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RESEARCH ARTICLE

T2 Protect AD: Achieving a rapid recruitment timeline in a multisite clinical trial for individuals with mild to moderate Alzheimer's disease

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Abstract

Introduction: The reporting of approaches facilitating the most efficient and timely recruitment of Alzheimer's disease (AD) patients into pharmacologic trials is fundamental to much-needed therapeutic progress.

Methods: T2 Protect AD (T2), a phase 2 randomized placebo-controlled trial of troriluzole in mild to moderate AD, used multiple recruitment strategies.

Results: T2 exceeded its recruitment target, enrolling 350 participants between July 2018 and December 2019 (randomization rate: 0.87 randomizations/site/month, or 3-fold greater than recent trials of mild to moderate AD). The vast majority (98%) of participants were enrolled during a 10-month window of intense promotion in news media, TV and radio advertisements, and social media. The distribution of primary recruitment sources included: existing patient lists at participating sites (72.3%), news media (12.3%), physician referral (6.0%), word of mouth (3.1%), and paid advertising (2.9%).

Discussion: The rapid recruitment of participants with mild to moderate AD was achieved through a range of approaches with varying success.

KEYWORDS
Alzheimer's disease, clinical trial, drug development, pharmacologic, recruitment

1 | INTRODUCTION

Recruitment into Alzheimer's disease (AD) trials is recognized as a barrier to therapy development, as it extends trial duration and increases resources to sustain trial infrastructure.[1] Slow recruitment is particularly evident in phase 2 and 3 AD clinical trials. For example, recent phase 3 trials of AD therapies have included an average of 342 participants and taken 185 weeks to recruit individuals with mild to moderate AD.[2]

The *National Strategy for Recruitment and Participation in Alzheimer's and Related Dementias Clinical Research*, published in October 2018 by the National Institute on Aging, outlined four goals to address the

challenge of recruiting patients into AD clinical trials. One of these goals was to "develop an applied science of recruitment," given that research on AD trial recruitment is largely lacking and that few trials have published their recruitment metrics to inform the evidence base around best practices for recruitment.[3] Thus, the National Strategy encouraged scientific investigators to report on their approaches and outcomes in AD trial recruitment. We report the strategies used to achieve a successful and rapid recruitment of individuals with mild to moderate AD into a phase 2 clinical trial of troriluzole, a glutamate modulator being tested for potential symptomatic benefits.

2 | METHODS

2.1 | Overview of the T2 Protect AD trial

T2 Protect AD was a phase 2, 48-week, randomized, double-blind, placebo-controlled trial to establish the safety and efficacy of troriluzole in participants ages 50 to 85 years with a diagnosis of mild to moderate AD. The Alzheimer's Disease Cooperative Study (ADCS) at the University of California, San Diego served as the central coordinating center for the trial. The trial was funded by Biohaven Pharmaceuticals, Inc., which served as the study sponsor and Investigational New Drug holder. Key eligibility criteria are provided elsewhere (Clinicaltrials.gov identifier: NCT03605667).

2.2 | Recruitment methods

2.2.1 | Overview

Our goal was to recruit 336 participants. Participants were recruited from 44 US sites, which included 14 (31.8%) National Institutes of Health (NIH)-designated Alzheimer's Disease Research Centers (ADRCs), 23 (52.3%) AD specialty clinics, and 7 (15.9%) clinical trials groups (e.g., clinical research organizations). We anticipated recruitment of 6 to 10 participants per site. All sites received institutional review board (IRB) approval for study conduct. The median time to approval to screen participants was lower for sites with only a central IRB (109.5 [range, 6.0–323.0] days) compared to sites with central and local IRBs (118.0 [range, 79.0–148.0] days) or only a local IRB (147.0 [range, 80.0–456.0] days). Sites obtained written informed consent from all individuals or legally authorized representatives prior to screening.

2.2.2 | Collaboration between sponsor and ADCS

Recruitment was led by ADCS, which provided a core roster of academic medical sites and investigators and staff experienced in AD trials, including a recruitment team comprising a faculty director with expertise in trial recruitment who supervised the overall recruitment effort; a recruitment manager with extensive experience in AD trial recruitment and vast knowledge of site-specific enrollment potential; a com-

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RESEARCH IN CONTEXT

1. **Systematic review**: Slow recruitment into Alzheimer's disease (AD) pharmacologic trials is a barrier to therapy development, with recent trials reporting an average of 185 weeks for recruitment of individuals with mild to moderate AD. Few studies have described the most effective recruitment strategies for efficient and timely recruitment of individuals with AD into pharmacologic trials.

