

Creating a Values based, R&D driven Global Biopharmaceutical Leader

December 5, 2018

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President & CEO
Takeda Pharmaceutical Company Limited

Better Health, Brighter Future

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Profit Forecast for Takeda for the year ending March 31, 2019

Takeda is currently in an offer period (as defined in the City Code on Takeovers and Mergers (the "Code")) with respect to Shire plc. Pursuant to Rule 28 of the Code, statements made regarding Takeda's guidance for FY2018 (including statements regarding forecasts for FY2018 revenue, Core Earnings, Operating profit, Profit before income taxes, Net profit attributable to owners of Takeda, Basic earnings per share, R&D expenses, Amortisation and impairment and other income/expense, Underlying Revenue, Underlying Core Earnings and Underlying Core EPS) constitute a profit forecast for the year ending March 31, 2019 (the "Takeda Profit Forecast").

For additional information regarding the Takeda Profit Forecast and the required statement by its Directors that such profit forecast is valid and has been properly compiled on the basis of the assumptions stated and that the basis of accounting used is consistent with Takeda's accounting policies, please see page 9 of Takeda's Summary of Financial Statements (Tanshin) for the Six Months Period Ended September 30, 2018.

VISION 2025

Our mission is to strive towards Better Health and a Brighter Future for people worldwide through leading innovation in medicine

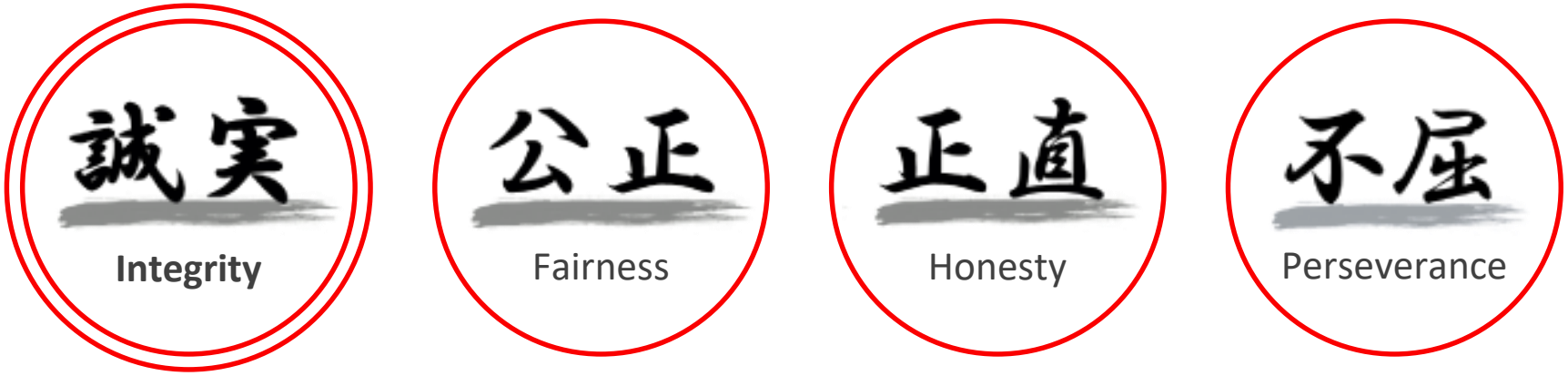
We serve the needs of our patients, wherever they are.

We earn the trust of society and customers through Takeda-ism.

We are recognized as best in class because of agility and innovation, qualities that help us build a steady pipeline and deliver growth, year on year.

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:

1 Putting the patient at the center

2 Building trust with society

3 Reinforcing our reputation

4 Developing the business

Takeda has created a unique R&D engine

THERAPEUTIC AREA FOCUS

Oncology, Gastroenterology, Neuroscience plus Vaccines

PARTNERSHIPS & CAPABILITIES	TRANSFORM OUR CULTURE

R&D TRANSFORMATION KEY IMPERATIVES

- Agile and lean
- Dynamic and sustainable research and early development engine
- Transformative advances via reciprocally advantageous partnerships
- Laser-focused on purposeful execution

With a very focused and lean footprint freeing up resources for pipeline development

