Sage Therapeutics®

PRECEDENT Study

PRECEDENT Study Results Call

April 17, 2024

Safe Harbor Statement

PRECEDENT Study

- The slides presented today and the accompanying oral presentations contain forward-looking statements, which may be identified by the use of words such as “may,” “might,” “will,” “should,” “can,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “opportunity”, “goal”, “mission”, “potential,” “target”, or “continue,” and other similar expressions.
- Forward-looking statements in this presentation include statements regarding: our expectations with respect to the timing of reporting of results from ongoing clinical trials of dalzanemdor; our belief in the unmet need for new treatment options for brain health disorders; the potential for positive results from ongoing studies of dalzanemdor in HD and AD, despite negative results from the PRECEDENT study in PD; our views regarding possible distinctions among indications as a result of the underlying pathophysiology and symptomatology in PD; our statements as to the potential for dalzanemdor in the treatment of cognitive impairment due to certain neurodegenerative diseases; our expectations regarding our cash runway; and the mission, goals, opportunity and potential for our business.
- These forward-looking statements are neither promises nor guarantees of future performance, and are subject to a variety of risks and uncertainties, many of which are beyond our control, whichcould cause actual results to differ materially from those contemplated in these forward-looking statements, including the risk that:
  - The results of our ongoing clinical studies of dalzanemdor in HD and AD may be negative like the results from the PRECEDENT study in MCI in PD. The possible distinctions among indications as a result of the underlying pathophysiology and symptomatology in PD may not prove to be relevant in the context of clinical trials of dalzanemdor. The ongoing studies of dalzanemdor may not meet their primary or key secondary endpoints. Results of earlier trials in HD and AD may not be replicated in ongoing or future trials. Clinical and nonclinical data we generate in the course of the dalzanemdor development program may not be sufficient to move to the next phase of development for an indication or may not support further development at all.
  - We may encounter unexpected safety or tolerability issues with respect to dalzanemdor or any of our product candidates or marketed products. We may encounter different or more severe adverse events at higher doses, different frequency or length of dosing or in new indications.
  - We may encounter delays in initiation, conduct or completion of ongoing or future clinical trials or reporting of clinical trial results, including as the result of the need to meet with regulatory authorities, or as a result of actions arising from those meetings, that may impact our ability to meet our expected time-lines.
  - The FDA may not agree with our view of the data we generate from our development efforts at any stage. Decisions or actions of the FDA or other regulatory agencies may affect the initiation, timing, design, size, or progress of ongoing or future clinical trials or the regulatory pathway for dalzanemdor in an indication or our ability to proceed with further development. The FDA may ultimately decide that the design or results of completed, ongoing and planned clinical trials, even if positive, are not sufficient for the next phase of development or ultimately for regulatory approval of dalzanemdor in any indication or of any of our other product candidates in any indications that are the focus of our development programs and plans.
  - Even if dalzanemdor or any of our other product candidates is successfully developed and approved, the number of patients with the diseases or disorders our products treat or the subset of such patients we believe will use our products, the need for new treatment options, and the actual market for such products may be smaller than our current estimates.
  - We may not be able to obtain and maintain adequate intellectual property protection or other forms of data and marketing exclusivity for dalzanemdor or any of our other products, or to defend our patent portfolio against challenges from third parties.
  - We may face competition from others developing products or with approved products for similar uses as those for which dalzanemdor or any of our other product candidates are being developed or for which our marketed products are sold.
  - Our operating expenses may be higher than forecasted and we may face unexpected expenses which could cause us to change our plans. Our revenues may be lower than we expect, including if we do not achieve market acceptance of ZURZUVAE in the treatment of women with PPD or if we do not achieve our access/reimbursement goals in this indication, or if our launch for other reasons is not as successful as we expect. We may not achieve expected milestones that trigger cash payments on the timing we expect, or at all. For these and other reasons, our expectations with respect to financial strength and cash runway may not prove to be accurate. We may need or choose to raise additional funding, which may not be available on acceptable terms, or at all.
  - We may not be able to establish and maintain key business relationships with third parties on acceptable terms or we may encounter problems with the performance of such third parties.
  - We may encounter technical and other unexpected hurdles in the manufacture, development or commercialization of our products.
  - Any of the foregoing or other factors may negatively impact our ability to achieve our goals, mission, opportunities, plans or expectations for our business and the potential for value creation.
- For additional disclosure regarding these and other risks Sage faces, see the disclosure contained in the "Risk Factors" section of our most recent report, and in our other public filings, with the Securities and Exchange Commission, available on the SEC's website at http://www.sec.gov. Any forward-looking statement represent our views only as of today, and should not be relied upon as representing our views as of any subsequent date. We undertake no obligation to update or revise the information contained in this presentation, whether as a result of new information, future events or circumstances or otherwise.