2. **Interpretation**: The vast majority (98%) of participants randomized into T2 Protect AD ($N = 350$), a phase 2 randomized controlled trial of troriluzole in mild to moderate AD, were enrolled during a 10-month window of intense promotion in news media, TV and radio advertisements, and social media. Existing lists of patients at participating sites and news media were the primary sources of recruitment.

3. **Future directions**: Increased investment in identifying newly diagnosed mild to moderate AD patients in the community will be imperative in helping sites access more inclusive databases and registries of patients to facilitate timely recruitment into pharmacologic AD trials.

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munications specialist with expertise in media communications; a marketing and graphic design expert to prepare visually appealing recruitment materials; and a trained recruitment interviewer to conduct centralized prescreening (described below). The sponsor and ADCS collaboratively developed an overarching recruitment plan. The senior leadership of the sponsor provided resources for recruitment and was fully engaged in recruitment planning and operations.

Participants self-reported their recruitment source at screening. Source statistics were carefully monitored with the rollout of each recruitment strategy.

2.2.3 | Recruitment toolkit

A trial website (https://t2protect.org) was developed, and sites were provided with a recruitment toolkit containing study brochures, infographics, flyers, postcards, PowerPoint presentations for public events, a press release, an FAQ document, a 2-minute animated video, and a physician-to-physician letter. The purpose of the engaging and upbeat animated video, which appeared on the trial website and was shared as part of a social media campaign, was to motivate potential participants, or their friends and family members, to contact the trial. The video emphasized the need to investigate new drugs aimed at slowing down and potentially improving memory and thinking problems among AD patients; described the trial, eligibility criteria, and study drug; and provided contact information. Another short animated video, which

can be viewed on the sponsor's website (www.biohavenpharma.com), described diseases related to glutamate regulation and was used as B-roll by the media in news stories. All recruitment materials were approved by central and local IRBs.

2.2.4 | Memory clinic patient rosters, patient registries, and electronic health records

Existing patient rosters from memory clinics, internal registries of patients willing and able to participate in AD clinical trials, and electronic health records (EHRs) were used for recruitment. Patients who appeared to meet eligibility based on age and existing clinical diagnosis of mild to moderate AD were contacted for potential participation.

2.2.5 | Media outreach

The ADCS recruitment team managed earned media outreach through distribution of trial-related information to broadcast, print, and electronic news media outlets to develop media interest in the trial. Both Forbes.com and Fox News published and broadcast national news stories about the trial.[4,5] Centrally coordinated media outreach also resulted in several local broadcast and news stories, including impactful editorials that raised public awareness about the trial, as well as local TV and radio interviews.[6,7]

Biohaven assigned Sam Brown, Inc., their public relations and communications team, to work with ADCS on recruitment. ADCS was focused on earning national and local news stories, whereas Sam Brown worked primarily on earning local news stories in select markets. Sam Brown also supported the recruitment toolkit with videos and infographics. Earned media was prioritized over paid media (particularly near sites without adequate AD patient pipelines), and paid advertising was pursued only when site AD patient pipelines began to dwindle.

2.2.6 | Broadcast and print advertising

In consultation with participating sites, ADCS and Sam Brown worked collaboratively to develop, purchase, and place radio, newspaper, and television advertisements in local media markets to address local recruitment needs.

2.2.7 | Algorithm-driven digital marketing campaign

The ADCS recruitment team worked with a digital marketing company to execute a multi-tiered, algorithm-driven, age and geographically targeted digital marketing campaign for recruitment. Advertisements were placed in various mediums targeting geographic locations close to participating sites and the following demographic groups: adults ≥35 years living with grandparents at home, adults ≥65 years, and adult children serving as caregivers. Text ads appeared in search engine results pages based on entered keywords (e.g., "Alzheimer's disease"). Custom advertisements were placed on Facebook, and an e-mail blast about the trial was sent to a subset of the company's existing mailing list (≈160,000 e-mails). ADCS continued the Facebook advertisement campaign after the end of the contract with the digital marketing company.