BOSTON, MA

R&D Center
Oncology, GI Research

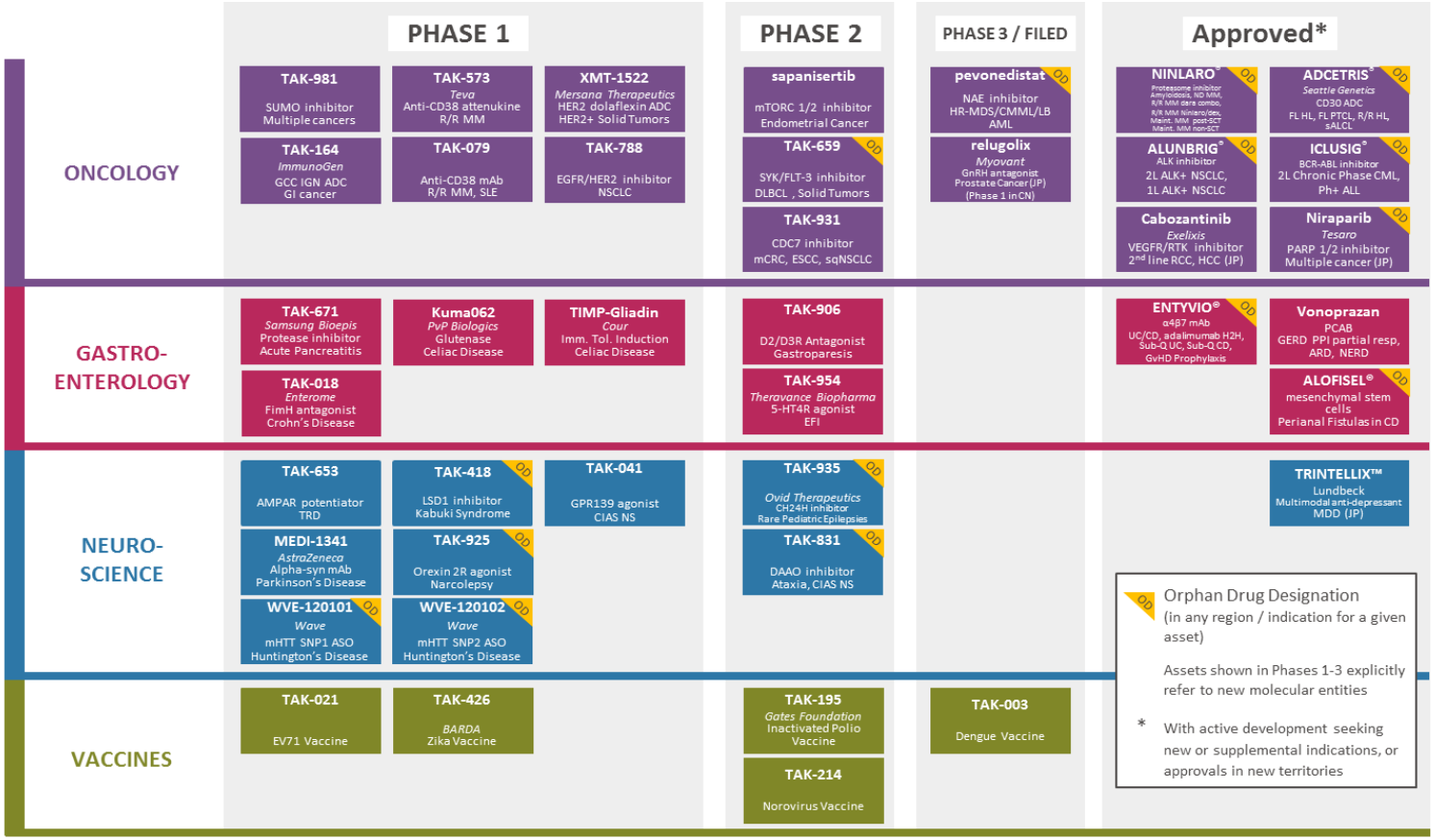
SHONAN, JAPAN

Neuroscience Research,
T-CiRA, iPark

SAN DIEGO, CA

Specialized drug discovery technologies, GI and Neuroscience

Resulting in a dynamic and re-invigorated pipeline



31 pipeline assets progressed since the start of FY2016

46% of pipeline is partnered

83% of pipeline with global development plans/rights

37% of pipeline has orphan drug designation

Pipeline as of October 31, 2018. Please refer to glossary for disease abbreviations

Shire acquisition will enhance Takeda R&D engine with an initial R&D budget greater than 400 Bn yen

Note: The greater than 400 billion JPY initial R&D budget is a reference to the combined historic R&D spend for the period ending March 31, 2017 for Takeda and December 31, 2017 for Shire, less the expected R&D cost synergies

