* Imm Tol Induction Celiac Disease TAK-018 *Enterome* FimH antagonist Crohn's Disease	TAK-906 D2/D3R antagonist Gastroparesis TAK-954 *Theravance Biopharma* 5-HT4R agonist Enteral Feeding Intolerance	TAK-721 (OD) (SHP621) BOS EoE TAK-647 (SHP647) MAdCAM-1 mAb IBD	ENTYVIO® (OD) α4β7 mAb UC/CD, adalimumab H2H, SC UC, SC CD, GvHD Prophylaxis Vonoprazan PCAB GERD PPI partial resp, ARD ALOFISEL (OD) mesenchymal stem cells Perianal Fistulas in CD GATTEX (OD) GLP-2 Adult-SBS, pediatric-SBS RESOLOR prucalopride CIC (US)
NEUROSCIENCE	TAK-653 AMPAR potentiator TRD TAK-418 (OD) LSD1 inhibitor Kabuki Syndrome TAK-041 GPR139 agonist CIAS NS MEDI-1341 *Astra Zeneca* Alpha-syn mAb Parkinson's Disease TAK-925 (OD) Orexin 2R agonist Narcolepsy TAK-680 (SHP680) Neurologic Conditions WVE-120101 (OD) *Wave* mHTT SNP1 ASO Huntington's Disease WVE-120102 (OD) *Wave* mHTT SNP2 ASO Huntington's Disease	TAK-935 (OD) *Ovid Therapeutics* CH24H inhibitor Rare Pediatric Epilepsies TAK-831 (OD) DAAO inhibitor Ataxia, CIAS NS		TRINTELLIX™ *Lundbeck* Multimodal anti-depressant MDD (JP) BUCCOLAM (OD) Seizures (US, JP) VYVANSE ADHD (JP) MYDAYIS ADHD
RARE DISEASES	TAK-611 (OD) (SHP611) ERT MLD TAK-531 (OD) (SHP631) ERT Hunter CNS TAK-754 (OD) (SHP654) Gene therapy HemA	TAK-607 (OD) (SHP607) IGF-1/ IGFBP3 Chronic Lung Disease TAK-609 (OD) (SHP609) Hunter (IT) TAK-752 (SHP652) SLE	TAK-755 (OD) (SHP655) ERT/ ADAMTS-13 cTTP TAK-620 (OD) (SHP620) CMV infection in transplant patients	FIRAZYR (OD) HAE (JP) VONVENDI (OD) vWD TAKHZYRO (OD) Anit-kallikrein mAb HAE prophylaxis (EU) OBIZUR (OD) CHAWI Surgery NATPARA (OD) Hypoparathyroidism (JP)
PLASMA-DERIVED THERAPIES				HYQVIA (OD) Pediatric PID, CIDP CINRYZE (OD) SC HAE prophylaxis, HAE prophylaxis (JP), pediatric HAE (US), AMR
VACCINES	TAK-021 EV71 Vaccine TAK-426 *BARDA* 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)

OD Orphan Drug Designation

*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

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, Immunine 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

BUSINESS AREA FOCUS

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 years[1]) 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

[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

BUSINESS AREA FOCUS

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 term[1] 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

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

FINANCIAL STRENGTH

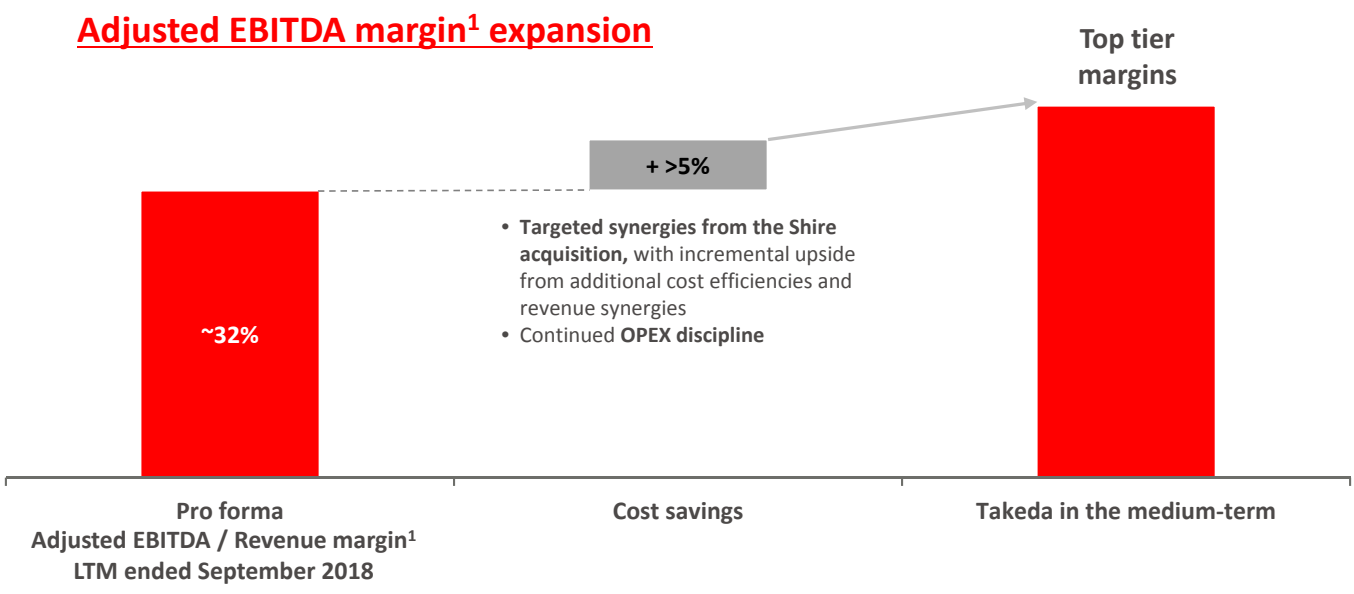
Profitability and cash flow will support R&D investment, deleveraging and cash returns to shareholders

- Significantly EPS accretive on underlying basis[1] 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.