2.2.8 | Age- and geo-targeted mass mailings

ADCS hired a direct mail marketing company in San Diego, California, to print and mail postcards targeting individuals in site metropolitan areas. This company used a commercially available, consumer-oriented mailing list compiled from public and other records. Postcards were mailed to adults 50 to 85 years who lived close to participating sites. Three of the sites participated in the mass mailing campaign, distributing a total of 20,000 postcards.

2.2.9 | Centralized prescreening

ADCS implemented a centralized prescreening program from April 29, 2019 to November 1, 2019. The primary goal was to reduce screen burden on sites and screen out candidates who were not qualified, thereby allowing sites to focus on their local recruitment activities. This approach was undertaken in response to the large volume of calls expected after the media and marketing campaigns. A centralized call center was established at ADCS with a trained recruitment interviewer to assess key eligibility criteria among interested candidates. A prescreening script for the recruitment interviewer was developed and IRB-approved prior to implementation. Participants were prescreened for fundamental inclusion and exclusion criteria. Those who seemed eligible were contacted by the participating site within 48 hours for further screening.

2.2.10 | Meetings with site principal investigators and study coordinators

The ADCS recruitment team and study sponsor engaged regularly in phone calls with site investigators and study coordinators. The calls were done in small enough groups to allow site-level reporting and interactive discussion of any barriers and new solutions to recruitment.

2.2.11 | Recruitment cost estimates

The total recruitment expenditures (not including personnel) were set at $585,213. This was divided between the central effort—focused on media outreach, the digital marketing campaign, and mass mailings—and participating sites, which were focused on recruiting participants from existing lists of patients. Approximately $484,393 was spent on recruitment (not including personnel); when including personnel costs, approximately $737,283 was spent on recruitment.

3 | RESULTS

3.1 | Screening

From July 2018 to December 2019, sites screened 687 individuals and randomized 350 participants with mild to moderate AD into the trial (Figure 1). The screen failure rate was 49.1%, and the screening ratio, or number screened for every enrolled participant, was 1.96. Major reasons for screen failure (*n* = 337) were a Mini-Mental State Examination (MMSE) score outside of 14 to 24 and prohibited medications

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687 participants screened (which included 87 referred from central prescreening)

Primary reasons for screen failure (n=337)
♦ MMSE outside of 14-24 (n=189)
♦ Prohibited medications (n=28)
♦ Cranial MRI shows evidence of infection, tumor, cortical infarction, white matter disease (Fazekas score >2), or multiple lacunes (n=28)
♦ Not treated with stable dosage of FDA-approved AD medications for ≥3 months (n=7)
♦ Contraindication to MRI (n=6)
♦ Medical comorbid illnesses (n=6)
♦ BMI >35 kg/m^2 at screening (n=6)
♦ ALT/SGPT, AST/SGOT >1.5x upper limit of normal, or total bilirubin >1x upper limit of normal (n=5)
♦ Untreated or insufficiently treated hypothyroidism, vitamin B12, or folate deficiency (n=5)
♦ Clinically significant ECG (n=5)
♦ Brain MRI scan within 6 months of screening inconsistent with diagnosis of AD (n=5)
♦ Missing reasons for screen failure (n=25)
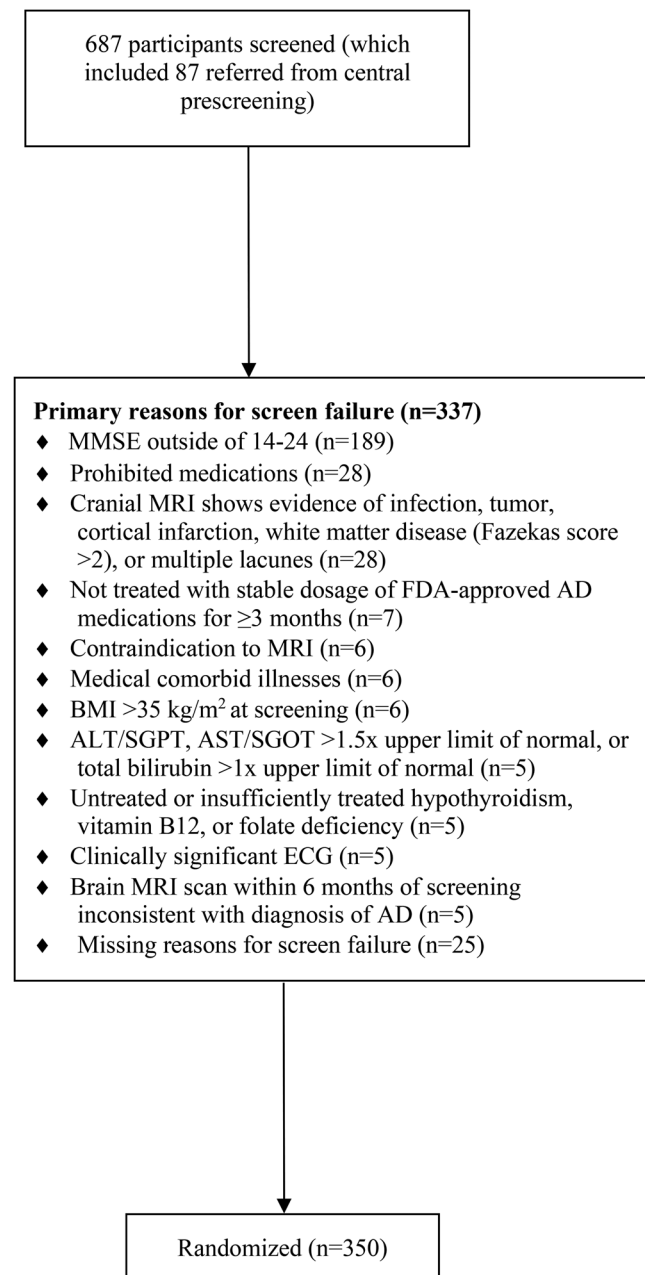
Randomized (n=350)

