AKCEA® THERAPEUTICS

First Quarter 2020 Earnings Call

May 5, 2020

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}, vupanorsen (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, including those related to the impact COVID-19 could have on our business including but not limited to the impact on our commercial products and the medicines in our pipeline, and 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® THERAPEUTICS

First Quarter Achievements

Delivering transformative treatments to people living with serious and rare diseases

Strong start to 2020

- ✓ $421M of cash and short-term investments to execute on strategic priorities for 2020 and beyond

Expanded and strengthened our leadership team and board of directors

Continued sequential growth for TEGSEDI and WAYLIVRA

Steadily advancing broad pipeline of products

- ✓ positive topline data readouts for vupanorsen (ANGPTL3-L_{Rx}) and APOCIII-L_{Rx}

Took immediate action to mitigate risks due to the COVID-19 pandemic

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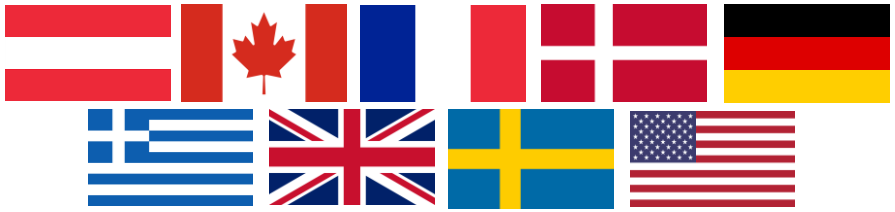
TEGSEDI



Commercially available in 12 countries with additional launches underway

AKCEA CONNECT

Continuing without interruption to provide patients the individualized support they need

94% of commercial lives currently secured with coverage and 75% of commercial lives secured with coverage through 2023 in the U.S.

hATTR Compass

Map Your Genetic Journey

> 1,800 physicians using hATTR Compass

TEGSEDI was discovered and developed by Ionis

AKCEA THERAPEUTICS

- **Approved in Europe**
- **Commercially available in Germany & Austria**
- **Continued ATU enrollment in France**
- **Ongoing partnership with PTC across Latin America; goal to file in Brazil 2H'20**
- **On track to refile with the FDA this year**

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

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

AKCEA THERAPEUTICS

Advancing Broad Pipeline to Commercialization*

Drug	Therapeutic Area	Preclinical	Phase 1	Phase 2	Phase 3	Key Near-term Pipeline Events	Partner
Cardiometabolic lipid disorders							
AKCEA-APO(a)-L_{Rx}	High Lp(a) with Established CVD					Novartis initiated Phase 3 CVD outcomes study	NOVARTIS
vupanorsen (AKCEA-ANGPTL3-L_{Rx})	Cardiovascular and Metabolic diseases					Reported positive Phase 2 data in January 2020	Pfizer
AKCEA-APOCIII-L_{Rx}	Hypertriglyceridemia with Established CVD					Reported positive Phase 2 data in January 2020	IONIS
ATTR amyloidosis (ATTR)							
AKCEA-TTR-L_{Rx}	ATTR					Phase 3 program in cardiomyopathy and polyneuropathy initiated	IONIS

*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. Akcea is looking to add additional rare disease medicines to its pipeline, both from Ionis and third parties

AKCEA THERAPEUTICS

Advancing Broad Pipeline to Commercialization

NOVARTIS

AKCEA-APO(a)-L_{Rx}

- ✓ Granted Fast Track Designation by the U.S. FDA
- ✓ First medicine that specifically targets Lp(a) - a genetic risk factor for CVD
- ✓ Phase 3 Lp(a) Horizon study is up and running and the first patients are on treatment

IONIS™

AKCEA-APOCIII-L_{Rx}

- ✓ Positive topline results in Phase 2 study
- ✓ 90% of patients at the highest monthly dose reached TG levels below the recognized threshold for CV risk
- ✓ Plan to present more detailed data at a future conference
- ✓ On track to initiate the Phase 3 study for FCS later this year

Pfizer

vupanorsen[1]