With the potential to deliver more value in the future

Takeda | Shire | OD Orphan Drug Designation

	PHASE 1	PHASE 2	PHASE 3/FILED	APPROVED*
ONCOLOGY	**TAK-573** Teva Anti-CD38-attenukine **Refractory MM** **XMT-1522** Mersana Therapeutics HER2 dolaflexin ADC **HER2 + solid tumors** **TAK-079** Anti-CD38 mAb Refractory MM **TAK-788** EGFR/HER2 inh **NSCLC**	**sapanisertib** mTORC 1/2 inhibitor Breast cancer **TAK-659** OD SYK inhibitor DLBCL **TAK-931** CDC7 inhibitor Solid Tumors	**relugolix** Myovant GNRH antagonist Prostate Cancer (JP) **pevonedistat** OD NAE inhibitor HR MDS	**NINLARO®** OD Proteasome inhibitor MM R/R (EM), R/R Amyloidosis, Front Line MM, R/R Myeloma doublet regimen, Maintenance MM post-SCT Maintenance MM w/o SCT **ADCETRIS®** OD Seattle Genetics CD30 ADC FL HL, FL MTCL, CTCL **ICLUSIG®** OD BCR-ABL inhibitor Imatinib resistant Chronic Phase CML Second-Line Chronic Phase CML, Ph+ ALL **ALUNBRIG®** (brigatinib) OD ALK inhibitor ALK+NSCLC (EU), FL ALK+ NSCLC **cabozantinib** Exelixis VEGFR/RTK inhibitor Solid tumors (JP) **Niraparib** OD Tesaro PARP 1/2 inhibitor Multiple cancer (JP)
GI	**TIMP-Gliadin** Cour Imm Tol Indcution Celiac Disease	**TAK-906** D2/D3R Antagonist Gastroparesis **TAK-954** Theravance Biopharma 5-HT4R ag Enteral Feeding Intolerance **SHP625** OD ASBTi PFIC, Alagille's **SHP626** ASBTi NASH	**SHP621** OD BOS EoE **SHP647** MAdCAM-1 mAb IBD	**ENTYVIO®** OD α4β7 mAb UC/CD (EM), UC (JP), CD (JP), adalimumab H2H Sub-Q UC, Sub-Q CD, GvHD Prophylaxis, GvHD SR, IO Colitis **Vonoprazan** PCAB ARD (Asia) , NERD (JP) PPI Partial Responder **AMITIZA®** Sucampo Chloride channel activator Pediatric constipation , New formulation **ALOFISEL** OD Tigenix mesenchymal stem cells Perianal Fistulas in CD **GATTEX** GLP-2 SBS **RESOLOR** prucalopride CIC
NEURO-SCIENCE	**TAK-653** AMPAR potentiator TRD **TAK-418** OD LSD1 inhibitor Kabuki Syndrome **MEDI-1341** Astra Zeneca Alpha-syn mAb Parknoson's Disease **TAK-925** OD Orexin 2R agonist Narcolepsy **SHP680** Neurologic Conditions **TAK-041** GPR139 agonist CIAS neg. symptoms	**TAK-935** OD Ovid Therapeutics CH24H inhibitor Rare Pediatric Epilepsies **TAK-831** OD DAAO inhibitor SCZ, Ataxia		**TRINTELLIX™** Lundbeck Multimodal anti-depressant Cognition data in label (CRL received) MDD (JP) **BUCCOLAM** seizures **VYVANSE** ADHD **MYDAYIS** ADHD
RARE DISEASES	**SHP611** OD ERT MLD **SHP631** OD ERT Hunter CNS **SHP654** OD Gene therapy HemA	**SHP607** OD IGF-1/ IGFBP3 Chronic Lung Disease	**Lanadelumab** OD Anit-kallikrein mAb HAE **SHP620** CMV infection in transplant patients **SHP609** OD Hunter (IT) **SHP655** OD ERT/ ADAMTS-13 cTTP	**FIRAZYR** OD HAE **VONVENDI** OD vWD **CINRYZE** OD HAE, AMR **OBIZUR** OD CHAWI Surgery
PLASMA-DERIVED THERAPIES				**HYQVIA** OD Pediatric PID, CIDP
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	
OPHTHAL-MOLOGY	**SHP639** Glaucoma	**SHP659** DED	**SHP640** Infectious conjunctivitis	**XIIDRA** DED

