



FY2018 First-Half Results Briefing Session

- Research and Development -

November 2, 2018













JCR Pharmaceuticals Co., Ltd.








Development Pipeline in Japan

■ Lysosomal Storage Disorder (LSD) ■ Other Biopharmaceuticals
■ Regenerative Medical Product

As of Nov 2, 2018

Code	Indication	Pre-clinical	Ph I / II	Ph III	Filed	Approved	Remarks
Agalsidase Beta BS I.V. Infusion [JCR]	Fabry disease						<ul style="list-style-type: none"> Enzyme replacement therapy (ERT) Biosimilar
JR-141	Hunter syndrome	   					<ul style="list-style-type: none"> ERT J-Brain Cargo®
JR-162	Pompe disease						<ul style="list-style-type: none"> ERT J-Brain Cargo® J-MIG System®
JR-171	Hurler syndrome						<ul style="list-style-type: none"> ERT J-Brain Cargo® J-MIG System®
JR-441 NEW	Sanfilippo syndrome Type A						<ul style="list-style-type: none"> ERT J-Brain Cargo® J-MIG System®
JR-131	Renal anemia						<ul style="list-style-type: none"> Co-developed with Kissei Pharmaceutical Co., Ltd. Biosimilar
JR-401X	SHOX deficiency						<ul style="list-style-type: none"> Expanded indication of GROWJECT®
JR-142	Growth disorders						<ul style="list-style-type: none"> Long-acting human growth hormone product J-MIG System®
JR-041	Infertility						<ul style="list-style-type: none"> Out-licensed to ASKA Pharmaceutical Co., Ltd.
JR-031EB NEW	Epidermolysis bullosa						<ul style="list-style-type: none"> Expanded indication of TEMCELL® HS Inj.
JTR-161/JR-161	Acute cerebral infarction						<ul style="list-style-type: none"> Co-developed with Teijin Limited

- May 28 JCR Receives Approval in Brazil to Initiate Phase 2 Clinical Trial of JR-141 for Hunter Syndrome 
- June 1 JCR Announces Completion of PMDA Review of Phase 3 Clinical Trial of JR-141 for Hunter Syndrome 
- June 29 JCR Initiates Phase 2 Clinical Trial of JR-141 for Hunter Syndrome in Brazil 
- July 2 JCR Initiates Phase 3 Clinical Trial for An Expanded Indication of GROWJECT®
for Short Stature Homeobox-containing Gene (SHOX) Deficiency
- Aug. 9 JCR Initiates Phase 3 Clinical Trial of JR-141 for Hunter Syndrome 
- Sep. 14 JCR to Initiate Development of a New Drug Candidate
for Sanfilippo Syndrome Type A Using J-Brain Cargo®
- Sep. 21 JCR Receives Marketing Approval for Agalsidase Beta BS I.V. Infusion [JCR] for Fabry Disease
- Sep. 28 JCR Files for Marketing Approval for JR-131, a Long-Acting Erythropoiesis-Stimulating Agent
- Oct. 19 Notice of Orphan Drug Designation by the US Food Drug Administration
for JR-141 for Hunter Syndrome 
- Oct. 29 JCR to Initiate Development of TEMCELL® HS Inj. (JR-031EB)
for the Indication of Epidermolysis Bullosa

	Product	Status	Indication
LSD Biosimilar	<u>Agalsidase Beta BS I.V. Infusion [JCR]</u> Recombinant Agalsidase Beta (rDNA origin)	Received marketing approval in Japan	Fabry disease
LSD	JR-441 BBB-Penetrating heparan N-sulfatase (rDNA origin)	Preclinical	Sanfilippo syndrome type A
LSD	JR-141 BBB-Penetrating iduronate-2-sulfatase (rDNA origin)	Japan: Phase III Brazil: Phase II	Hunter syndrome
Regenerative Medical Product	JR-031EB Expanded indication of TEMCELL®HS Inj.	Application for marketing approval in preparation	Epidermolysis bullosa
Regenerative Medical Product	JTR-161/JR-161 Dental pulp-derived stem cells	Phase I/II	Acute cerebral infarction
Biosimilar	JR-131 Darbepoetin (rDNA origin)	Filed	Renal anemia
Growth Hormone	JR-401X Expanded indication of GROWJECT®	Phase III	SHOX deficiency
Growth Hormone	JR-142 Long-acting growth hormone (rDNA origin)	Preclinical	Growth disorders



