Avadel Pharmaceuticals plc

(NASDAQ: AVDL)

February 2022

Safe Harbor Statements

This presentation may include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. The words “will,” “may,” “believe,” “expect,” “anticipate,” “estimate,” “project” and similar expressions, and the negatives thereof, identify forward-looking statements, each of which speaks only as of the date the statement is made. Although we believe our forward-looking statements are based on reasonable assumptions within the bounds of our knowledge of our business and operations, our business is subject to significant risks, and, as a result, there can be no assurance that actual results of our research, development and commercialization activities and our results of operations will not differ materially from the results contemplated in such forward-looking statements. These risks include: (a) risk relating to potential negative impacts resulting from public health epidemics, such as the current COVID-19 pandemic (including any subsequent waves of same), on our employees, contractors, government entities (e.g., the US Food & Drug Administration), and clinical trial sites, as well as the global economy; (b) risks relating to our investigational FT218 sodium oxybate product, including risks that (i) the FDA may determine there are deficiencies in the NDA for FT218, may delay approval, or may never approve the NDA for FT218, (ii) FT218 may not have the therapeutic benefits we anticipate, (iii) the long-term safety and maintenance of efficacy data generated from the RESTORE study may be delayed, may not be completed, or may include unanticipated results, (iv) the commercial launch of FT218 could be delayed or not occur at all, (v) FT218 may not achieve commercial acceptance or may not align with Company forecasts/projections, if approved and launched, and (vi) other companies may develop competing products or such products may receive FDA approval before FT218; (c) risks that our projected financial performance, including, but not limited to projected revenues, expenses, and use of cash on hand may differ materially from such projections; and (d) the other risks, uncertainties and contingencies described in the Company's filings with the U.S. Securities and Exchange Commission, including our annual report on Form 10-K for the year ended December 31, 2020, which we filed with the Securities and Exchange Commission (SEC) on March 9, 2021, and subsequent SEC filings. You should not place undue reliance on forward-looking statements, which speak only as of the date they are made and are not guarantees of future performance. We do not undertake any obligation to publicly update or revise these forward-looking statements.

Avadel is a global biopharmaceutical company focused on transforming medicines to transform lives – starting with narcolepsy.

Avadel™

Avadel: All the Components for Success

7 Years
of **R&D experience** within narcolepsy

FT218
a differentiated investigational oxybate product designed to be **taken just once** at bedtime

Orphan Drug Designation
granted by FDA as FT218 may be clinically superior to the 2x-nightly formulation of sodium oxybate

Clinically meaningful improvement for two prominent symptoms of narcolepsy demonstrated in **pivotal Phase 3 REST-ON**

Conducting **RESTORE Study**
an OLE/switch study of FT218

FT218 NDA Review
ongoing with FDA

The current oxybate market value:
~$1.8B

Represents only:
~40%

of oxybate **eligible patients in the U.S.**

Oxybate eligible patients ranked once at bedtime dosing (FT218) as the **most important driver** of their treatment preference

16 Years
intellectual property protection – until mid-2037; additional patent applications pending

Avadel

Management Team

Gregory Divis
Chief Executive Officer,
Board of Directors Member

Schering-Plough · Lumara Health · SANOFI

Richard Kim
Chief Commercial Officer

Schering-Plough · Bristol-Myers Squibb · Intercept

Doug Williamson
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Lundbeck · parexel · Lilly