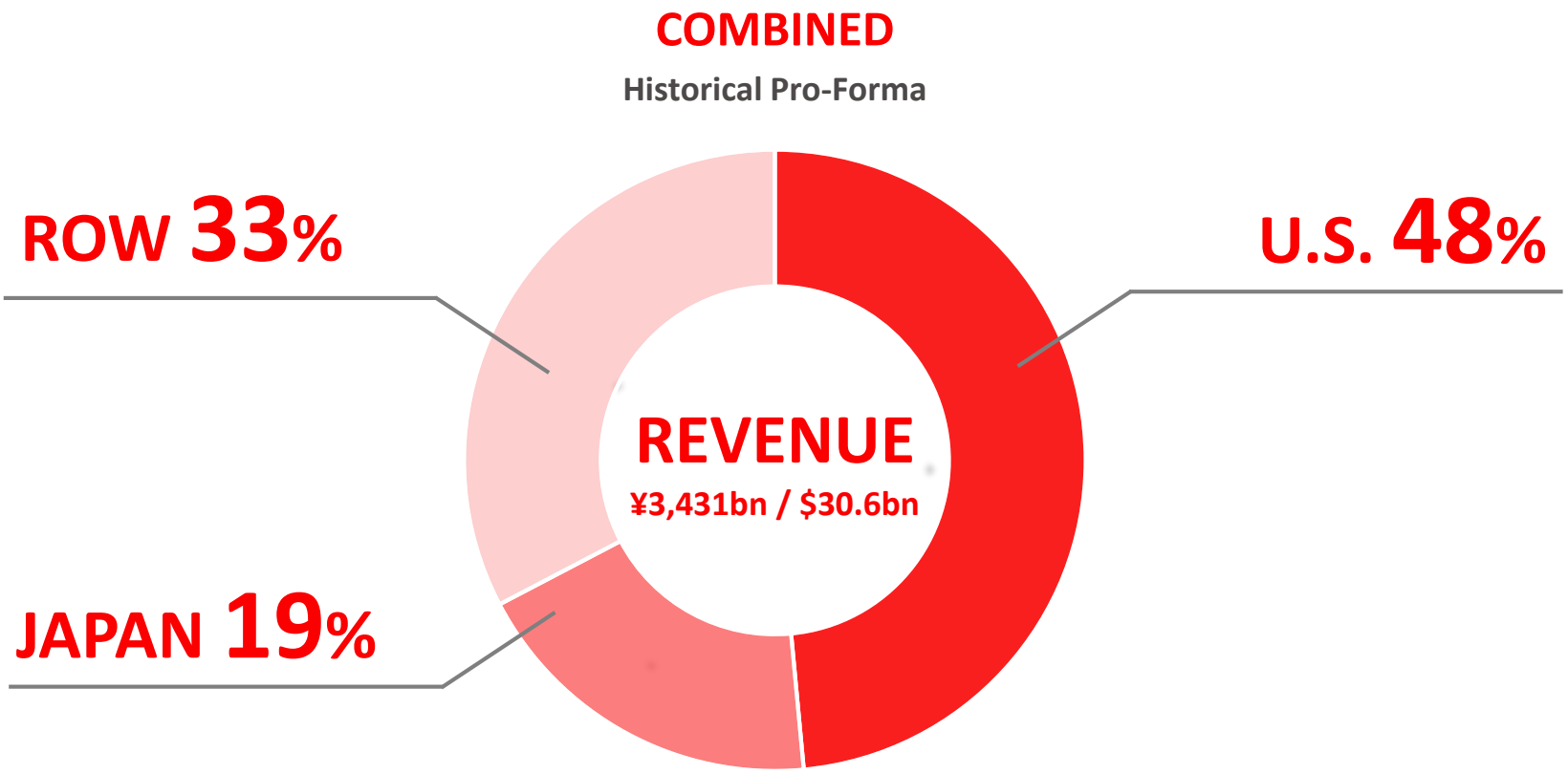
Note: SHP652 and Natpara classified as "other" and not shown here *With ongoing clinical development activities. Pipeline as of February 1, 2018
As announced on 27 October 2018, Takeda has proposed a remedy to the European Commission of a potential divestment of SHP647 and certain associated rights

Accelerates Takeda transformation with a more distinctive focus on key therapy areas

ONCOLOGY	GI	NEUROSCIENCE	RARE DISEASES: LYSOSOMAL STORAGE DISORDERS	RARE DISEASES: HAE[2]	RARE DISEASES: HEMATOLOGY	PLASMA DERIVED THERAPIES	OTHERS (example of key products)	
NINLARO ixazomib capsules ADCETRIS brentuximab vedotin ALUNBRIG ICLUSIG VELCADE (bortezomib)	Entyvio vedolizumab Takecab amitiza lubiprostone DEXILANT dexlansoprazole ALOFISEL	Trintellix vortioxetine 5mg·10mg·20mg tablets AZILECT				kenketu glovenin-I KENKETU NONTHRON® KENKETU ALBUMIN	Nesina alogliptin Uloric (febuxostat) Colcrys (colchicine, USP) tablets AZILVA® Neosaldina® Magnyl Ebrantil Xefo ...etc.	TAKEDA KEY PRODUCTS
	Gattex (teduglutide [rDNA origin]) for injection 500-mg capsules PENTASA (mesalamine) controlled-release capsules Lialda (mesalamine) 1.2g delayed release tablets	Vyvanse intuniv Mydayis BUCCOLAM	elaprase (idursulfase) VPRIV REPLAGAL	CINRYZE (C1 inhibitor [human]) firazyr (icatibant) KALBITOR (ecallantide)	ADVATE [Antihemophilic Factor (Recombinant)] FEIBA ADYNOVATE [Antihemophilic Factor (Recombinant), PEGylated] vonvendi [von Willebrand factor (Recombinant)] RIXUBIS [COAGULATION FACTOR IX (RECOMBINANT)] AGRYLIN (anagrelide hydrochloride) Obizur [Antihemophilic Factor (Recombinant), Porcine Sequence]	Cuvitru GAMMAGARD LIQUID [Immune Globulin Intravenous (Human)] 10% HyQvia [Immune Globulin Infusion 16% (Human) with Recombinant Human Hyaluronidase] Flexbumin [Albumin (Human)], USP Glassia Aralast NP (alpha1-proteinase inhibitor [human])	xiidra Natpara ...etc.	SHIRE KEY PRODUCTS

Source: Shire plc Annual Report 2017, Takeda Consolidated Financial statements for the Fiscal Year Ended March 31, 2017
Notes: Percentage calculated using (a) the amount for the 12 month period ending on March 31, 2017 and converted using the $/¥ of 111.43 as at that date (in the case of Takeda) and (b) the amount for the 12 month period ending on December 31 2017 and converted using the $/¥ of 112.65 as at that date (in the case of Shire). 1Management Data. 2Hereditary Angioedema

Create an attractive geographic footprint with leading positions in Japan and the U.S.