FIGURE 1 T2 Protect AD screening flow diagram. AD, Alzheimer's disease; ALT/SPGT, alanine aminotransferase; AST/SGOT, aspartate aminotransferase; BMI, body mass index; ECG, electrocardiogram; FDA, Food and Drug Administration; MMSE, Mini-Mental State Examination; MRI, magnetic resonance imaging
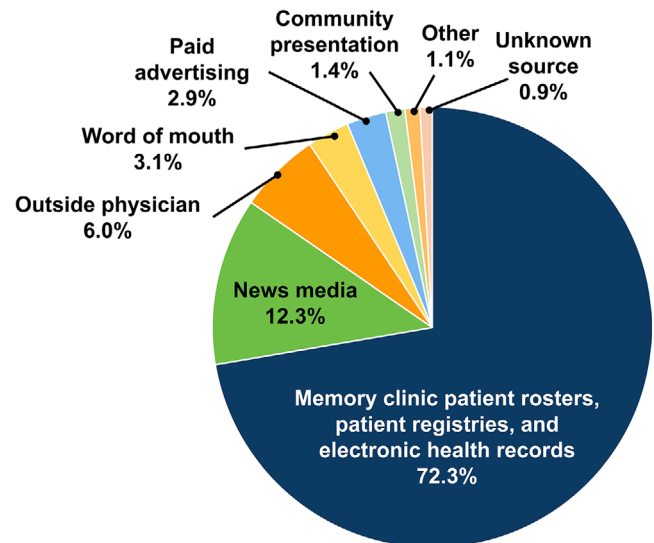

FIGURE 2 Sources of recruitment of randomized participants in the T2 Protect AD trial among individuals with mild to moderate AD (*N* = 350)

(Figure 1). When stratified by race and ethnicity, these were among the primary reasons for screen failure among White individuals, Blacks, and individuals of Hispanic/Latino ethnicity (Tables S1 and S2 in supporting information). In total, 428 people underwent centralized prescreening, among whom 169 (39.5%) were screened out, 172 (40.2%) were lost to follow-up, and 87 (20.3%) were referred for further screening. Approximately 100 hours were spent conducting centralized prescreening.

3.2 | Recruitment sources

Of the randomized participants, 72.3% were recruited from existing lists of patients from memory clinics, patient registries, and EHRs (Figure 2). Additional sources were earned news media (12.3%), physician referrals (6.0%), word of mouth (3.1%), paid advertisements (2.9%), and community presentations (1.4%).