Therapeutic enzyme for Fabry disease Biosimilar to Fabrazyme (α -galactosidase A)



JCR's first enzyme replacement therapy for LSD

Agalsidase Beta BS I.V. Infusion [JCR]



(left) Agalsidase Beta BS I.V. Infusion 5mg
(right) Agalsidase Beta BS I.V. Infusion 35mg

First domestic
ERT product
for LSD

High quality
manufacturing in
serum-free culture
in Japan

Equivalence in
efficacy and safety
compared with the
innovator product

To be launched in Nov. 2018



Therapeutic enzyme for Fabry disease Biosimilar to Fabrazyme (α -galactosidase A)



JCR's first enzyme replacement therapy for LSD

Agalsidase Beta BS I.V. Infusion [JCR]

➤ **Fabry disease**

MHLW designated intractable disease

- Disease condition:
 - Skin : Angiokeratomas, lymphedema of the lower limbs
 - Circulatory : Cardiac failure, enlarged heart, valvular disease, arrhythmia
 - Digestive system: Abdominal pain, diarrhea
 - Kidney : Renal failure, proteinuria
 - Nerves : Extremity pain, hypohidrosis
 - Eye : Cloudy cornea

■ Market size* : **24** billion JPY est. (FY2017 Japan), **135** billion JPY est. (2017 WW)

■ Patient population* : **800** (Japan), **18,000** (WW) est.

*Internal analysis

JR-441 BBB-penetrating heparan N-sulfatase **NEW**

➤ Sanfilippo syndrome Type A (MPS IIIA)

MHLW designated
intractable disease

- Cause : an inborn deficiency or defect in heparan N-sulfatase within lysosomes in cells throughout the body
- Disease condition : CNS disorders, sleep disorders, hepatosplenomegaly and seizures
- Treatment : **effective treatment is not available** → **development of a new treatment option has been long awaited**
- Patient population* : **60** (Japan), **6,890** (WW) est

Total of Type A&B (Internal analysis)

A animal studies demonstrated delivery of JR-441 not only into peripheral tissues but also into the brain, along with significant reduction of heparan sulfate accumulated in these tissues.

JR-141 BBB-penetrating iduronate-2-sulfatase

➤ Hunter syndrome (MPS type II)

MHLW designated intractable disease

- Disease condition
 - Bone : characteristic face, bone deformity, arthrogryposis
 - Heart : cardiac valvular disease
 - Soft tissue : thick skin, hairiness, macroglossia
 - Liver : hepatomegaly
 - CNS : **CNS disorders**

Existing enzyme replacement therapy does **not show effect on CNS symptoms** due to non-penetration of BBB

■ Patient population* : **100-200** (Japan), **2,000** (WW) est.

*Internal analysis

■ Market size* : **8 billion JPY est.** (FY2017 Japan) , **65 billion JPY est.** (2017 WW)