FINANCIAL STRENGTH

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



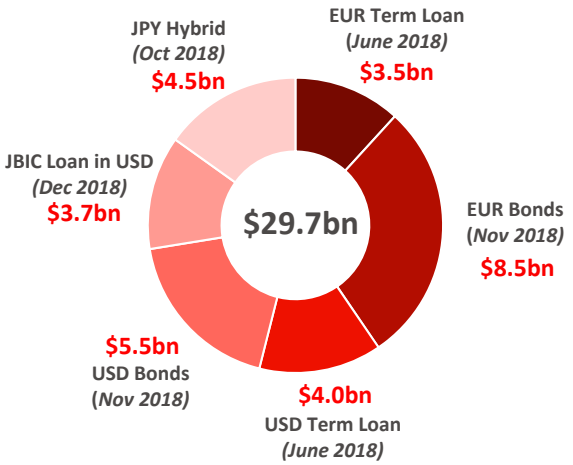
Note: does not include potential divestitures

[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.

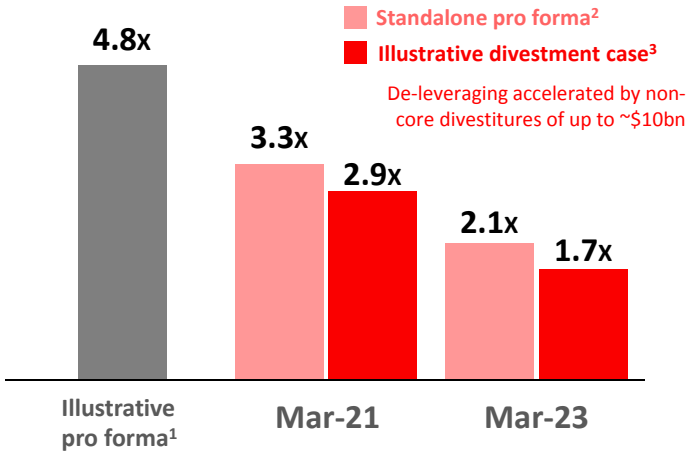
FINANCIAL STRENGTH

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 Debt[5] / Adjusted EBITDA[6] 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.

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-centric[1], 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

- PDT[2] BU
- Oncology BU
- Vaccine BU

[1] Local Operating Company; [2] Plasma Derived Therapies

INTEGRATION

An experienced and diverse executive team with a strong track record

CHRISTOPHE WEBER
President & CEO

COSTA SAROUKOS
Chief Financial Officer

HARUHIKO HIRATE
Corporate Communications & Public Affairs Officer

YOSHIHIRO NAKAGAWA
Global General Counsel

PADMA THIRUVENGADAM
Chief Human Resources Officer

MILANO FURUTA
Corporate Strategy Officer & Chief of Staff

MWANA LUGOGO
Chief Ethics & Compliance Officer

RAMONA SEQUEIRA
President, US Business Unit

MASATO IWASAKI
President, Japan Pharma Business Unit

GILES PLATFORD
President, Europe & Canada Business Unit

RICARDO MAREK
President, Growth & Emerging Markets Business Unit

CHRISTOPHE BIANCHI
President, Global Oncology Business Unit

RAJEEV VENKAYYA
President, Global Vaccine Business Unit

JULIE KIM
President, Plasma-Derived Therapies Business Unit

ANDY PLUMP
President, Research & Development

THOMAS WOZNIEWSKI
Global Manufacturing & Supply Officer

GERARD (JERRY) GRECO
Global Quality Officer

CAMILLA SOENDERBY
Chief Patient Value & Product Strategy Officer

MARCELLO AGOSTI
Global Business Development Officer

HELEN GIZA
Chief Integration & Divestiture Management Officer

GOVERNANCE

Board composition for best-in-class governance

INTERNAL DIRECTORS

Christophe Weber (NC)
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 (NC)
Independent Director
Chair of the Board meeting
Chair of Nomination Committee

Michel Orsinger
Independent Director

Toshiyuki Shiga (CC)
Independent Director
Chair of Compensation Committee

Emiko Higashi (NC)
Independent Director

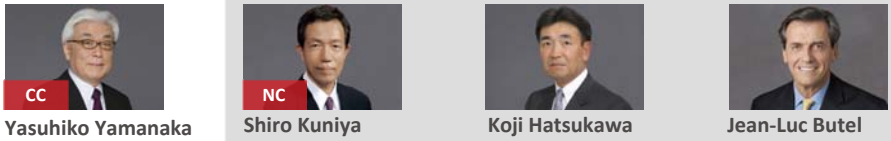
Yoshiaki Fujimori (CC)
Independent Director

Ian Clark
Independent Director

Olivier Bohuon
Independent Director

Steven Gillis
Independent Director

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



Yasuhiko Yamanaka (CC)
Director, A&SC member

Shiro Kuniya (NC)
Independent Director, Chair A&SC

Koji Hatsukawa
Independent Director, A&SC member

Jean-Luc Butel
Independent Director, A&SC member

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

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

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.

Reconciliation from net profit to EBITDA / Adjusted EBITDA of Takeda

	Full year ended Mar 31			6 months ended Sep 30	
(Bn JPY)	**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**

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.

	Full year ended Dec 31			9 months ended Sep 30	
(USDmm)	**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

Glossary of Abbreviations

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