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Technical Operations

patheon by Thermo Fisher Scientific · BANNER LIFE SCIENCES

Jerad Seurer
Vice President,
General Counsel

Mallinckrodt Pharmaceuticals · WYATT

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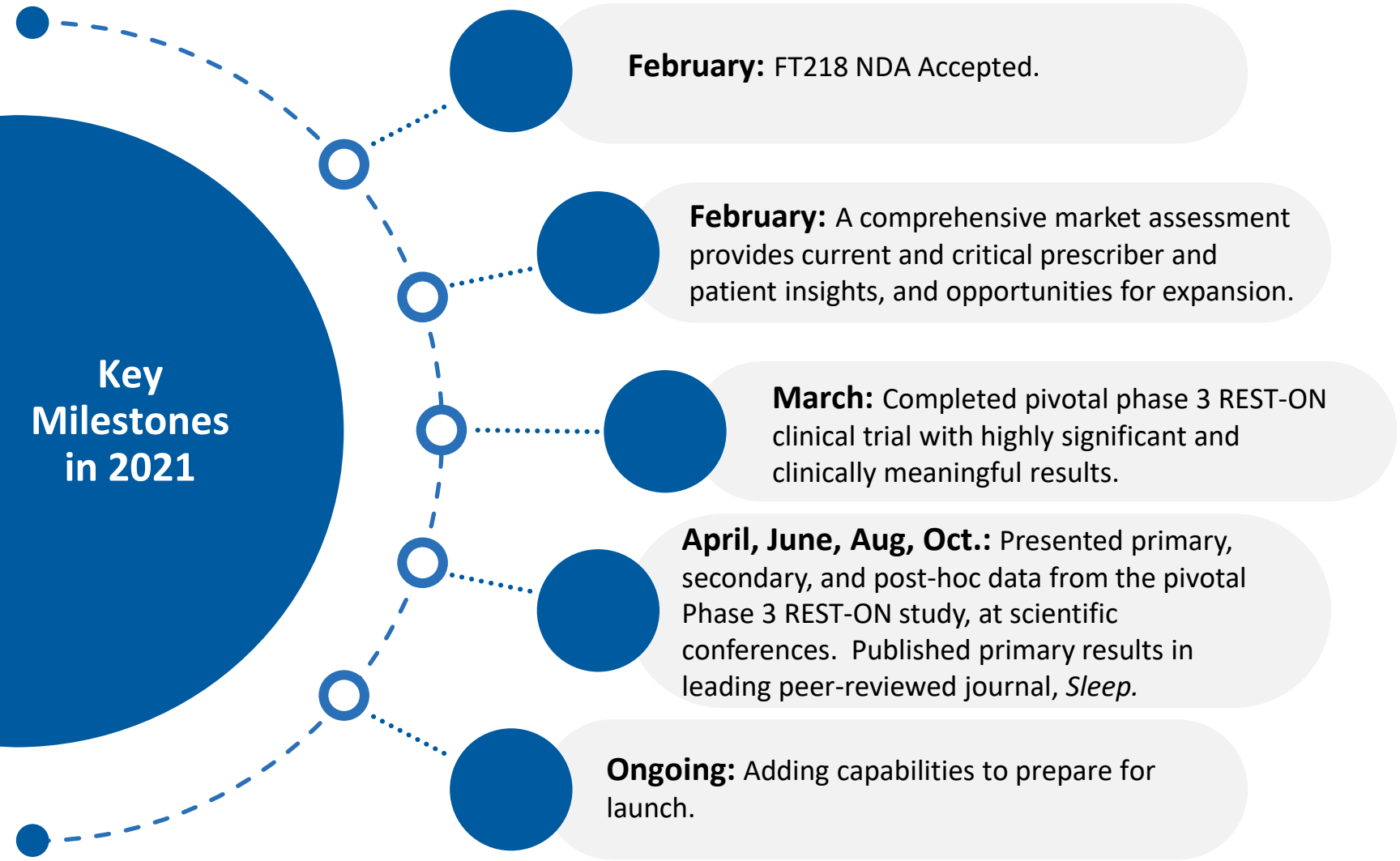
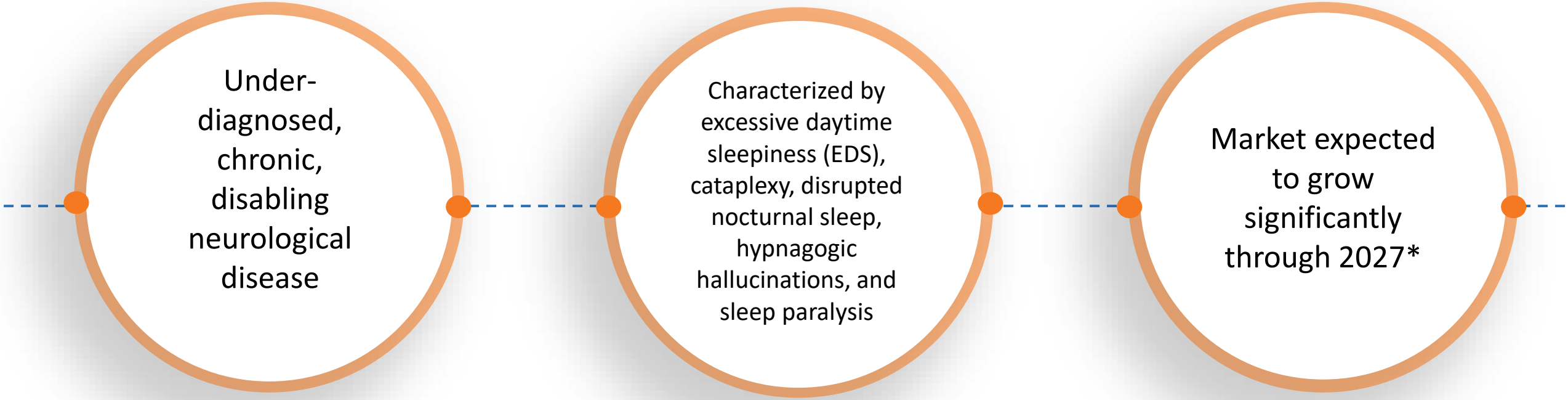
Avadel Positioned for Success and Poised for the Future



Upcoming Milestones

- **FDA review of FT218 NDA** ongoing
- **RESTORE study –** generating long term safety/tolerability data and patient preference
- Add **Sales Force** post - approval; Complete development of **REMS program**; Build of **commercial supply** following PDUFA

Characteristics of Narcolepsy – Serious Disease with Large Unmet Need

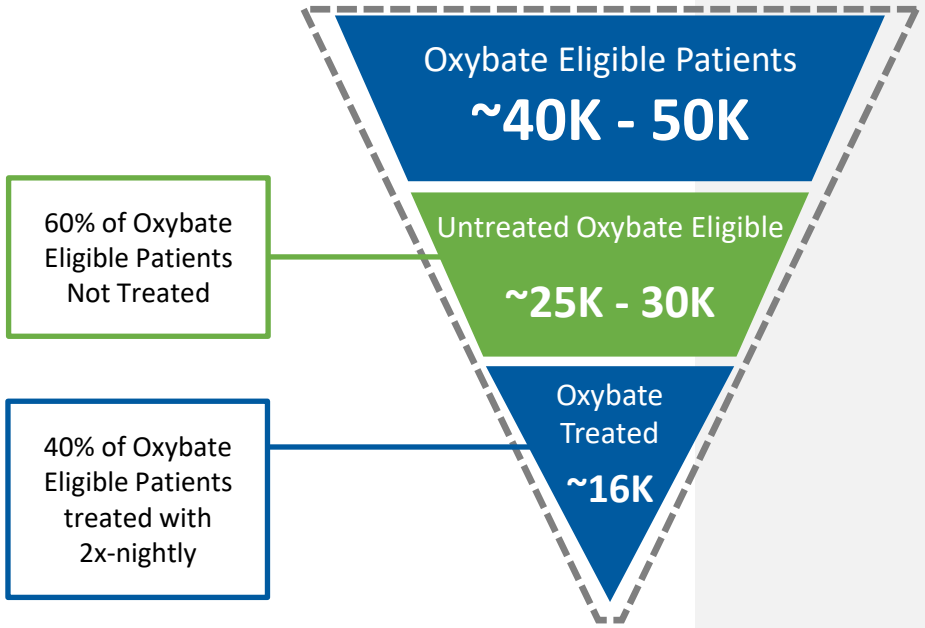


Oxybate is the current standard of care (SoC) for both cardinal symptoms of narcolepsy:

- **Excessive daytime sleepiness** (EDS)
- **Cataplexy:** a sudden loss of muscle tone, which can be triggered by strong emotion

Notes: *Narcolepsy Drugs Market by Type, Application, and Drug Formulation: Global Opportunity Analysis and Industry Forecast, 2019 - 2026 Source: Research and Markets Syndicated Report – October 2019

Significant Unmet Need in the Multi-billion Dollar Sodium Oxybate Market



- Once-at-bedtime dosing **ranked higher in importance** than efficacy and side effect profile*
- **Significant opportunity** to capture a meaningful market share of a multi-billion oxybate-eligible patient population
- **~60%** of oxybate-eligible patients are not currently receiving treatment primarily due to 2x-nightly dosing-related challenges[1] represents opportunity for market expansion
- **~40%** of oxybate-eligible patients currently receiving 2x-nightly treatment represents existing $1.8B annual market

Notes: *Data based on in-depth commercial research conducted on behalf of Avadel, which included over 200 sodium oxybate prescribers, over 220 current or previously treated SO patients, greater than 75 caregivers, 20 office and nursing staff from sodium oxybate treating offices, and 15 large national and regional health plans and PBMs

Oxybate Treatment and Dosing Opportunity

Oxybate is the SoC for treating EDS and cataplexy in narcolepsy patients

2x-Nightly Dosing

All approved oxybate therapies require 2x-nightly dosing

- Sodium oxybate approved by FDA for treatment of cataplexy in narcolepsy in 2002
- Sodium oxybate approved by FDA for treatment of EDS in narcolepsy in 2005
- Mixed salts formula of sodium oxybate approved by FDA to treat EDS and cataplexy in 2020
- Authorized generic versions of sodium oxybate expected to enter market in 2023

Once-at-Bedtime Dosing

FT218 will be the only once-at-bedtime oxybate

- NDA review ongoing
- Pivotal Phase 3 REST-ON trial data demonstrated clinically meaningful improvement for two cardinal symptoms of narcolepsy, EDS and cataplexy, as well as improvements in disturbed nocturnal sleep

A New Treatment Paradigm is Welcomed by Physicians and Patients

There is high unmet need in patients treated with the 2x-nightly product

"… I don't know of another medication where the patient has to wake up in the middle of the night to take it again, this is a serious problem for patients that already have a sleep disorder …"

Sleep Specialist KOL,
Major Academic Hospital SleepCenter in PA

"… The dosing schedule makes it complicated. It's hard for them to wake up, so they may miss their second dose or take it at the wrong time. It's also a burden on their spouse or parents or roommates …"

Primary Care Physician,
Private Clinic in NJ

81%* of physicians would prescribe FT218

Notes: *Data on file - proprietary market research

Investigational FT218 is Positioned to Disrupt the Narcolepsy Market

Targeting Orphan Disease

~40 – 50K

oxybate eligible patients in U.S.; only 16K currently treated with 2x nightly oxybate

Dissatisfaction with 2x-nightly oxybate primarily due to dosing

~50%

of new patients

on 2x nightly discontinue treatment within one year

Differentiated Solution

FT218 will be the only available

Once-at-bedtime

oxybate treatment, if approved

Positive Phase 3 Clinical Results

Phase 3

study for FT218 reported clinically meaningful improvement for two prominent symptoms of narcolepsy

Focused Strategy

Market preparation

underway to maximize share of a multi-billion market, with opportunities to expand

All the Capabilities to Succeed

Avadel's Proprietary Drug Delivery Technology for Once-at-Bedtime Delivery

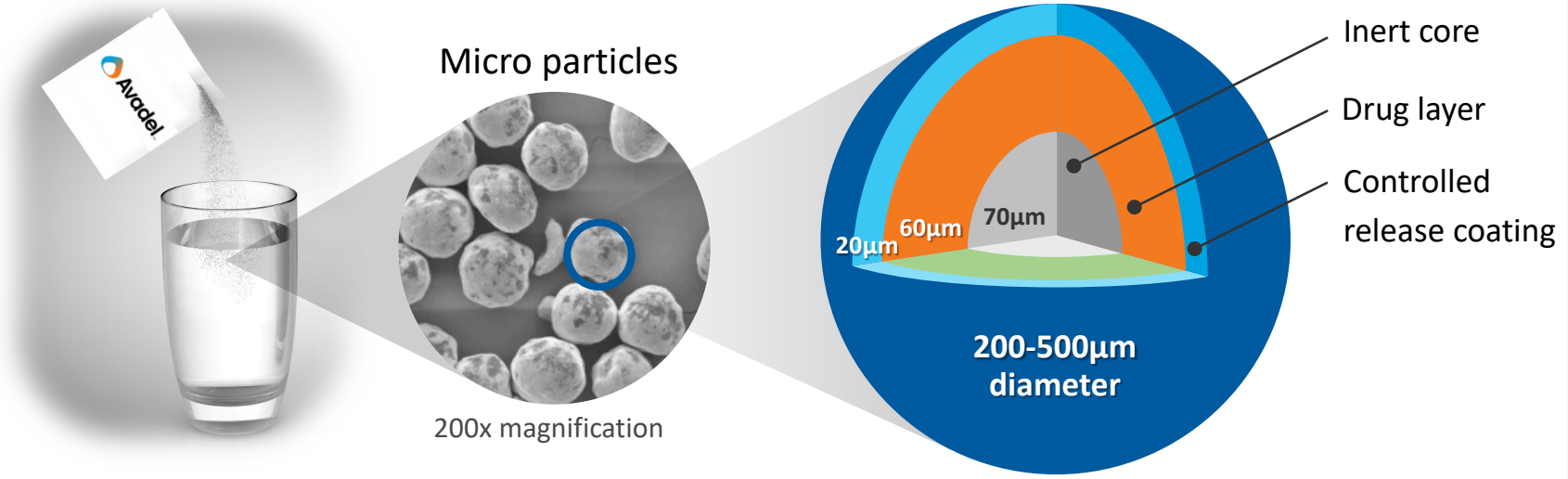
The Technology

Contains thousands of microparticles

- Each is a miniature delivery system

Microparticulate design can be adapted to drug's specific challenges

- Modify coatings / thickness



The Advantages

- Controlled delivery of small molecule drugs taken orally
- Potential to improve efficacy, reduce toxicity, improve compliance