Recruitment started in July 2018 with the approval of the first site. Recruitment momentum built in proportion to the number of sites approved to screen over time (Figure 3). The vast majority (98%) of participants were screened and enrolled during a 10-month period from January 2019 to October 2019. This period of rapid recruitment was initiated when 21/44 (47.7%) sites were actively recruiting. The paid advertisements, news stories, digital marketing campaign, Facebook advertisements, and mass mailings all occurred during this 10-month period. While the social media efforts resulted in considerable engagement (e.g., comments or interactions on Facebook posts), they did not appear to result in large numbers of eligible participants. Age- and geo-targeted mass mailings also did not appear to generate eligible participants. Thus, we focused our efforts on lists of eligible patients from sites and on earning news media stories. We actively monitored site-level recruitment and engaged in frequent calls to ensure that enrollment was proceeding smoothly. Because sites had a reasonable goal of
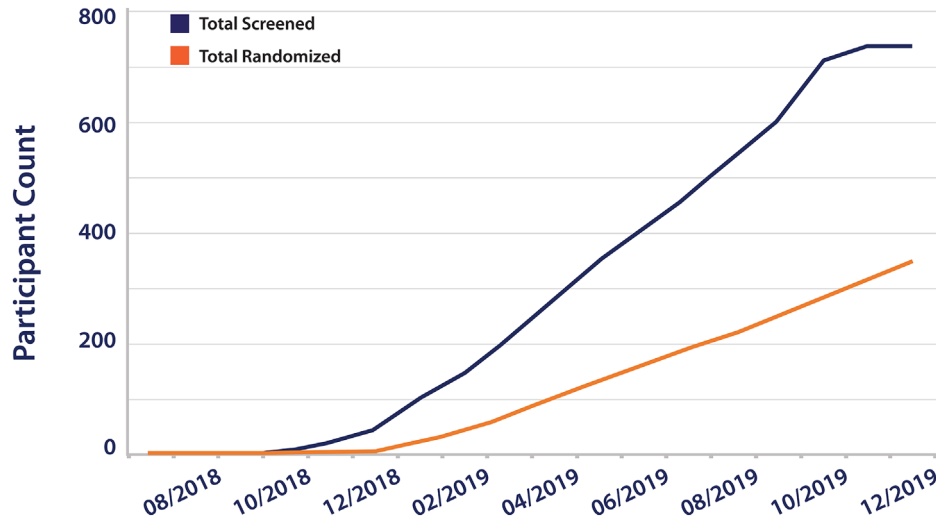
FIGURE 3 Timeline of screening and randomization of participants into the T2 Protect AD trial among individuals with mild to moderate Alzheimer's disease
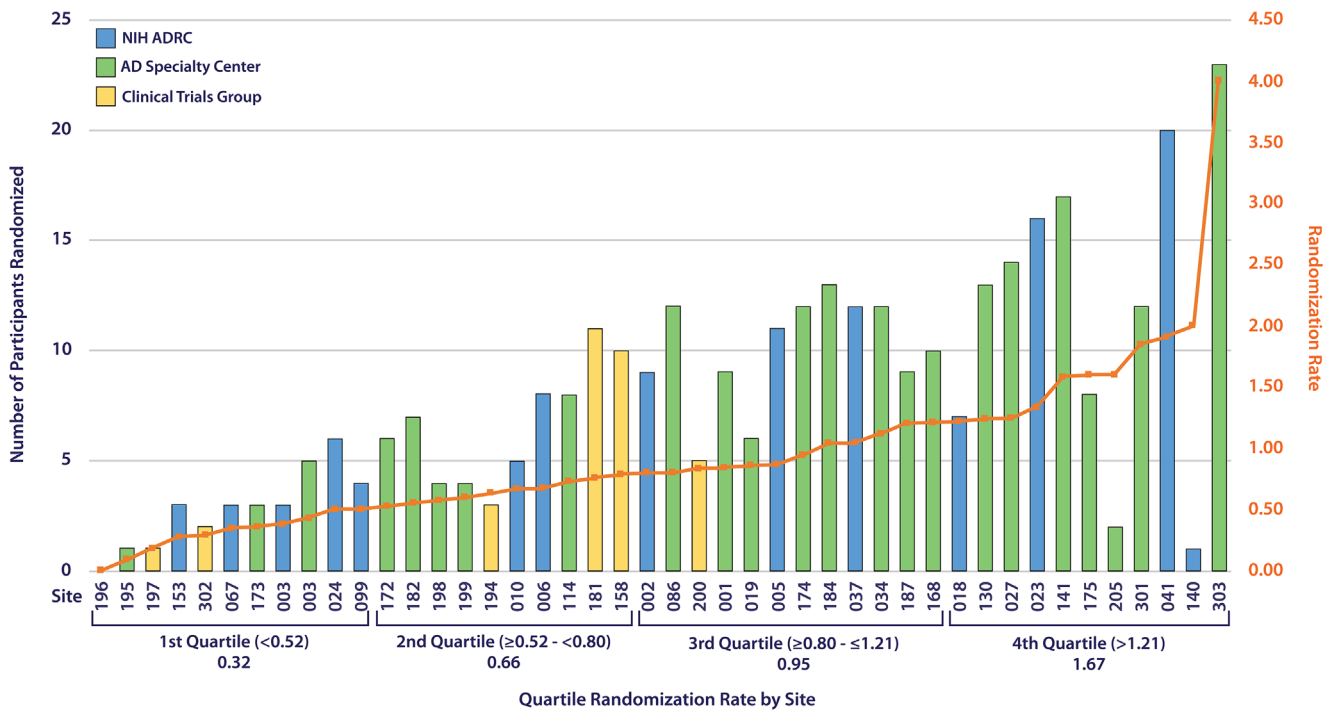

