AKCEA® THERAPEUTICS

Third Quarter 2019 Earnings Call

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.

Akcea by Year End 2019

2 Commercial Products

Tegsedi® (inotersen) injection 284 mg/1.5 mL

waylivra® (volanesorsen) injection 285 mg/1.5 mL

2 Products in Phase 3 Development

AKCEA-APO(a)-L_{Rx}

NOVARTIS

AKCEA-TTR-L_{Rx}

IONIS™

2 Products Nearing Ph 2 Data

AKCEA-APOCIII-L_{Rx}
in patients with CVD due to high triglycerides

AKCEA-ANGPTL3-L_{Rx}

Pfizer

Strong cash balance supporting our execution across the business

All products were discovered and either developed by Ionis or co-developed by Ionis and Akcea
AKCEA-APO(a)-L_{Rx} was licensed by Novartis in February 2019; Novartis refers to AKCEA-APO(a)-L_{Rx} as TQJ230

AKCEA THERAPEUTICS

An Experienced Management Team

Damien McDevitt
Interim Chief Executive Officer

Mike MacLean
Chief Financial Officer

Louis St. L. O'Dea
Chief Medical Officer

Kyle Jenne
Chief Commercial Officer

Maura Bullock
VP, Human Resources

Kathleen Gallagher
VP, Corporate Communications & Investor Relations

Third Quarter Highlights

- ✓Introduced new executive leaders
- ✓Advanced our pipeline
- ✓Signed a worldwide exclusive licensing agreement with Pfizer for AKCEA-ANGPTL3-L_{Rx} with $250M upfront milestone
- ✓Began treating patients in the UK with TEGSEDI
- ✓Launched WAYLIVRA in Germany & ATU in France

TEGSEDI

Tegsedi® (inotersen) injection 284 mg/1.5 mL

AKCEA CONNECT

hATTR Compass
Map Your Genetic Journey

>40%

New prescriptions from first time prescribers

TEGSEDI now launched in multiple countries with Akcea Connect up and running

>1,000

Physicians using hATTR Compass

- PTC announced approval of TEGSEDI in Brazil with strong indication statement
- Completed initial free pricing period and successfully finalized pricing negotiations in Germany
- Received acceptance from NICE, Scottish Medicines Consortium, the New Therapies Council in Sweden and the Sickness Insurance Funds in Austria

TEGSEDI was discovered and developed by Ionis

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waylivra®
(volanesorsen) injection 285 mg/1.5 mL

- **Approved in Europe**
- **Launched in Germany**
- **Beginning ATU in France**

WAYLIVRA was discovered by Ionis and co-developed by Ionis and Akcea

Only Approved Treatment for FCS Patients

- Approximately 1,000 patients eligible for treatment
- Patients at risk for potentially fatal acute pancreatitis, chronic pancreatitis and diabetes
- Major emotional and psychosocial effects
- Many unable to work, must declare bankruptcy due to repeat pancreatitis

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Financials

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Q3 Total Revenue	**$21M**
Q3 TEGSEDI Revenue	**$12M**
Cash and short-term Investments as of September 30, 2019	**$253M**