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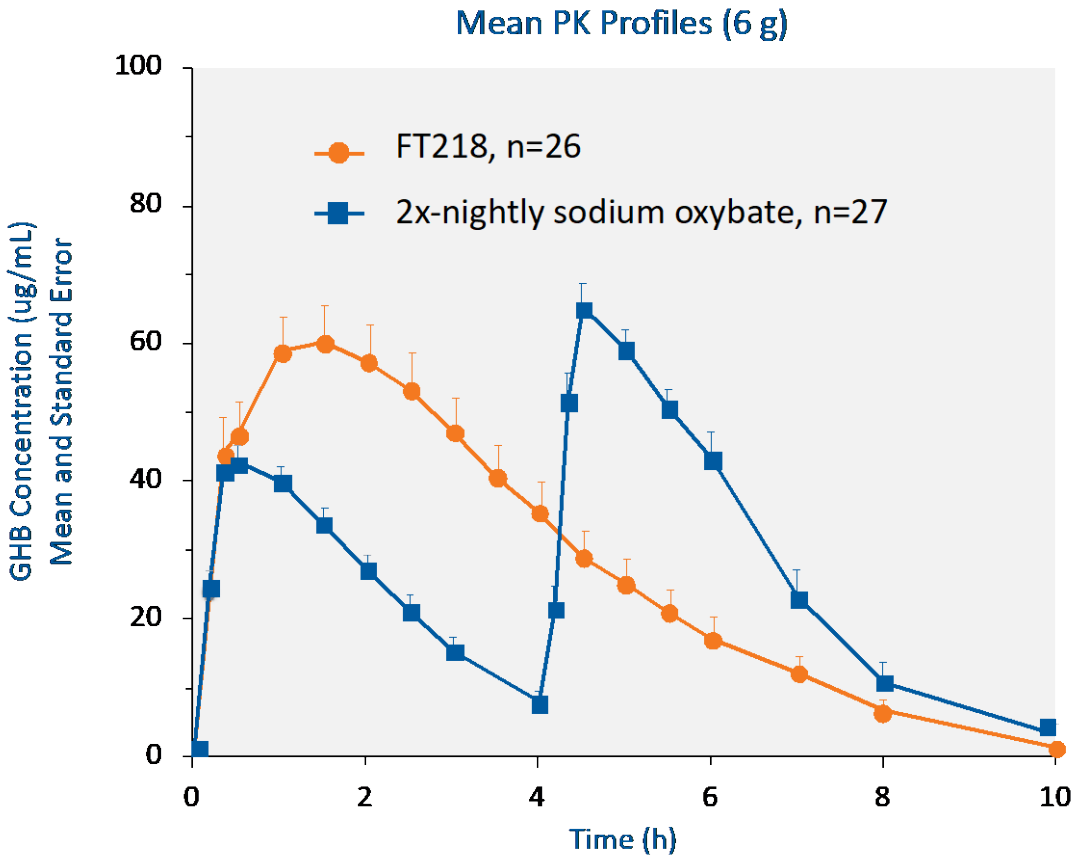
PK Profile Optimized for Once-Nightly Dosing



Comparison to 2x-Nightly

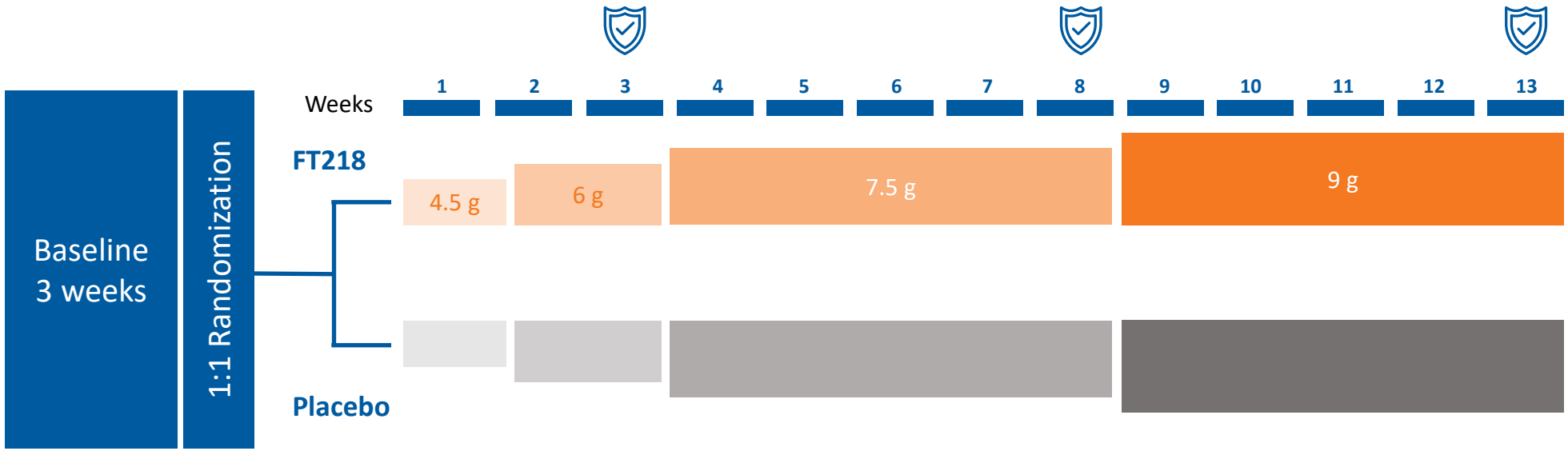
Single pre-measured nightly dose	**Advantage**
No middle-of-the-night dosing	**Advantage**
Overall exposure (AUC) – bioequivalent to SoC	**Similar**
Onset time	**Similar**

