AKCEA THERAPEUTICS

Fourth Quarter and Year End 2018 Earnings Call

February 26, 2019

Forward-Looking Language Statement

This presentation includes forward-looking statements regarding the business of Akcea Therapeutics, Inc., and the therapeutic and commercial potential of TEGSEDI® (inotersen), WAYLIVRA™ (volanesorsen), AKCEA-APO(a)-L_{Rx}, AKCEA-ANGPTL3-L_{Rx}, AKCEA-APOCIII-L_{Rx} and AKCEA-TTR-L_{Rx}. Any statement describing Akcea's goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Akcea's forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Akcea's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Akcea. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Akcea's programs are described in the most recent quarterly report on Form 10-Q and in the most recent annual report on Form 10-K. Copies of these and other documents are on file with the SEC.

In this presentation, unless the context requires otherwise, "Akcea," "Company," "we," "our," and "us" refers to Akcea Therapeutics. Akcea Therapeutics®, TEGSEDI® and WAYLIVRA™ are trademarks of Akcea Therapeutics, Inc.

A Pivotal Year for Akcea Therapeutics

Established Global, Commercial Company

- Launch of TEGSEDI in US, Germany and Canada
- Track record of execution
- Broad, novel pipeline
- Strategic partnership with Novartis
- Foundational Ionis relationship

Licensed TTR Franchise from Ionis

- Focused beyond cardiometabolic disease
- Grew from ~90 employees to +250
- Expanded Global footprint from five to 12 countries
- Further strengthened relationship with Ionis

Received AKCEA-APO(a)-L_{Rx} study results

- Longest and largest study to date from Ionis LICA technology
- Strong efficacy, favorable safety and tolerability profile
- Novartis exercised its option to AKCEA-APO(a)-L_{Rx}
- Novartis is preparing to initiate Phase 3 cardiovascular outcomes study

TEGSEDI® (inotersen) Commercial Launch

Positive Early Results

- Launched in Germany (Oct. 2018), U.S. (Dec. 2018) and Canada (2019)
- Treated patients from early access and open label extension programs, as well as naïve patients
- Received reimbursement from both public and private payers

Full Commercial Infrastructure

- Experienced team executing drug launches
- Supply chain working and fully integrated with our specialty pharmacy Accredo
- hATTR Compass genetic testing program launched to enable faster diagnosis

Supporting Patients and Physicians through Akcea Connect

- Guides patients and physicians through reimbursement support
- Aids patients in creating a straight forward monitoring routine that meets an individual patient's needs
- Provides disease education and assistance with injection training

Tegsedi™ (inotersen) injection 284 mg/1.5 mL

**TEGSEDI was discovered and developed by Ionis and licensed to Akcea in 2018*

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Serving Patients Around the Globe