Source: Shire plc Annual Report 2017 and management information, Takeda Consolidated Financial statements for the Fiscal Year Ended March 31, 2017, Takeda Consolidated Financial statements for the Nine Month Period Ended December 31, 2017

Notes: Percentages calculated using (1) the revenue by geography for the 12 month period ending on December 31, 2017 (the final quarter of FY2016 and the first three quarters of F2017) and converted using the $:¥ of 1:112.65 as at that date (in the case of Takeda) and (2) the revenue by geography for the 12 month period ending on December 31, 2017 (in the case of Shire). Percentages for the combined group are calculated by aggregating the revenue by geography for Takeda and Shire. The historical revenue of the combined group represent the aggregate consolidated revenue of (a) the amount for the 12 month period ending on March 31, 2017 and converted using the $/¥ of 1:112.65 as at that date (in the case of Takeda) and (b) the amount for the 12 month period ending on 31 December 2017 and converted using the $/¥ of 1:112.65 as at that date (in the case of Shire). These results are historic and do not take into account any divestures or other events that may have occurred since these dates. The aggregate revenue figure comprises the aggregate of Takeda's reported revenue and Shire's Non GAAP revenue.

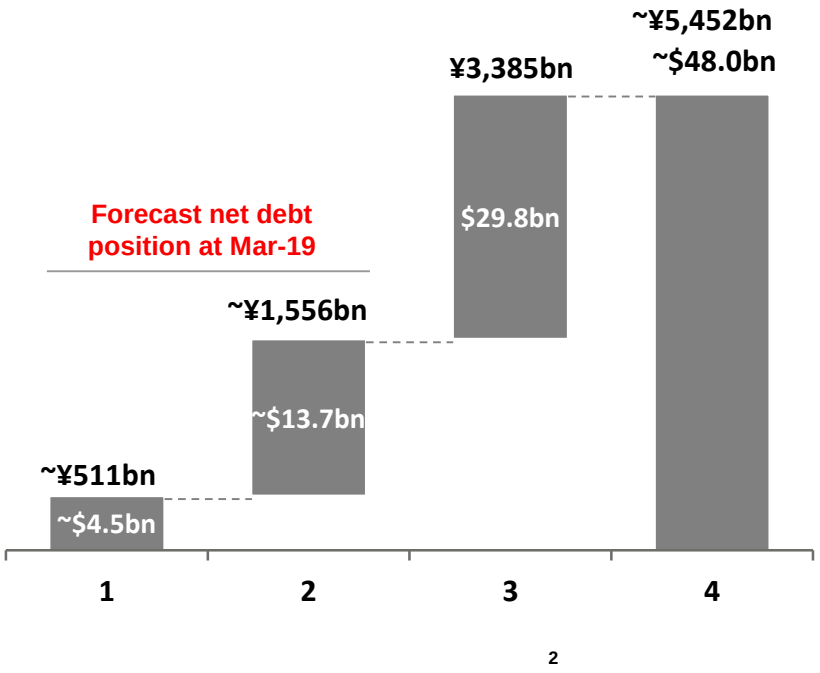
Transaction will be significantly EPS accretive and generate strong cash flow

- The recurring pre-tax cost synergies for the combined group are expected to reach a run-rate of at least ¥153bn / $1.4bn per annum by the end of the third fiscal year following completion[1]
- The number of issued Takeda shares will essentially double but EBITDA[2] is approximately three times larger on a historical combined basis[3].
  The acquisition will be significantly EPS accretive[4] on an underlying basis from the first full fiscal year following completion and on a reported basis within 3 fiscal years post completion.
- Low risk of impairments to combined goodwill (¥4,000 bn to ¥4,400 bn) and intangible assets (¥6,300 bn to ¥6,700 bn)
- The transaction's Return on Invested Capital (ROIC) is expected to exceed Takeda's weighted average cost of capital (WACC) within the first full fiscal year following completion
- Intend to maintain our well-established dividend policy with 180 JPY dividend per share
- Committed to maintaining investment grade credit rating