Adequate drug concentrations maintained throughout the night and gradual decline to lowest levels by 8-10 hours after dosing

Pivotal Phase 3 REST-ON Trial

REST-ON was a pivotal Phase 3 double-blind, randomized, placebo-controlled trial

- Assessed the efficacy and safety of investigational FT218, an extended-release formulation of sodium oxybate, for the once-at-bedtime treatment of excessive daytime sleepiness and cataplexy in narcolepsy
- Special Protocol Assessment agreement with FDA
- Dosed a total of 212 patients, completed in March 2020 and announced positive topline data in April 2020



Positive Topline Results Across All Co-Primary Endpoints For All Doses

Once-at-bedtime FT218 at 9 g demonstrated a high degree of statistical significance, compared to placebo, for each of the three co-primary endpoints

FT218 7.5 g and 6 g also demonstrated statistical significance for the three co-primary endpoints, compared to placebo

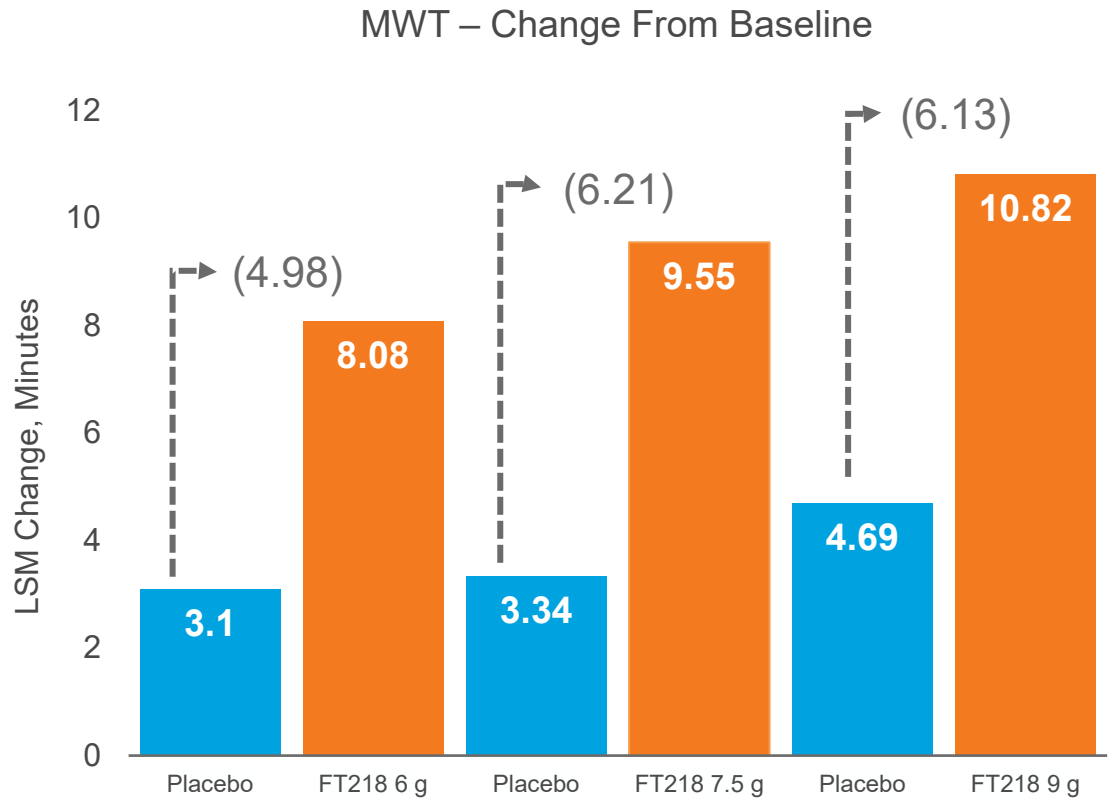
FT218 was generally well-tolerated; commonly known sodium oxybate adverse reactions occurred at low rates at the highest dose (9 g)

- Improvement of excessive daytime sleepiness
- Improvement of the clinician's overall assessment of the patients' functioning
- Reduction in cataplexy attacks

Statistically Significant Results on the MWT Compared to Placebo

Change From Baseline in Maintenance of Wakefulness Test (MWT)

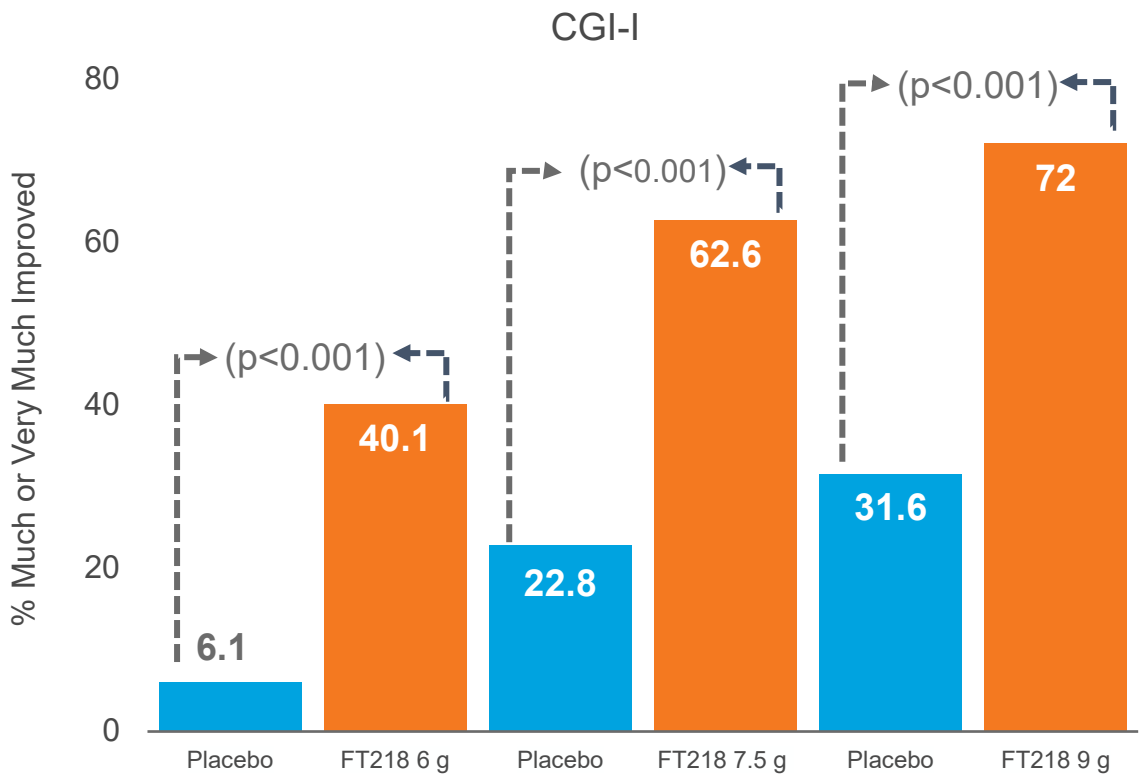
- p<0.001 for all three doses compared to placebo
- Significant change at Week 3 for the lowest dose assessed
- Efficacy sustained through Week 12
- 7.5 g achieved similar efficacy to 9 g, by Week 8