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Sage Therapeutics call participants

PRECEDENT Study

Barry Greene
Chief Executive Officer

Laura Gault
Chief Medical Officer

1. **Introduction**
   Barry Greene, *Chief Executive Officer*

2. **Review of PRECEDENT Phase 2 Data**
   Laura Gault, *Chief Medical Officer*

3. **Closing Remarks and Q&A**
   Barry Greene, *Chief Executive Officer*

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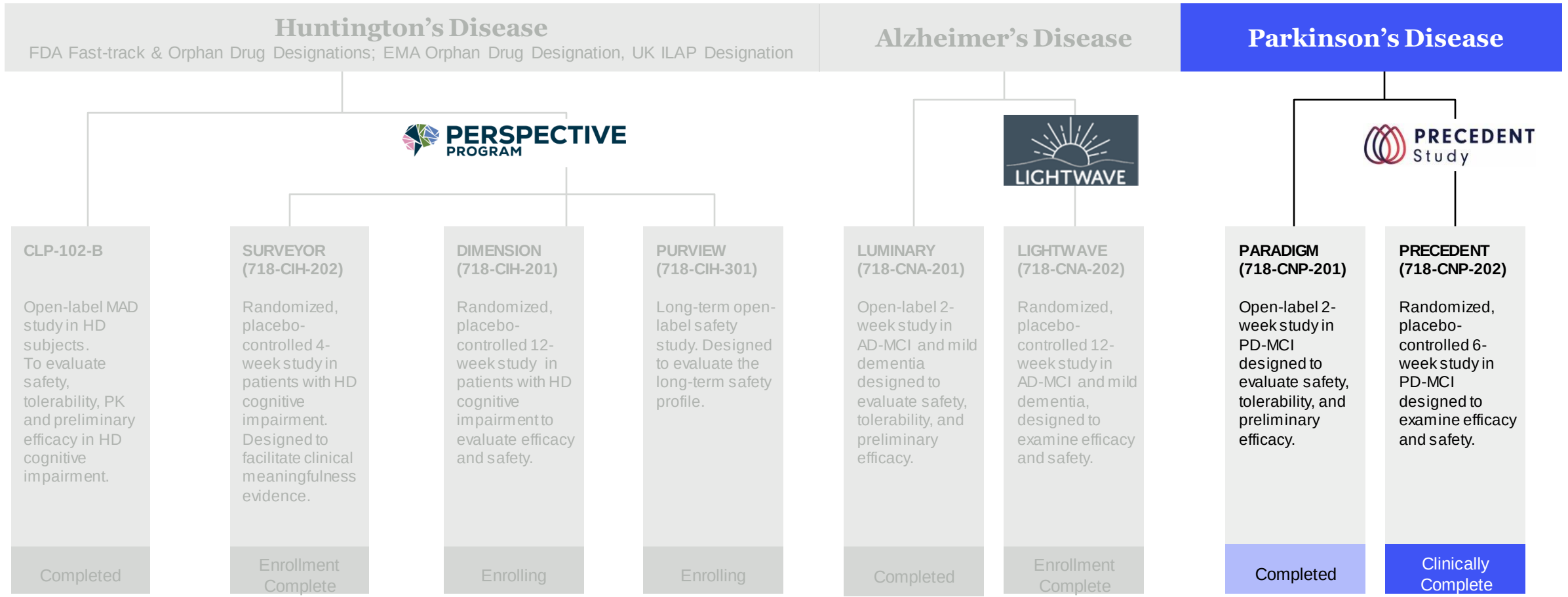
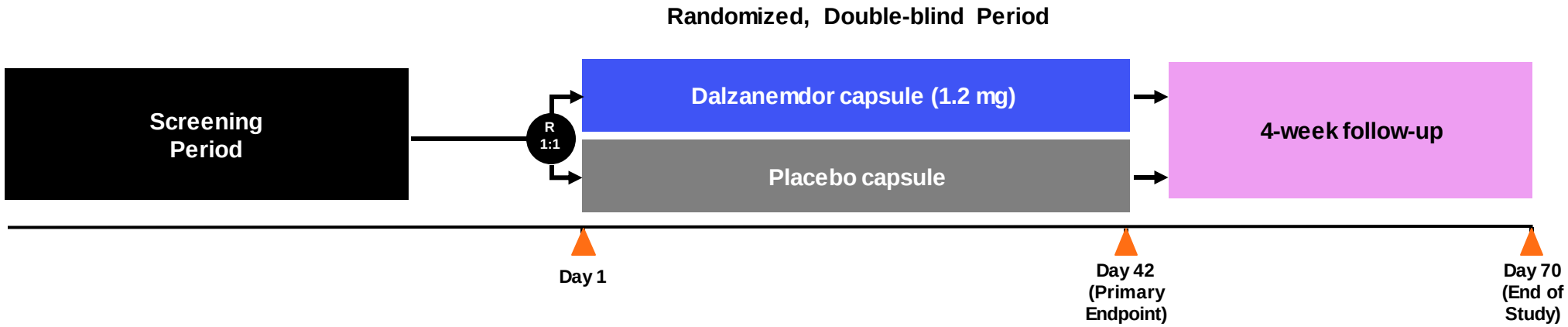
The Dalzanemdor Clinical Development Program