Designated under
"SAKIGAKE
Designation System

Aug. 2018;
Ph3 clinical trial initiated



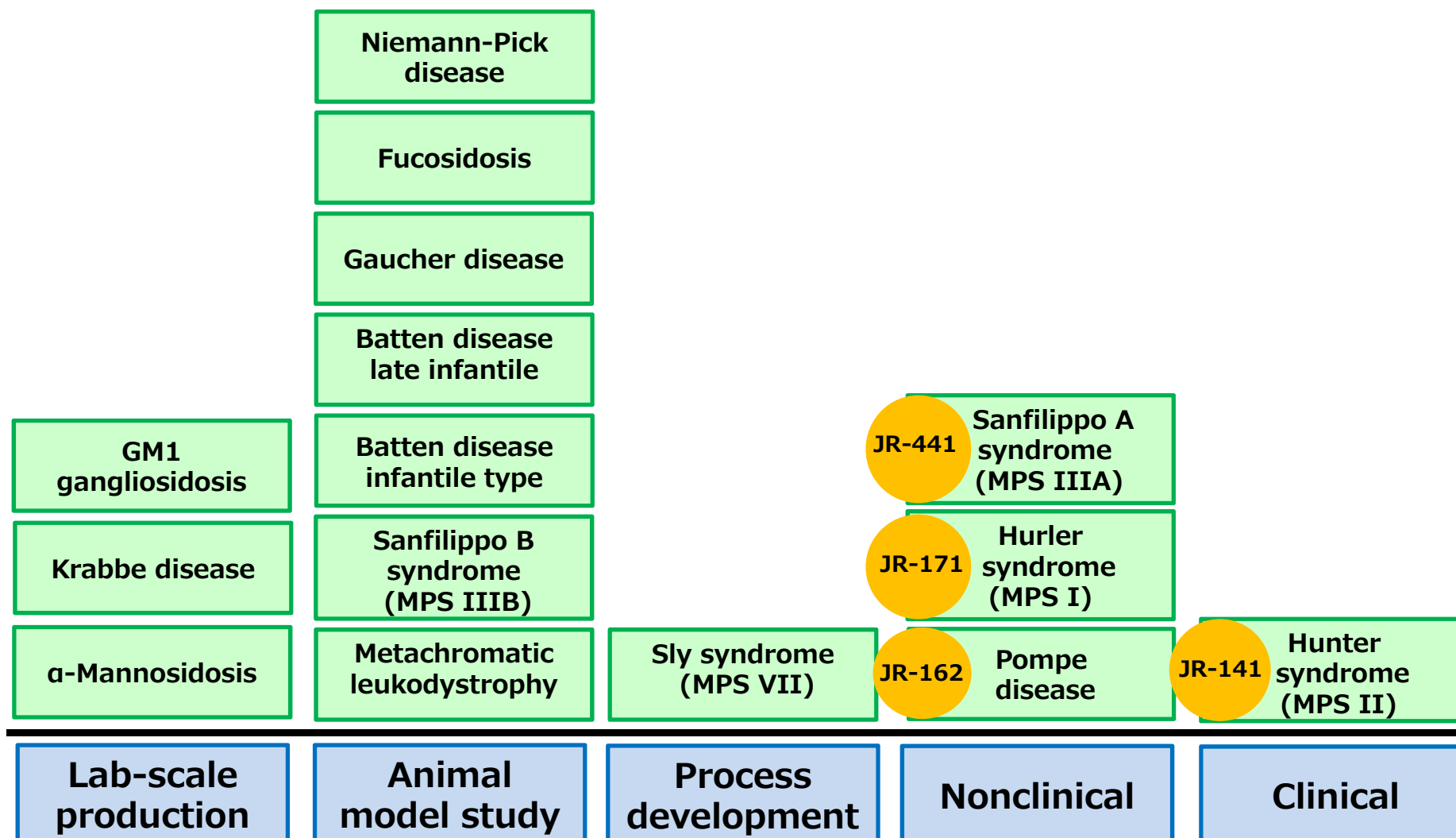