FIGURE 4 Randomization rate by site into the T2 Protect AD trial among individuals with mild to moderate AD ($N = 350$). AD, Alzheimer's disease; ADRC, Alzheimer's Disease Research Center; NIH, National Institutes of Health

6 to 10 participants to enroll, 14 sites exceeded their enrollment target, with the top two performing sites randomizing 20 to 23 participants.

3.3 | Randomization rate

Figure 4 shows the average randomization rate by site, defined as the number of participants randomized divided by the number of active site recruitment months. The overall randomization rate was 0.87 randomizations per site per month (range, 0 to 4.0). Among the top 10 per-

forming sites according to randomization rate, 70% were AD specialty centers and 30% were NIH-designated ADRCs.

3.4 | News media and digital marketing campaign metrics

The central recruitment activities (e.g., earned news media and digital marketing campaign) generated interest in the trial, as demonstrated by the numbers of trial website visitors. From October 15, 2018

TABLE 1 Baseline demographic characteristics of participants randomized into the T2 Protect AD trial among individuals with mild to moderate AD (N = 350)

Characteristic	Total (N = 350)	Men (N = 147)	Women (N = 203)
Age, mean (SD), years	72.3 (7.9)	72.4 (8.1)	72.2 (7.8)
Race, n (%)			
Black/African American	9 (2.6%)	5 (3.4%)	4 (2.0%)
Asian	5 (1.4%)	3 (2.0%)	2 (1.0%)
Native Hawaiian/Other Pacific Islander	1 (0.3%)	0 (0.0%)	1 (0.5%)
White	333 (95.1%)	139 (94.6%)	194 (95.6%)
Other	2 (0.6%)	0 (0.0%)	2 (1.0%)
Ethnicity			
Hispanic or Latino	9 (2.6%)	3 (2.0%)	6 (3.0%)
Not Hispanic or Latino	337 (96.3%)	143 (97.3%)	194 (95.6%)
Not reported	4 (1.1%)	1 (0.7%)	3 (1.5%)
Education, mean (SD), years	15.3 (3.1)	15.9 (3.1)	14.8 (2.9)

Abbreviations: AD, Alzheimer's disease; SD, standard deviation

to October 31, 2019, 24,325 people visited the trial website, which had a total of 41,550 page views. There was an approximate 2-fold increase in trial website visitors after the distribution of a Fox News article about the trial from Nashville to Fox affiliates in January 2019. Activities from the digital marketing campaign, including advertisements in newspapers and magazines and the e-mail blast, each resulted in > 2000 new visitors to the trial website, generated > 9,000,000 audience impressions (i.e., appearances on a screen), 428 unique centralized prescreening calls, and 87 prescreened referrals to sites.

3.5 | Randomized participant characteristics

Among randomized participants, mean age was 72.3 (standard deviation [SD] 7.9) years, and mean years of education was 15.3 (SD 3.1) years (Table 1). Racial makeup was distributed as follows: White (95.1%), Black (2.6%), Asian (1.4%), Native Hawaiian/other Pacific Islander (0.3%), and other race (0.6%). Overall, 2.6% were Hispanic/Latino.