Phase 2 PRECEDENT Study Design



Objectives

- To evaluate the effect of dalzanemdor (SAGE-718) on cognitive performance in participants with Mild Cognitive Impairment (MCI) in Parkinson's Disease (PD)
- To evaluate the safety and tolerability of dalzanemdor (SAGE-718) oral capsule in participants with PD-MCI

Primary Endpoint: Change from Baseline to Day 42 in the Wechsler Adult Intelligence Scale-IV (WAIS-IV) Coding test

Secondary Endpoints: Proportion of participants experiencing treatment emergent adverse events (TEAEs) and severity of TEAEs. Number of participants who withdraw due to adverse events (AEs)

Other Endpoints: Cognitive and functional endpoints

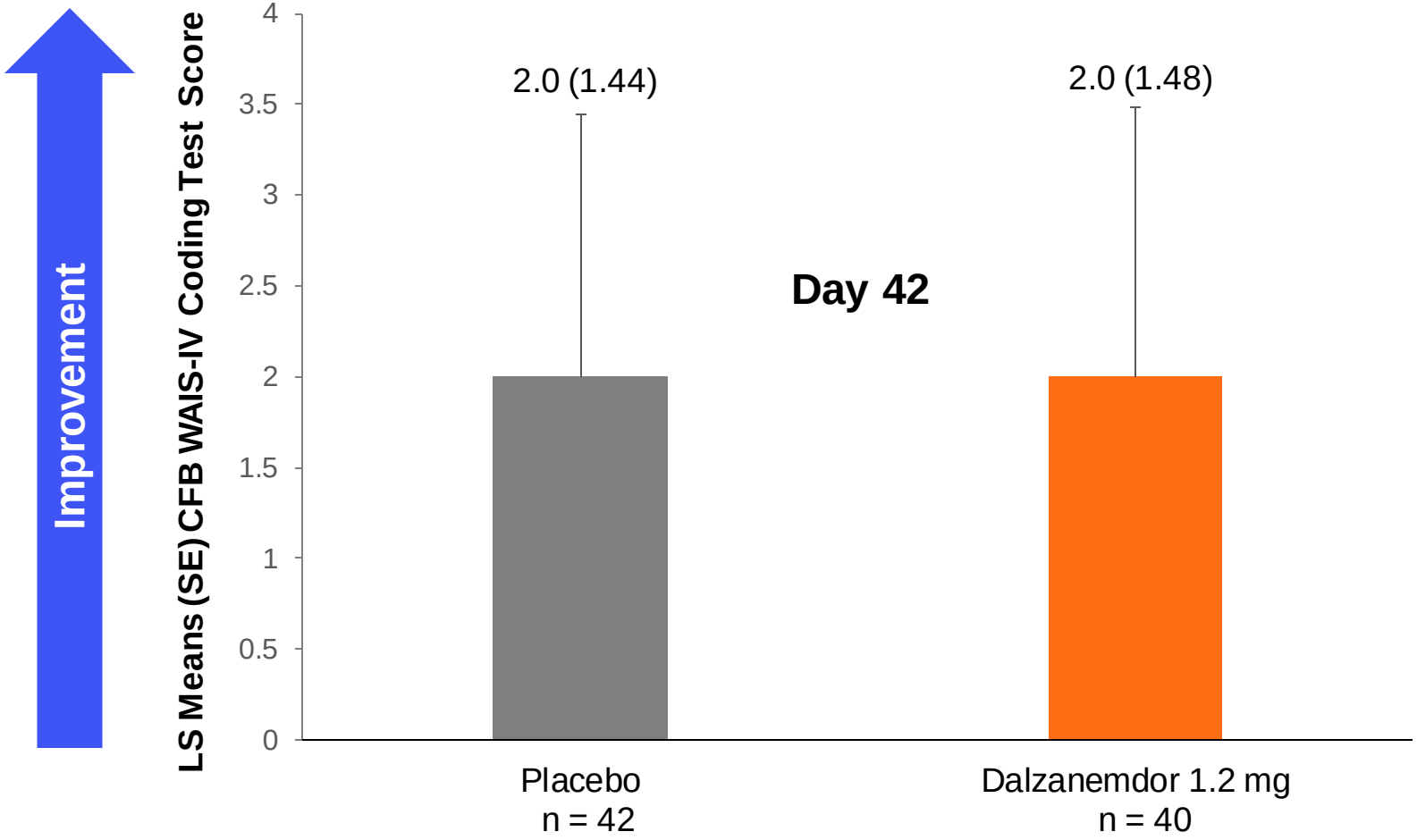
PRECEDENT Study: Participant Disposition, Demographics and Characteristics at Baseline