Jun. 2018;
Ph2 clinical trial initiated



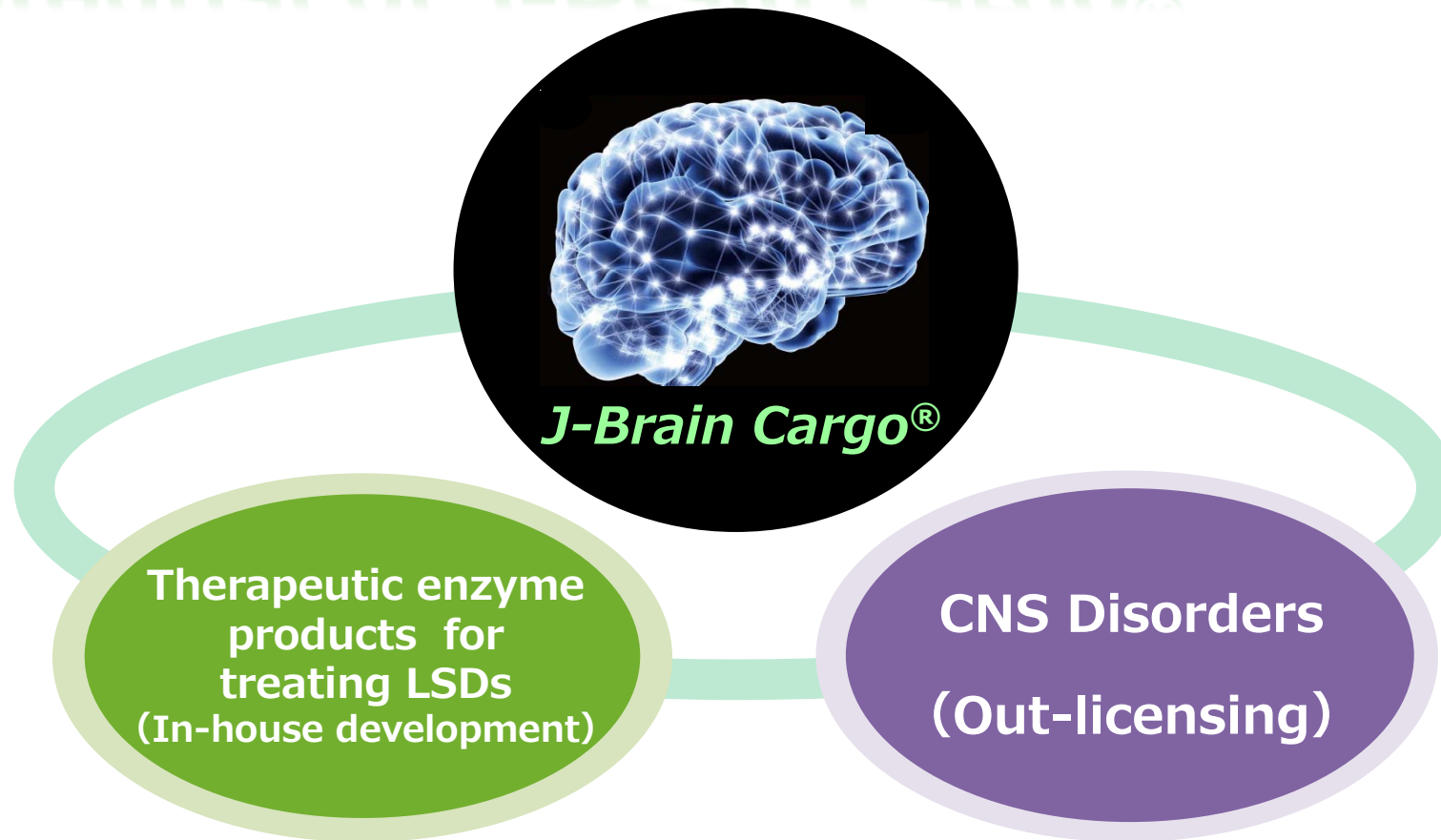
Oct. 2018;
Designated under Orphan
Drug Designation