Significant Improvement in CGI-I Compared to placebo

Clinical Global Impression-Improvement (CGI-I) - Percent Much or Very Much Improved

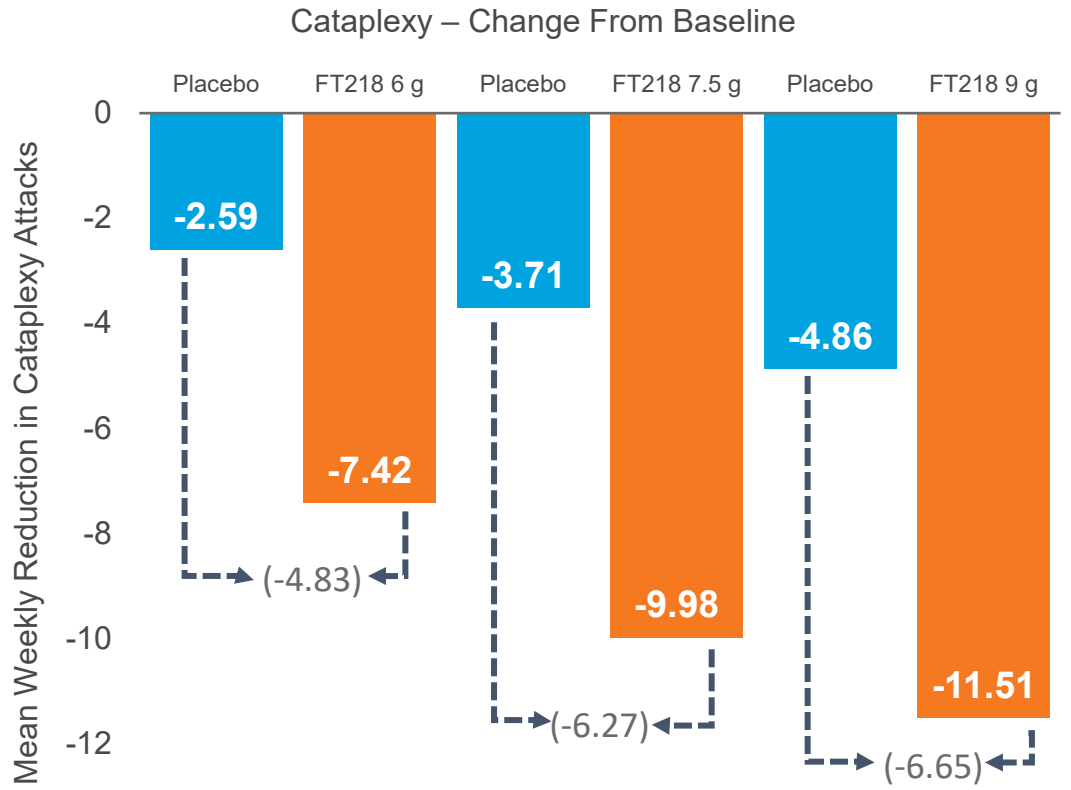
- Odds ratio between FT218 6 g and placebo at week 3 was 10.29 (p<0.001)
- Odds ratio between FT218 9 g and placebo at week 8 was 5.67 (p<0.001)
- Odds ratio between FT218 9 g and placebo at week 13 was 5.56 (p<0.001)



Significant Reduction in Mean Weekly Cataplexy Attacks Compared to Placebo

Change From Baseline in Weekly Cataplexy Attacks

- LS Mean difference between FT218 6 g and placebo was -4.83 (p<0.001)
- LS Mean difference between FT218 7.5 g and placebo was -6.27 (p<0.001)
- LS Mean difference between FT218 9 g and placebo was -6.65 (p<0.001)



FT218 9 g was Generally Well Tolerated

	FT218 (%) | N=77	Placebo (%) | N=80
Any Adverse Drug Reaction (ADR)	35.1	5.0
Any Serious ADR	1.3	0.0
ADR Leading To Discontinuation	3.9	0.0
ADRs ≥2% and greater than placebo in FT218		
Decreased Weight	3.9	0.0
Vomiting	5.2	0.0
Decreased Appetite	2.6	0.0
Dizziness	5.2	0.0
Somnolence	3.9	0.0
Enuresis	9.1	0.0