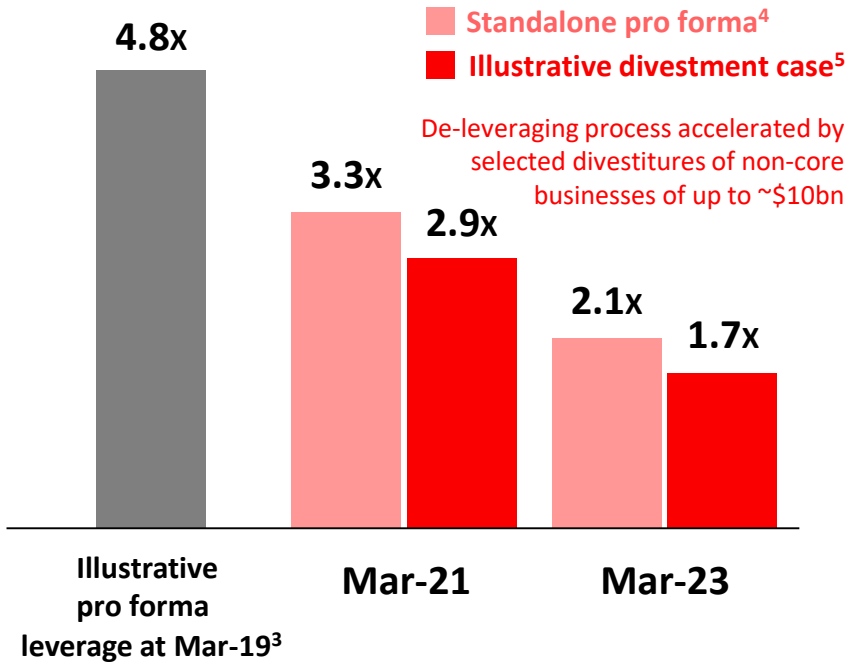
Notes: [1] The Takeda Directors expect recurring pre-tax cost synergies for the Combined Group to reach a run - rate of at least $1.4 billion per annum by the end of the third fiscal year following completion of the Acquisition ($/¥ of 1:108.97 as at May 8, 2018]. Reported under Rule 28.1 of the Takeover Code; related reports can be found in the Rule 2.7 Announcement made by Takeda on May 8, 2018, as well as information regarding the method of calculation of the synergies and the costs to achieve such synergies. [2] Earnings Before Interest Taxes Depreciation and Amortization [3]The historical pro-forma EBITDA figure comprises Takeda's EBITDA (Operating Profit adjusted for other operating income and expenses, intangible amortization & impairment, software amortization, PP&E depreciation & impairment and other non-recurring items) for the Fiscal Year Ended March 31, 2018 based on the exchange rates of $:¥ of 1:108.97 as at May 4, 2018 and Shire's EBITDA for the 12 month period ending on Mar 31, 2018 (the final three quarters of FY2017 and the first quarter of FY2018). [4] The statement that the Acquisition is underlying earnings accretive is not intended as a profit forecast and should not be construed as such, and is therefore not subject to the requirements of Rule 28 of the Takeover Code. The statement should not be interpreted to mean that the earnings per share in any future fiscal period will necessarily match or be greater than those for the relevant preceding financial period.

Committed to investment grade with a target net debt to EBITDA ratio of 2.0x or less in the medium term

Net Debt Build Up (bn[1])