		Placebo (n=43)	Dalzanemdor 1.2 mg (n=43)
Participant Disposition			
Randomized, n		43	43
Dosed, n		43	43
Completed treatment, n (%)		41 (95.3)	39 (90.7)
Discontinued treatment*, n (%)		2 (4.7)	4 (9.3)
Completed study, n (%)		42 (97.7)	39 (90.7)
Demographics and Characteristics at Baseline			
Age, mean (SD), y		68.5 (4.76)	68.2 (6.37)
Sex, n (%)	Male	34 (79.1)	29 (67.4)
Race, n (%)	Black/African American	1 (2.3)	2 (4.7)
	White	41 (95.3)	40 (93.0)
	Other†	1 (2.3)	1 (2.3)
Ethnicity, n (%)	Hispanic/Latino	11 (25.6)	6 (14.0)
Years since initial diagnosis of PD, mean (SD), y		5.8 (3.72)	4.3 (3.90)
MDS-UPDRS Part III, TMS, mean (SD)		33.5 (13.61)	35.3 (17.36)
Modified Hoehn and Yahr Stage, n (%)	≤2	29 (67.4)	22 (51.2)
	>2	14 (32.6)	21 (48.8)
MoCA Educational Adjusted Total Score, mean (SD)		22.9 (1.88)	23.0 (1.65)