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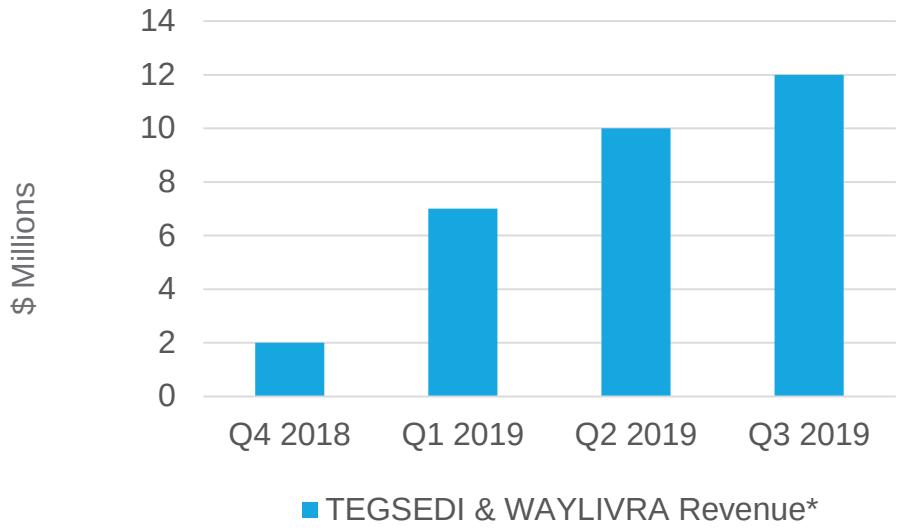
waylivra® (volanesorsen) injection 285 mg/1.5 mL



- $250M upfront license fee from our worldwide exclusive licensing agreement with Pfizer for AKCEA-ANGPTL3-L_{Rx}*
- With substantial liquidity due to our cash balance and the license fee from Pfizer, Akcea is well positioned to continue to execute on the ongoing launches and broaden the pipeline.
- Generated $4M from PTC in Q4 for the approval of TEGSEDI in Brazil**

*Awaiting HSR clearance; 50% due to Ionis settled by issuance of shares of common stock

**Milestone from PTC to be split 40% to Akcea and 60% to Ionis

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An Update on WAYLIVRA

- ✓Continuing to work toward a path forward with regulatory agencies in U.S. and Canada
- ✓Phase 3 APPROACH study was published in the August 8th issue of the *New England Journal of Medicine*
- ✓Reviewing data from the BROADEN study with experts in the field to determine next steps

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

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	Novartis initiating Phase 3 CVD outcomes study
AKCEA-ANGPTL3-L$_{Rx}$	Cardiovascular and Metabolic diseases				Pfizer	Report Phase 2 data early 2020
AKCEA-APOCIII-L$_{Rx}$	Hypertriglyceridemia with Established CVD				NOVARTIS	Report Phase 2 data early 2020
ATTR amyloidosis (ATTR)						
AKCEA-TTR-L$_{Rx}$	ATTR				IONIS	Phase 3 program initiating in late 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

Future potential pipeline: Ionis granted AKCEA right of first negotiation in rare cardiometabolic and rare inherited metabolic diseases

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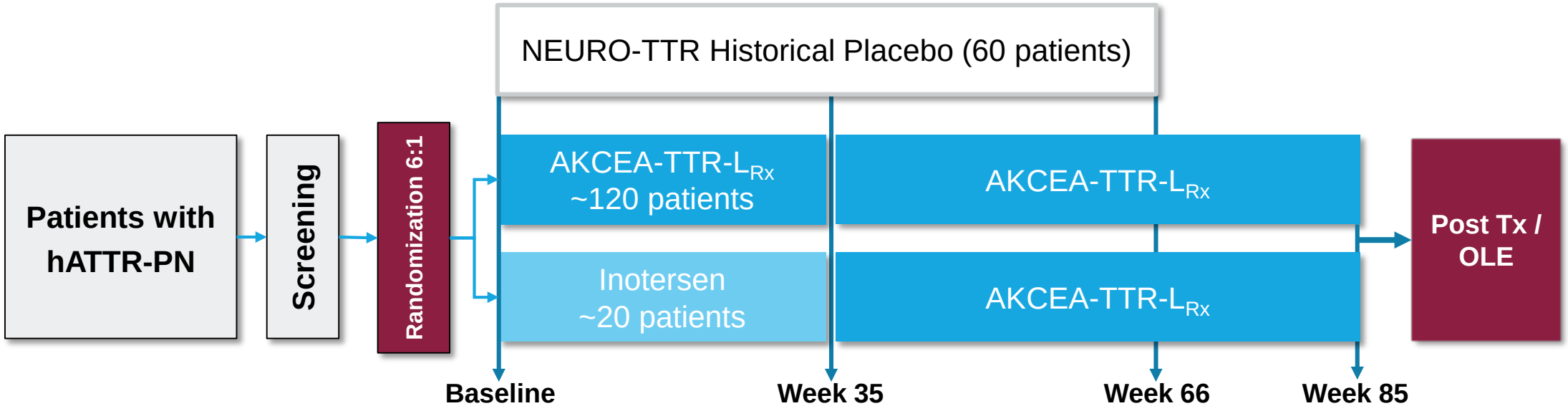
AKCEA-TTR-L_{Rx}: NEURO-TTRansform