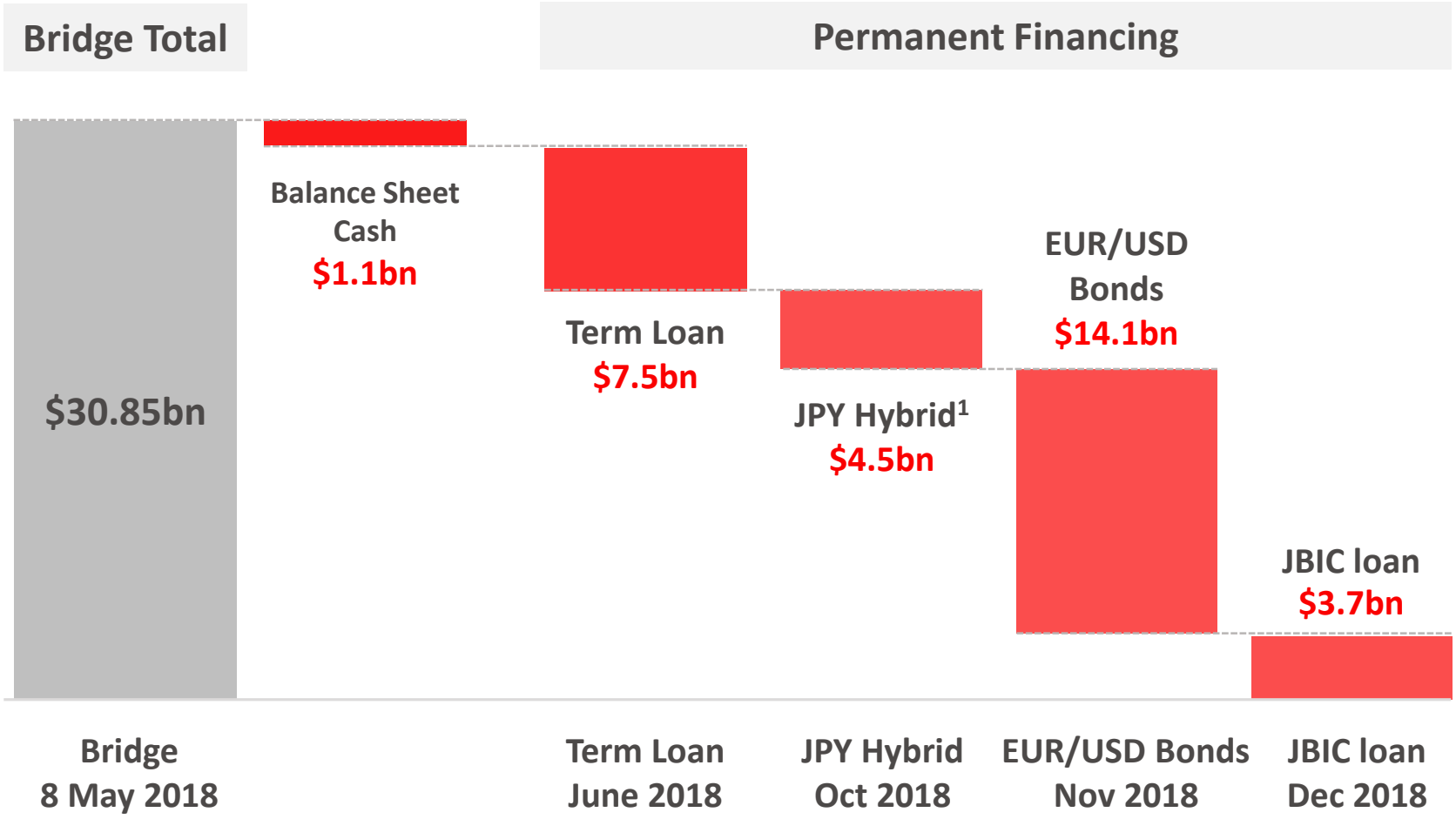
Illustrative Net Debt / EBITDA Ratio



Takeda has a strong track record in deleveraging and portfolio optimisation

Notes: [1] Net debt converted based on the exchange rate of $:¥ of 1:113.6 as at Sep 30, 2018, [2] New debt expected to be raised in order to finance the acquisition of Shire, [3] Illustrative pro forma net debt / EBITDA of 4.8x calculated using the illustrative pro forma net debt of ~$48.0bn. The EBITDA is calculated by adding : i) Takeda's EBITDA (Operating Profit adjusted for other operating income and expenses, intangible amortisation & impairment, software amortisation, PP&E depreciation & impairment and other non-recurring items) of $3,552mm as per Consolidated Financial statements for the Fiscal Year Ended March 31, 2018 released on May 14, 2018 and based on the exchange rates of $:¥ of 1:106.35 as at March 31, 2018; and ii) Shire's EBITDA of $6,523mm for the 12 month period ending on March 31, 2018 (the final three quarters of FY2017 as disclosed in Shire's year end results released on Feb 14, 2018 and the first quarter of FY2018 as disclosed in Shire's Q1 results released on Apr 26, 2018), [4] Based on forecast net debt taking into account the expected cash balance, annual cash generation and forecast FY EBITDA, [5] 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)

Financing supported by leading global financial institutions



Note: [1] ¥500 billion (approx. $4.5 billion) senior short term loan entered into on 26 October 2018 (which will in turn be refinanced using a ¥500 billion (approx. $4.5 billion) hybrid loan, also entered into on 26 October 2018)