4 | DISCUSSION

T2 Protect AD, a phase 2, placebo-controlled, randomized clinical trial, was undertaken to evaluate the efficacy of troriluzole in individuals with mild to moderate AD at 44 sites. The trial exceeded its enrollment target of 336 participants, ultimately enrolling 350 participants into the trial. The majority (72.3%) of participants were recruited from existing lists of patients connected to the participating sites. National and local news stories raised public awareness of the trial, contributing to 12.3% of randomized participants. Other sources (e.g., digital marketing campaign, mass mailings, or social media advertisements) recruited fewer participants.

Average recruitment rates into AD pharmacologic trials are generally low. A previous summary of 12 phase 2 and 3 AD trials among individuals with mild to moderate AD reported monthly recruitment rate and screening ratio averages of 0.79 (range, 0.10–2.77) and 1.35 (range, 1.22–1.47), respectively.[8] We reported a screening ratio of 1.96, indicating that, relative to this prior average, more individuals needed to be screened to enroll a participant into T2 Protect AD. According to the most recent published estimate from clinicaltrials.gov, active pharmacologic trials of mild to moderate AD recruited at a rate of 0.29 participants per site per month as of February 27, 2020.[2] The randomization rate observed in T2 Protect AD, 0.87 randomizations per site per month, was 3-fold higher than this estimate.

Nearly 5% of randomized participants in T2 Protect AD were from underrepresented populations. Historically, individuals from underrepresented populations have not been well represented in clinical trials. Hispanic and Black individuals represent 18.5% and 13.4% of the US population, respectively, but only 5% of clinical trial participants.[9,10] With this industry-sponsored trial, we did not set specific minority recruitment goals or dedicate resources for minority outreach. We were instead focused on a "competitive recruitment" targeting all eligible individuals with mild to moderate AD within the shortest time frame to address whether there was a clinical signal with which to launch a more comprehensive set of trials with broader focus. Thus, we screened few underrepresented minorities relative to White individuals. In contrast, a recent National Institute on Aging (NIA)-funded trial of aerobic exercise conducted by ADCS among individuals with amnestic mild cognitive impairment (MCI; the EXERT trial) achieved a minority participation rate of 13.2%, largely due to a concerted effort by the ADCS recruitment team that involved the development of culturally appropriate and sensitive multimedia messaging, geo-targeting of mass mailings of postcards and brochures in areas with demographic diversity, and prioritization of underrepresented minorities for screening and clinic appointments.[11] As an NIA-funded trial, EXERT had

specific minority recruitment goals. Similar to EXERT, we found that major reasons for screen failure in T2 Protect AD were similar across racial and ethnic groups.[11] Thus, enrollment of underrepresented populations into future AD clinical trials will require concerted and targeted recruitment strategies.

An important aspect of our recruitment strategy was to "test, evaluate, adapt, and learn" by continuously collecting and monitoring recruitment metrics. If certain recruitment strategies were not working, we focused our efforts elsewhere during the course of the trial. The central coordination of the trial by ADCS was instrumental in guiding sites to evolve their recruitment strategy. For example, mass mailings of postcards and brochures; paid advertisements in TV, radio, or newspapers; the digital marketing campaign; or Facebook advertisements were not effective for recruitment into T2 Protect AD. Similarly, Facebook advertisements helped recruit only a small proportion (3%) of participants into the University of California Irvine Consent-to-Contact (UCI (C2C) registry for preclinical AD trials.[12] While mass mailings have been used for recruitment into AD prevention trials and brain health registries, our findings suggest that mass mailings may be ineffective for recruitment into pharmacologic trials of mild to moderate AD.[13–16] Mass mailings accounted for more than half of participants randomized into EXERT, whereas 25% were recruited from existing lists of eligible patients from participating sites.[11] This underscores the need to publish AD trial recruitment metrics to inform the evidence base around best practices for recruitment.