A Phase 3 Study to Evaluate the Efficacy and Safety of AKCEA-TTR-LRx in Participants With Hereditary Transthyretin-Mediated Amyloid Polyneuropathy

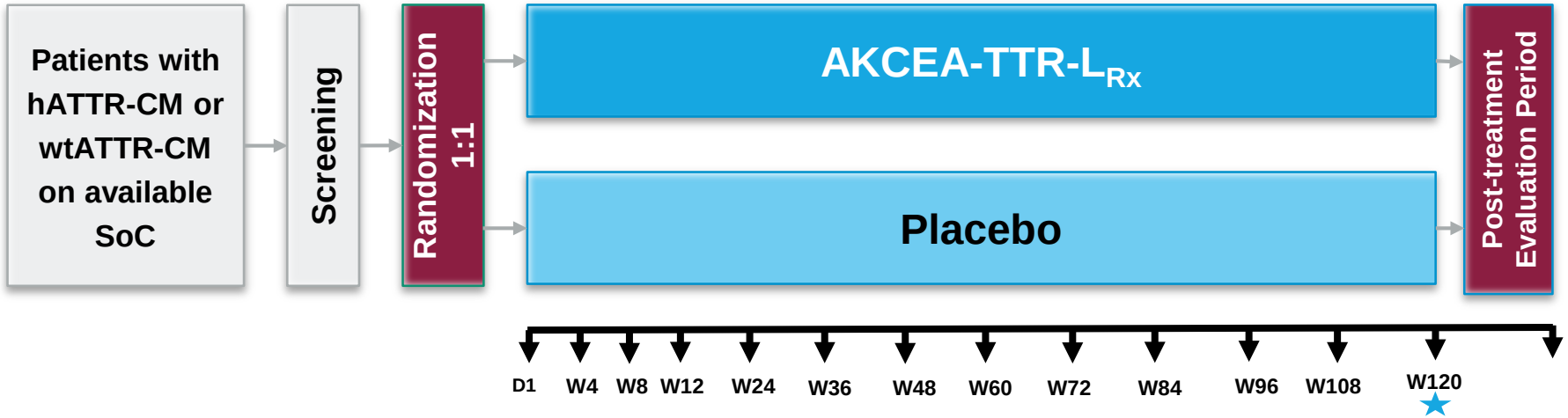


Adults with hATTR-PN meeting all 3 of the following criteria:

- Stage 1 or Stage 2
- Documented TTR genetic mutation
- Symptoms and signs consistent with polyneuropathy (NIS ≥ 10 and ≤ 130)

AKCEA-TTR-L_{Rx}: CARDIO-TTRansform

A Phase 3 Global, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy and Safety of AKCEA-TTR-L_{Rx} in Patients with Transthyretin-Mediated Amyloid Cardiomyopathy (ATTR-CM)



- Sample size: ~750
- Primary composite endpoint: CV death and CV clinical events
- Secondary endpoints: 6MWT, KCCQ, CV clinical events
- Exploratory endpoints: Echo, biomarkers, PROs, (potential CMRI sub-study)

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Our mission is to be the trusted patient-focused, global company delivering innovative solutions that improve the lives of those affected by serious diseases.