Board of Directors for Best-in-Class Governance

INTERNAL DIRECTORS

Christophe Weber
Representative Director,
President & CEO

Masato Iwasaki
Director,
JPBU President

Andrew Plump
Director, Chief Medical
& Scientific Officer

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

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

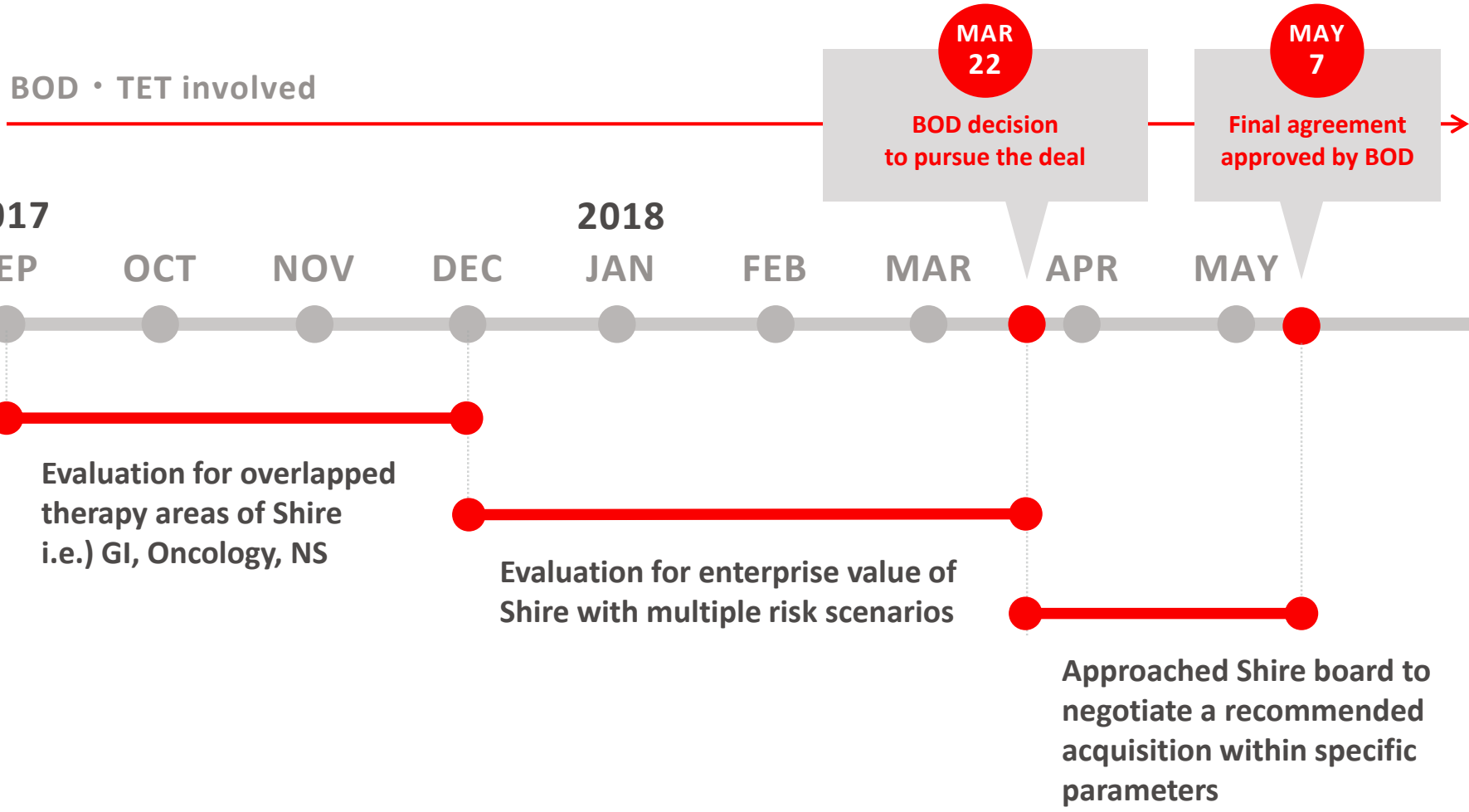
Yasuhiko Yamanaka
Director,
A&SC member

Shiro Kuniya
Independent Director,
Chair A&SC

Koji Hatsukawa
Independent Director,
A&SC member

Jean-Luc Butel
Independent Director,
A&SC member

Takeda board (BOD) and Takeda Executive Team (TET) have been fully involved early in the acquisition with many reviews starting in 2017



The acquisition has been approved by the board after multiple extensive reviews with detailed risk assessment

MAJOR RISKS	MITIGATION
Financial Market Risks Examples: ▪ Interest rate risk ▪ Currency risk	• Remain investment grade credit rated • Denominate the debt with competitive aggregate interest rate with the right currency balance • Consider disposal of non-core assets
Business Risks Examples: ▪ Competitive pressure ▪ Pricing pressure	• Model future business outlook with prudent forecasts • Risk of impairments to goodwill and intangible assets mitigated by Shire's in market products and prudent forecasts also applied to its pipeline
Integration Risks Examples: ▪ Cultural difference ▪ Shire talent retention	• Experienced leadership well prepared for integration • Keep consistent with Takeda's name, culture and purpose • Promote shared intention to become a patient centric and R&D driven company • Build the operating model to leverage Takeda and Shire employee know-how

Integration planning is well underway

Creating our 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 empowering General Managers to make local decisions
- Minimizing complexity

*Local Operating Company

Lean & Focused

- Focusing on six business drivers
- Leveraging global scale while keeping the right balance of country resources
- Making us fit to deal with demanding healthcare environments

4 Regional Business Units

3 Global Specialty Business Units

- PDT* BU
- Oncology BU
- Vaccine BU

*Plasma Derived Therapies

Global, diverse and experienced new Takeda Executive Team (Post-closing)

CHRISTOPHE WEBER
President & CEO

COSTA SAROUKOS
Global Finance

HARUHIKO HIRATE
Corporate Communication & Public Affairs

YOSHIHIRO NAKAGAWA
Global Legal

PADMA THIRUVENGADAM
Global Human Resources

MILANO FURUTA
Corporate Strategy

MWANA LUGOGO
Global Ethics & Compliance

RAMONA SEQUEIRA
U.S. Business Unit

MASATO IWASAKI
Japan Pharma Business Unit

GILES PLATFORD
Europe & Canada Business Unit

RICARDO MAREK
Emerging Markets Business Unit

CHRISTOPHE BIANCHI
Global Oncology Business Unit

RAJEEV VENKAYYA
Global Vaccine Business Unit

JULIE KIM[1]
Global Plasma-Derived Therapy Business Unit

ANDY PLUMP
R&D

THOMAS WOZNIEWSKI
Global Manufacturing and Supply

GERARD (JERRY) GRECO
Global Quality

CAMILLA SOENDERBY[1]
Global Patient Value & Product Strategy

MARCELLO AGOSTI
Global Business Development

HELEN GIZA
Integration

[1] New executive members from Shire plc

Reinforce the diversity and strength of the board with appointment of three new independent external directors

INTERNAL DIRECTORS

Christophe Weber
Representative Director,
President & CEO

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Independent Director
Chair of Compensation Committee

Emiko Higashi
Independent Director

Yoshiaki Fujimori
Independent Director

Ian Clark[1]
Independent Director

Olivier Bohuon[1]
independent Director

Steven Gillis[1]
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

[1] New independent external directors from Shire plc









The acquisition of Shire will enable Takeda to significantly accelerate its transformational journey to become a values-based, R&D driven global biopharmaceutical leader headquartered in Japan

Takeda

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