*Participants who discontinued treatment could complete remaining study visits through Day 70. †Placebo group: American Indian or Alaska Native; Dalzanemdor group: Native Hawaiian or Pacific Islander.
PD = Parkinson's Disease; MDS = Movement Disorders Society; MoCA = Montreal Cognitive Assessment; SD = standard deviation; TMS = Total Motor Score; UPDRS = Unified Parkinson's Disease Rating Scale.
Data on file.

PRECEDENT Study: Primary Endpoint

Change from Baseline in WAIS-IV Coding Test Score* at Day 42† (FAS)



Primary Endpoint

WAIS-IV Coding Test Score
CFB at Day 42
LS Means (SE) Dalzanemdor vs. Placebo:
2.0 (1.48) vs. 2.0 (1.44)
TRT Difference (95% CI):
-0.0 (-4.13, 4.09)
p-value = NS

*WAIS-IV Coding Test score = Total correctly decoded items completed in 120 seconds. †Baseline mean (SD) WAIS-IV Coding Test score: 40.5 (13.27) placebo; 39.7 (13.06) dalzanemdor.
CFB = change from baseline; CI = confidence interval; FAS = full analysis set; LS = least squares; NS = non-significant; SE = standard error; TRT = treatment; WAIS-IV = Wechsler Adult Intelligence Scale-IV.
Data on file.

PRECEDENT Study: Safety/Tolerability[1,2]

	Placebo (n=43)	Dalzanemdor 1.2 mg (n=43)
At least 1 TEAE, n (%)	27 (62.8)	21 (48.8)
Severe TEAE, n (%)	2 (4.7)	2 (4.7)
SAE, n (%)	2 (4.7)	3 (7.0)
Deaths during study*, n (%)	0	0
Discontinuation of treatment due to TEAEs, n (%)	1 (2.3)	0
Discontinuation from study due to TEAEs, n (%)	0	0
TEAEs >5% in any treatment group		
Urinary tract infection, n (%)	3 (7.0)	3 (7.0)
Fall, n (%)	2 (4.7)	3 (7.0)
Cough, n (%)	1 (2.3)	3 (7.0)

Dalzanemdor 1.2 mg was generally well tolerated

- The incidence of TEAEs in the dalzanemdor group was 48.8% and 62.8% in the placebo group.
  - The vast majority of TEAEs were mild to moderate in severity.
- No participants in the dalzanemdor group and 1 (2.3%) participant in the placebo group discontinued study drug due to TEAEs.
- No TEAEs in either treatment group led to withdrawal from the study.
- No SAEs were considered related to dalzanemdor.
- No deaths were reported during the study.*
- The most common TEAEs in the dalzanemdor group (observed in >5% of participants in either treatment group) were urinary tract infection, fall, and cough.
- There was no signal for increased suicidal ideation or behavior compared to baseline as assessed by C-SSRS.

SAE = serious adverse event; TEAE = treatment-emergent adverse event; C-SSRS = Columbia Suicide Severity Rating Scale.
*One death was reported in the placebo group after the end of the study and was reported as not related to study drug by the investigator.
1. PRECEDENT Press Release. April 17, 2024. Accessed April 17, 2024. https://investor.sagerx.com/press-releases. 2. Data on file.

Additional Phase 2 data expected for dalzanemdor over the course of 2024

PRECEDENT Study

EARLY 2024 (Q1/Q2)

- Topline data from the **PRECEDENT Study in PD**

MID 2024 (Q2/Q3)

- Topline data from the **SURVEYOR Study in HD**

LATE 2024 (Q3/Q4)

- Topline data from the **LIGHTWAVE Study in AD**
- Topline data from the **DIMENSION Study in HD**

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Q&A

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