Proactive development of LSD pipeline

-15 early to late stage J-Brain Cargo® programs-



Potential of J-Brain Cargo®



**J-Brain Cargo® potential applications
to various CNS disorders**

	Product	Status	Indication
LSD Biosimilar	Agalsidase Beta BS I.V. Infusion [JCR] Recombinant Agalsidase Beta (rDNA origin)	Received marketing approval in Japan	Fabry disease
LSD	JR-441 BBB-Penetrating heparan N-sulfatase (rDNA origin)	Preclinical	Sanfilippo syndrome type A
LSD	JR-141 BBB-Penetrating iduronate-2-sulfatase (rDNA origin)	Japan: Phase III Brazil: Phase II	Hunter syndrome
Regenerative Medical Product	JR-031EB Expanded indication of TEMCELL®HS Inj.	Application for marketing approval in preparation	Epidermolysis bullosa
Regenerative Medical Product	JTR-161/JR-161 Dental pulp-derived stem cells	Phase I/II	Acute cerebral infarction
Biosimilar	JR-131 Darbepoetin (rDNA origin)	Filed	Renal anemia
Growth Hormone	JR-401X Expanded indication of GROWJECT®	Phase III	SHOX deficiency
Growth Hormone	JR-142 Long-acting growth hormone (rDNA origin)	Preclinical	Growth disorders

JR-031EB

Expanded indication of TEMCELL[®]HS Inj.



Oct. 2018 :

Designed the orphan regenerative medical product for EB in Japan

➤ Epidermolysis bullosa : EB

MHLW designated intractable disease

- Cause: Hereditary disorder of abnormal gene expressed in the cutaneous basement membrane zone
- Disease condition: Slight friction may cause the skin to detach from its basement membrane, producing burn-like blisters and ulcers
- Treatment: Basically, none. Gauze dressings and Vaseline are used to protect wounds
- Patient population (Japan): **500-640** est. (**approx. 300 severe cases eligible for treatment**)

*Internal analysis

- investigator-initiated trial by
the Graduate School of Medicine, Osaka University

Dosing completed and demonstrated promising results

Application for marketing approval planned in FY2018

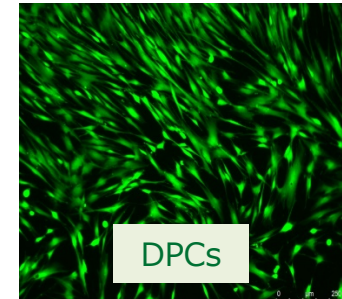
JTR-161/JR-161

Human dental pulp stem cells (DPCs)

a new product in cell therapy and regenerative medicine
succeeded TEMCELL[®] HS Inj.

TEIJIN

Co-development and license agreement
with Teijin Limited in July 2017
Indication : **Acute cerebral infarction**



➤ **Acute cerebral infarction**

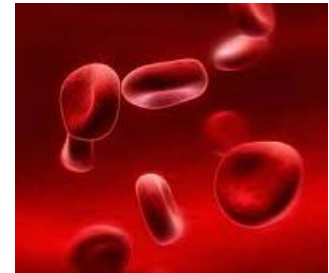
- Cause : Major risk factors are generally the same as for atherosclerosis:
high blood pressure, diabetes mellitus, tobacco smoking, obesity, and dyslipidemia
- Patient population* (Japan): **300,000** est. *Internal analysis
- Treatment : Use of thrombolytic therapy, antiplatelet therapy,
and anticoagulant therapy is advocated within a few hours of onset