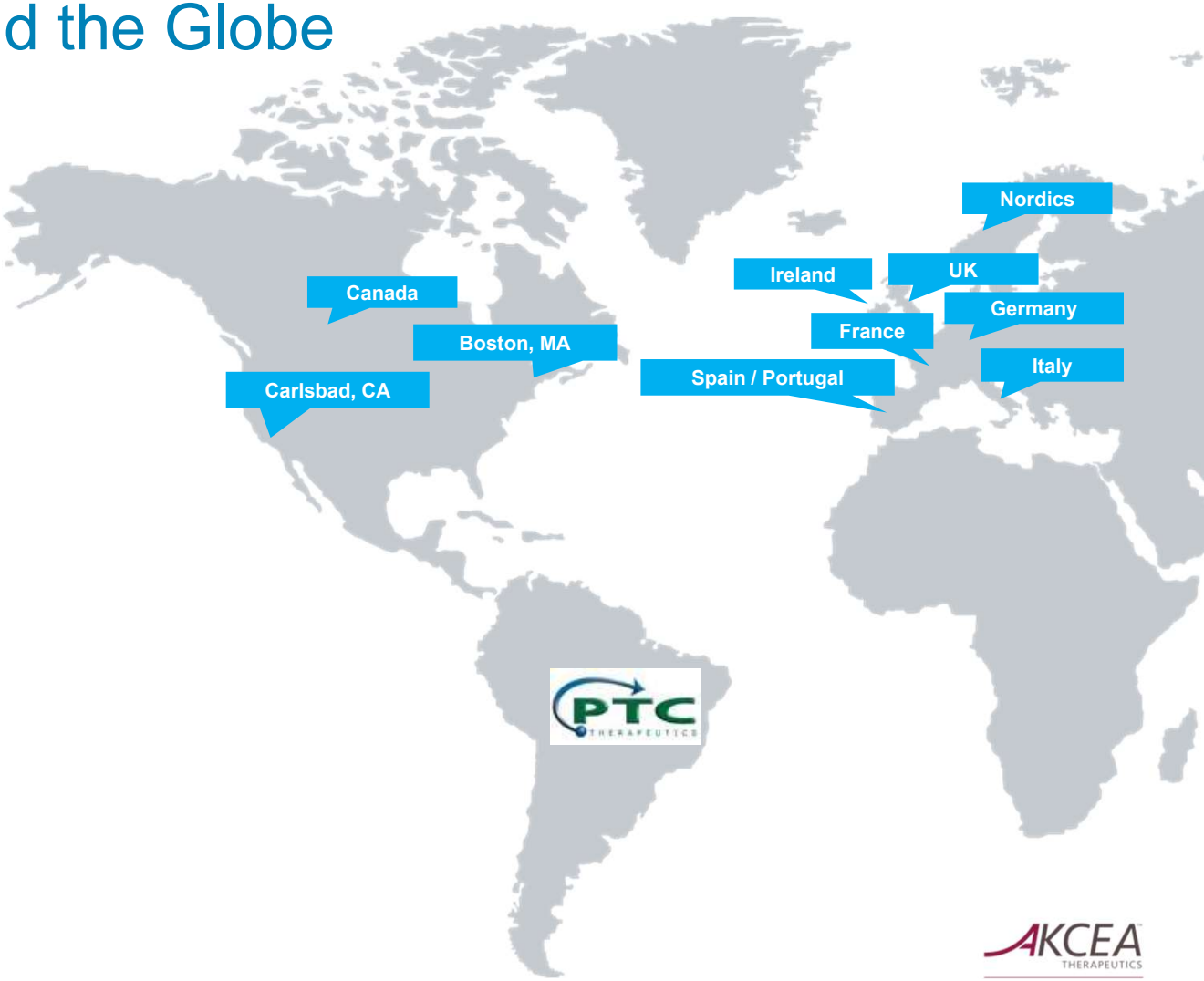
~50,000 Patients Worldwide

- ~ 16,000 patients in the U.S.
- ~ 16,000 patients in the E.U.
- ~ 6,000 patients in Latin America

~60% of patients with symptoms of polyneuropathy

Active dialogue with payers covering over 75% of lives in the U.S.

Strategic partnership with PTC in Latin America



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An Update on WAYLIVRA™

- ✓Review ongoing in the E.U.
- ✓Continuing our discussions with FDA in US
- ✓Expect data from WAYLIVRA FPL in Mid 2019

waylivra™
(volanesorsen sodium)
Injection 300mg in 1.5mL

Our patients matter…

- Patients, physicians and medical societies have spoken out in support of WAYLIVRA™
- FCS carries a heavy disease burden including frequent, unpredictable and potentially fatal pancreatitis
- There is no available treatment

WAYLIVRA™ was discovered by Ionis Pharmaceuticals and co-developed by Ionis Pharmaceuticals and Akcea Therapeutics

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Advancing Broad Pipeline to Commercialization*

Drug	Therapeutic Area	Preclinical	Phase 1	Phase 2	Phase 3	Key Near-term Pipeline Events
Cardiometabolic lipid disorders						
AKCEA-APO(a)-L_{Rx}	High Lp(a) with Established CVD					Novartis to initiate Phase 3 CVD outcomes study
AKCEA-ANGPTL3-L_{Rx}	Rare Hyperlipidemias					Report pilot study data mid-2019
	NAFLD with Metabolic Complications					Report Phase 2 data 1H 2020
AKCEA-APOCIII-L_{Rx}	Hypertriglyceridemia with Established CVD					Report Phase 2 data 1H 2020
ATTR amyloidosis (ATTR)						
AKCEA-TTR-L_{Rx}	ATTR					Phase 1 Data with a goal of initiating Phase 3 - H2 2019

*All products were discovered and either developed by Ionis or co-developed by Ionis and Akcea; LICA technology allows for significantly lower doses than non-LICA drugs, more flexible dosing and favorable safety and tolerability profile

Financials

Market Cap as of Feb. 25, 2018	$2.8B
Cash and Short –term Investments as of December 31, 2018	$253M
REVENUE:	
Q4 TEGSEDI	$2.2M
FY2018 Total	$65M

Impact of Novartis Option Exercise:

Earned $150M when Novartis exercised its option to license AKCEA-APO(a)-L_{Rx}.

Will settle $75M payment obligation to Ionis in shares.

Sufficient cash to fund commercial activities and progression of current pipeline to decision events.

Akcea positioned for strong and sustainable future

Established commercial company

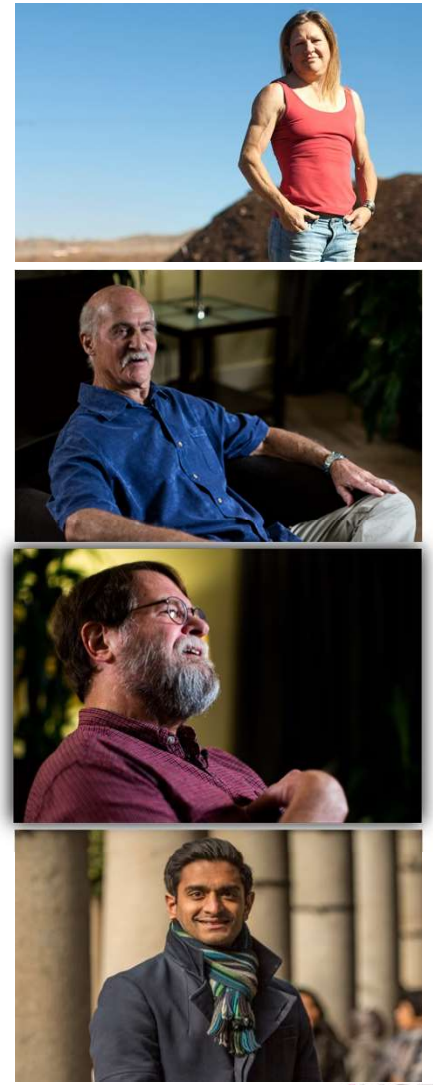
Successful launch of TEGSEDI™

Broad, advancing pipeline

Experienced management team

Foundational Ionis relationship and strong strategic partnerships

Sufficient cash on hand*



*With year end cash plus $150M from Novartis, have sufficient cash to fund commercial activities as well as fund progression of current pipeline to decision events.

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