- ✓ Positive topline results in Phase 2 study
- ✓ Met the primary endpoint – TG lowering as well as significant reduction in additional lipid parameters and ANGPTL3
- ✓ Plan to present detailed results at a future medical congress

IONIS™

AKCEA-TTR-L_{Rx}

- ✓ CARDIO-TTransform and NEURO-TTransform Phase 3 studies underway
- ✓ Potential to be an important treatment option
- ✓ Continue to build on our expertise and expand commitment within the TTR community

[1]ANGPTL-3-L_{RX}

All medicines were discovered and either developed by Ionis or co-developed by Ionis and Akcea

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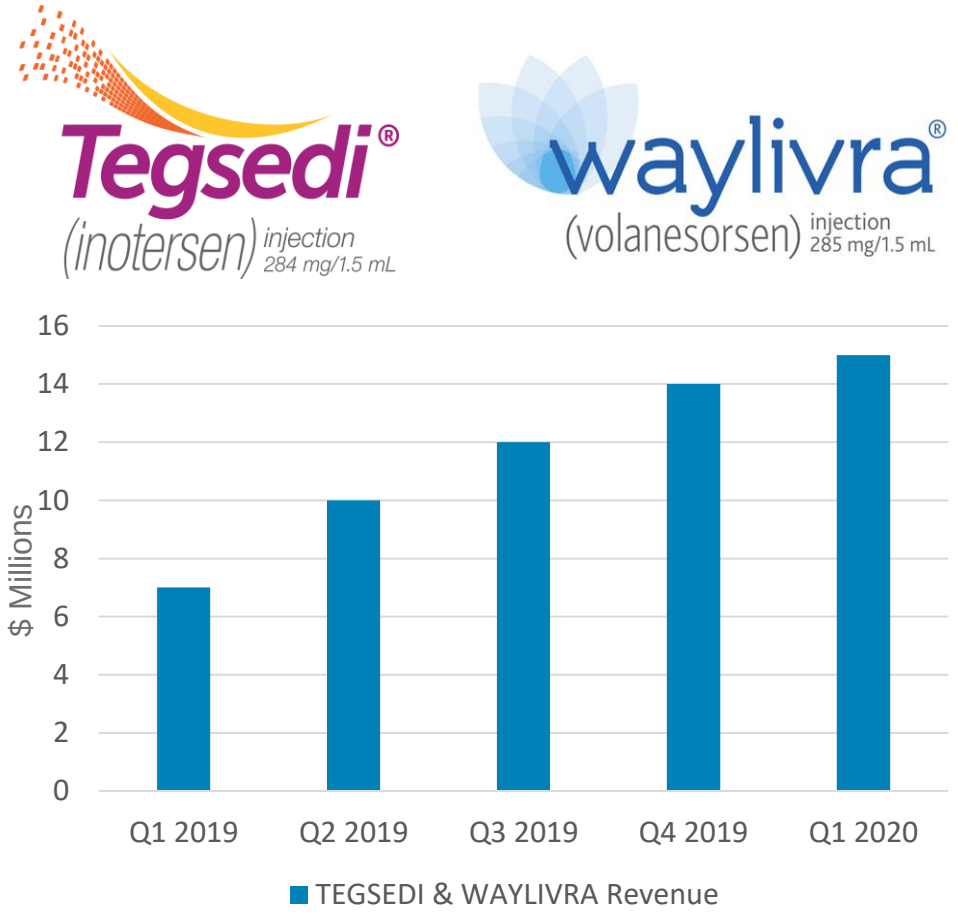
Financials

Q1 2020 Total Revenue	**$16M**
Q1 2020 Product Revenue	**$15M**
Cash and short-term Investments as of March 31, 2020	**$421M**



- Strong balance sheet positions Akcea well to continue to execute on the ongoing launches and broaden the pipeline

First Quarter Achievements

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Strong start to 2020

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Continued sequential growth for TEGSEDI and WAYLIVRA

Steadily advancing broad pipeline of products

- ✓ positive topline data readouts for vupanorsen (ANGPTL3-LRx) and APOCIII-LRx

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