Strong Secondary Endpoint Data from REST-ON*

Polysomnographic Measures of Sleep Continuity in Patients with Narcolepsy

- FT218 demonstrated significant consolidation of sleep on polysomnography (randomized, n=212) for the 6 g dose at Week 3, the 7.5 g dose at Week 8, and 9 g dose at Week 13 compared to placebo
- Data from the randomized, double-blind, placebo-controlled, multicenter, parallel-group study showed that the mean difference between FT218 and placebo for disturbed nocturnal sleep (shifts from deeper to lighter stages of sleep and wake) was statistically significant (P<0.001) at all doses tested: –22.63 at 9 g (week 13), –17.70 at 7.5 g (week 8), and –11.00 at 6 g (week 3)
- The mean difference between FT218 and placebo for number of arousals was –23.68 (P<0.001) at 9 g, –19.41 (P<0.001) at 7.5 g and –11.29 (P<0.021) at 6 g
- FT218 was generally well tolerated, and the most common adverse reactions were well-known and established sodium oxybate adverse reactions

Daytime Sleepiness, Sleep Quality, Hallucinations, and Sleep Paralysis in Patients with Narcolepsy

- FT218 demonstrated significant (P<0.001) improvement in the Epworth Sleepiness Scale (ESS) versus placebo at all doses tested: LS mean difference –3.86 at 9 g (week 13), –3.16 at 7.5 g (week 8), and –2.06 at 6 g (week 3)
- FT218 showed a statistically significant (P<0.001) improvement compared to placebo at all doses tested for sleep quality and refreshing nature of sleep on a visual analogue scale, and for sleep paralysis on a sleep symptom diary (P=0.037, 0.021, 0.039 at 9, 7.5, 6 g, respectively)
  - FT218 did not demonstrate significant improvement for hypnagogic compared to placebo
- Adverse events were similar to the known sodium oxybate safety profile

Notes: *Posters presented at 2021 American Academy of Neurology Annual (AAN) Meeting; April 2021

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Post Hoc Data Analyses Further Support Clinical Benefit of FT218*

Efficacy by Narcolepsy Subtype

- FT218 demonstrated statistically significant improvement in excessive daytime sleepiness (EDS) at all evaluated doses in patients with narcolepsy subtypes 1 (NT1, with cataplexy) and 2 (NT2, without cataplexy), with greater improvement in measures of EDS, including mean sleep latency on maintenance of wakefulness test (MWT) and Clinical Global Impression-Improvement (CGI-I) in overall condition, compared to placebo.
- The least squares (LS) mean difference in mean sleep latency (in minutes) on MWT between FT218 and placebo was 6.0 for 9 g (week 13), 7.0 for 7.5 g (week 8), and 4.9 for 6 g (week 3) in NT1 patients (all $p<0.001$), and 6.3 for 9 g ($P<0.05$), 4.0 for 7.5 g (P=NS), and 5.3 for 6 g ($P<0.05$) in NT2 patients. The mean difference between FT218 and placebo for number of arousals was –23.68 ($P<0.001$) at 9 g, –19.41 ($P<0.001$) at 7.5 g and –11.29 ($P<0.021$) at 6 g
- A significantly greater percentage of patients with NT1 receiving FT218 were rated as much or very much improved on the CGI-I compared to placebo: 75.5% vs. 35.9% at 9 g, 66.9% vs. 27.9% at 7.5 g, and 39.9% vs. 7.8% at 6 g (all $P<0.001$). A greater percentage of NT2 patients receiving FT218 were rated as much/very much improved at all three doses vs. placebo.

Efficacy by Stimulant Use

- FT218 demonstrated statistically significant improvement in EDS at all evaluated doses in narcolepsy patients with or without stimulant use, with improvement over placebo on MWT and CGI-I.FT218 showed a statistically significant ($P<0.001$) improvement compared to placebo at all doses tested for sleep quality and refreshing nature of sleep on a visual analogue scale, and for sleep paralysis on a sleep symptom diary (P=0.037, 0.021, 0.039 at 9, 7.5, 6 g, respectively)
- The LS mean difference in mean sleep latency (in minutes) on MWT between FT218 and placebo was 6.0 for 9 g (week 13), 5.5 for 7.5 g (week 8), and 5.4 for 6 g (week 3) for patients with concomitant stimulant use (all $P\leq0.001$). For patients not taking stimulants, the LS mean difference was 6.3 for 9 g ($P=0.001$), 7.1 for 7.5 g ($P<0.001$), and 4.2 for 6 g ($P<0.01$).
- More patients receiving FT218 were rated much/very much improved on CGI-I compared to placebo: 80.5% vs. 35.3% at 9 g, 66.3% vs. 26.5% at 7.5 g, and 39.8% vs. 4.4% at 6 g for patients with stimulant use (all $P<0.001$); 55.1% vs. 27.2% at 9 g ($P<0.05$), 54.5% vs. 17.5% at 7.5 g ($P=0.006$), and 40.0% vs. 7.7% at 6 g ($P<0.01$) for patients without stimulant use.

Weight Loss with FT218

- Patients receiving FT218 experienced a significantly greater decrease in weight and body mass index (BMI) from baseline to study end (week 13) compared to placebo.
- At study end, the mean (SD) change in weight from baseline was –1.3 (3.6) kg for patients receiving FT218 compared to 0.2 (2.6) kg for patients receiving placebo. Overall, 17.8% of patients receiving FT218 compared to 3.8% of patients receiving placebo experienced ≥5% weight loss. The mean difference between FT218 and placebo for number of arousals was –23.68 ($P<0.001$) at 9 g, –19.41 ($P<0.001$) at 7.5 g and –11.29 ($P<0.021$) at 6 g
- At study end, the LS mean (SE) change in BMI from baseline was –0.5 (0.13) kg/m^2 for patients receiving FT218 and 0.1 (0.13) kg/m^2 for patients receiving placebo (P=0.001).