Phase I / II started in Oct. 2018

	Product	Status	Indication
LSD Biosimilar	<u>Agalsidase Beta BS I.V. Infusion [JCR]</u> Recombinant Agalsidase Beta (rDNA origin)	Received marketing approval in Japan	Fabry disease
LSD	JR-441 BBB-Penetrating heparan N-sulfatase (rDNA origin)	Preclinical	Sanfilippo syndrome type A
LSD	JR-141 BBB-Penetrating iduronate-2-sulfatase (rDNA origin)	Japan: Phase III Brazil: Phase II	Hunter syndrome
Regenerative Medical Product	JR-031EB Expanded indication of TEMCELL®HS Inj.	Application for marketing approval in preparation	Epidermolysis bullosa
Regenerative Medical Product	JTR-161/JR-161 Dental pulp-derived stem cells	Phase I/II	Acute cerebral infarction
Biosimilar	JR-131 Darbepoetin (rDNA origin)	Filed	Renal anemia
Growth Hormone	JR-401X Expanded indication of GROWJECT®	Phase III	SHOX deficiency
Growth Hormone	JR-142 Long-acting growth hormone (rDNA origin)	Preclinical	Growth disorders

JR-131

Darbepoetin (Biosimilar to Nesp)



- Co-development agreement with Kissei Pharmaceutical Co., Ltd. in Sep. 2013

Leveraging JCR's proprietary **Glycoengineering Technology to approach complex sugar chain structure**

Patent filed

- Phase III study : demonstrated equivalence in efficacy and safety compared with darbepoetin



- In a primary endpoint of efficacy, the equivalence was verified for variations in hemoglobin concentration
- Similarity with regard to the safety profile was confirmed

Application for marketing approval in Sep. 2018

Growth Hormone

JR-401X

Somatotropin

Expanded Indication of GROWJECT®

- Indication : **Short stature homeobox containing gene (SHOX) deficiency**

Phase III started in July 2018

JR-142

Long-acting growth hormone

- JCR's proprietary half-life extension technology based on a novel modified albumin allows various biotherapeutic products to increase drug half-life significantly

Clinical trials aimed to start in FY2019



Development Pipeline in Japan

■ Lysosomal Storage Disorder (LSD) ■ Other Biopharmaceuticals
■ Regenerative Medical Product

As of Nov 2, 2018

Code	Indication	Pre-clinical	Ph I / II	Ph III	Filed	Approved	Remarks
Agalsidase Beta BS I.V. Infusion [JCR]	Fabry disease						<ul style="list-style-type: none"> Enzyme replacement therapy (ERT) Biosimilar
JR-141	Hunter syndrome	 					<ul style="list-style-type: none"> ERT J-Brain Cargo®
JR-162	Pompe disease						<ul style="list-style-type: none"> ERT J-Brain Cargo® J-MIG System®
JR-171	Hurler syndrome						<ul style="list-style-type: none"> ERT J-Brain Cargo® J-MIG System®
JR-441 NEW	Sanfilippo syndrome Type A						<ul style="list-style-type: none"> ERT J-Brain Cargo® J-MIG System®
JR-131	Renal anemia						<ul style="list-style-type: none"> Co-developed with Kissei Pharmaceutical Co., Ltd. Biosimilar
JR-401X	SHOX deficiency						<ul style="list-style-type: none"> Expanded indication of GROWJECT®
JR-142	Growth disorders						<ul style="list-style-type: none"> Long-acting human growth hormone product J-MIG System®
JR-041	Infertility						<ul style="list-style-type: none"> Out-licensed to ASKA Pharmaceutical Co., Ltd.
JR-031EB NEW	Epidermolysis bullosa						<ul style="list-style-type: none"> Expanded indication of TEMCELL® HS Inj.
JTR-161/JR-161	Acute cerebral infarction						<ul style="list-style-type: none"> Co-developed with Teijin Limited



– JCR Biotech for a New Tomorrow –

FORWARD- LOOKING STATEMENT

This presentation contains, and answers given to questions that may be asked today may constitute, forward-looking statements that are subject to a number of risks and uncertainties, many of which are outside our control. All forward-looking statements regarding our plans, outlook, strategy and future performance are based on judgments derived from the information available to us at this time.

All forward-looking statements speak only as of the date of this presentation.

Except as required by law, we assume no obligation to update these forward-looking statements publicly or to update the factors that could cause actual results to differ materially, even if new information becomes available in the future.