Notes: *Posters presented at SLEEP 2021; June 2021

Extensive Additional Data Supports FT218 Above and Beyond Positive Co-Primary Endpoints

- Mean end-of-study Epworth Sleepiness Scale for FT218 of 10.4, from baseline of 16.6
  - Scores of ≥16 characteristic of narcolepsy; scores of ≤10 **considered normal**
- Significant improvements in *disturbed nocturnal sleep (DNS);* DNS present in **~65%** of patients with narcolepsy
  - FT218, as measured by pre-specified endpoints:
    - Reduced nocturnal arousals
    - Reduced sleep stage shifts
    - Improved patient-reported visual analogue scales (VAS) sleep quality
    - Improved VAS on the refreshing nature of sleep
- FT218 demonstrated efficacy in the stratified NT1 ***and*** NT2 subgroups, both in improving EDS and the clinician's overall assessment of functioning (CGI-I)
- FT218 demonstrated improvement in narcolepsy symptoms in <u>both</u> those with and without concomitant stimulant use (post-hoc)
- FT218 demonstrated modest weight loss reduction (post-hoc)

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Landmark Moments for FT218

Program Milestones

Pivotal Phase 3 Data March 2020. Demonstrated clinically meaningful improvement for two prominent symptoms of narcolepsy.

OLE/Switch Study – First Patient Dosed July 2020. Shifting the focus to longer-term safety- and efficacy-related use data, as well as data for HCPs and patients considering switches.

FDA Accepted NDA Submission in February 2021. Review ongoing

Secondary Endpoint Analysis Announced April 2021. Secondary endpoint data from the REST-ON study are consistent with the primary analyses and further reinforce clinical benefit of FT218.

Commercial Strategy. Planning and execution underway: significant opportunity to capture a meaningful market share of oxybate eligible narcolepsy patient population.

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Avadel Financial Summary*

Nine Months, Ended September 30	2021	2020
Product Sales	**$ -**	**$ 22.3**
Cost of Products	-	5.7
Operating Expenses **	**$ 62.5**	**$ 38.6**
R&D Expense	15.0	15.2
SG&A Expense	47.5	23.4
Gain on Sale of Hospital Products	**$ -**	**$ 45.8**
Net (Loss) Income	**$ (55.0)**	**$ 18.3**
Ordinary Shares Outstanding (millions)	58.6	58.2
Cash and Cash Equivalents	**$ 181.1**	**$ 231.6**
Long Term Debt	**$ 143.8**	**$ 143.8**

($ and Shares in millions)

- Expansion of **commercial and medical affairs capabilities**
- **Strong balance sheet** with > $180M of cash to support launch of FT218, if approved
- **Convertible Notes mature Feb. 2023**; $10.79 conversion price

**Refer to Forms 10-Q for quarters ended September 30, 2021 & 2020 filed on November 8, 2021, and November 9, 2020, respectively, for full financial statements and results of operations.*
***Includes only R&D and SG&A. Refer to Forms 10-Q as referenced above for full operating expenses.*

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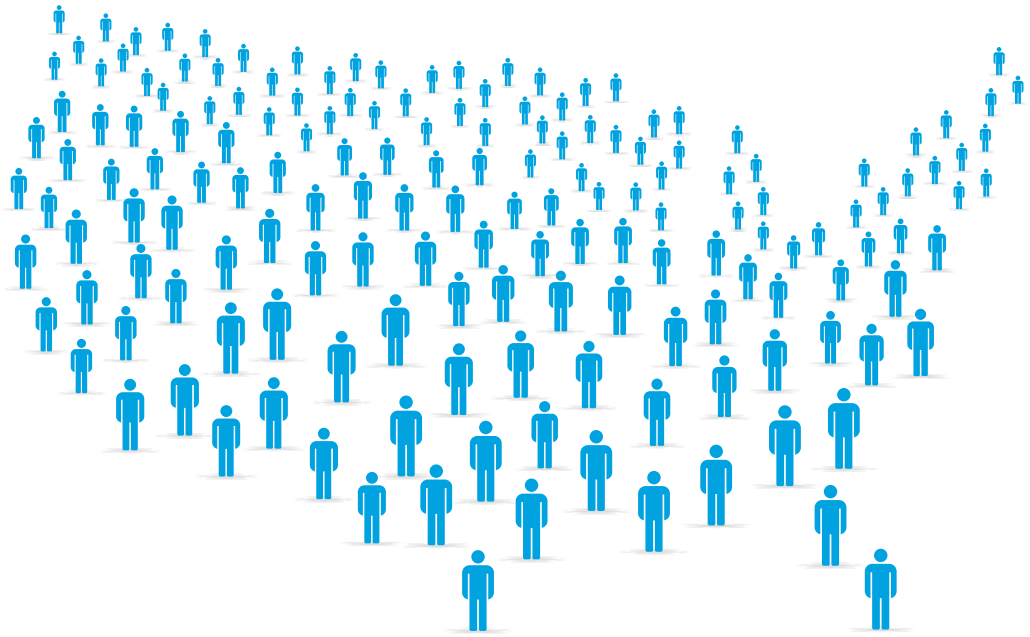
Avadel Poised for the Future

Focused HCP Universe Enables Efficient Product Launch



Plan for Concentrated Market Outreach

- ~450 prescribers make up 50% of current sodium oxybate total prescription volume in U.S.
- ~1,600 prescribers make up > 80% of current sodium oxybate total prescription volume in U.S. NDA approval

U.S. Commercial Team: Building an exceptional customer-facing team

- Commercial leadership team complete
- Market access and distribution personnel hiring on-going
- Salesforce of ~ 50 people onboarding post NDA approval

Avadel

Avadel: All the Components for Success

7 Years
of **R&D experience** within narcolepsy

FT218
a differentiated investigational oxybate product designed to be **taken just once** at bedtime

Orphan Drug Designation
granted by FDA as FT218 may be clinically superior to the 2x-nightly formulation of sodium oxybate

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an OLE/switch study of FT218

FT218 NDA Review
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The current oxybate market value:
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Represents only:
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Oxybate eligible patients ranked once at bedtime dosing (FT218) as the **most important driver** of their treatment preference

16 Years
intellectual property protection – until mid-2037; additional patent applications pending

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Thank You