Given the failure of mass mailings, the digital marketing campaign, and social media advertisements for recruitment, we focused our efforts on recruiting from existing lists of eligible patients from participating sites and on earning news media. We benefited from having a large number of sites, as low randomization rates in certain sites were offset by higher rates in others. The variation in randomization rate across sites will provide a set of reference data for coordinating centers or sponsors planning mild to moderate AD trials and additionally will be useful in guiding future ADCS site selection for its trials. The reasonable and achievable goal of 6 to 10 randomizations per site enabled sites to recruit the majority of their participants from existing lists of eligible patients. The ADCS recruitment team's broad familiarity with each site and intimate knowledge of its historical recruitment patterns facilitated the development of individualized strategies to leverage each site's unique recruitment landscape and predict its likely enrollment. The IRB approval process for each site to begin screening was efficient due to the recruitment team's existing relationships with central and local IRBs. Compared to sites with local IRBs, sites with central IRBs took less time to receive study approval, which facilitated timely recruitment. Finally, we successfully leveraged existing ADCS relationships with site principal investigators and study coordinators, underscoring the benefit of having dedicated trial infrastructure and networks in place to accelerate trial conduct (Table S3 in supporting information).

Other strategies that contributed to successful recruitment included that media outreach and centralized prescreening were not implemented until January 2019 when close to half of the sites were approved to enroll. This ensured that all sites benefited from

our extensive recruitment efforts. More than 100 hours were spent conducting centralized prescreening, enabling sites to invest their time and energy in enrolling qualified participants. It is also possible that we benefited from the fact that there were only 12 trials of mild to moderate AD at the time of recruitment, which may have partially contributed to interest in trial participation.[2,17]

The effectiveness of news media in recruiting mild to moderate AD patients into pharmacologic trials has not been widely reported. Earned news media contributed to 12.3% of randomized participants in T2 Protect AD, underscoring the success of the key messages conveyed in the news stories. While the media campaign accounted for a smaller proportion of enrollees than internal lists of patients, by generating community interest, it likely served a fundamental accelerating role for sites to more successfully develop their participant pipelines. Because we were unable to capture whether a participant's recruitment was due to multiple sources, it is possible that the influence of news media in this recruitment was underestimated. News media has shown success in recruiting participants into brain health registries;[12,18] however, its effectiveness in directly recruiting mild to moderate AD patients is not established. News stories were the most effective method to recruit participants into the UCI C2C registry focused on preclinical AD trials, contributing to 37% of enrollees.[18] Local newspaper coverage helped increase enrollment into the Alzheimer's Disease Neuroimaging Initiative 3 cohort, but specific metrics on its effectiveness were not reported.[19] In the EXERT trial led by ADCS, earned news media accounted for 1.7% of randomized participants, much smaller than the proportion who learned about T2 Protect AD from earned news media (12.3%).[11] This demonstrates that each trial has unique features that need to be adapted and responded to, including the type of trial (pharmacologic vs. non-pharmacologic) and population under study (e.g., MCI vs. AD), which will impact the success of a specific recruitment strategy.

In conclusion, recruitment into T2 Protect AD, a randomized controlled trial of a symptomatic therapy among individuals with mild to moderate AD, outperformed its enrollment target, enrolling almost all of the 350 participants during a 10-month period of rapid recruitment. The trial's randomization rate was three-fold greater than the most recently published randomization rate for active pharmacologic trials of mild to moderate AD.[3] Overall, our findings suggest that mass mailings of postcards, digital marketing campaigns, or Facebook advertisements may not be effective for recruitment of mild to moderate AD patients into pharmacologic trials. The majority of patients were recruited from existing lists of patients at memory clinics, patient registries, and EHRs. A relatively large number of sites with modest and achievable recruitment goals also contributed to the speed and success of recruitment. Our findings also suggest that a stronger commitment to minority recruitment is required than existed in this recruitment, including specific minority recruitment goals and targeted recruitment strategies, to enroll representative samples into AD pharmacologic trials. Finally, our findings suggest that increased investment should be made in identifying newly diagnosed mild to moderate AD patients in the community, perhaps similar to what is done by the Surveillance, Epidemiology, and End Results (SEER) program funded by the

National Cancer Institute.[20] This would help sites access more inclusive databases and registries of patients to facilitate timely recruitment into future AD trials.

CONFLICTS OF INTEREST

Stephen Kaplita is employed by the sponsor, Biohaven Pharmaceuticals, Inc., and has stock ownership in the company. Stephen Kaplita reports that Biohaven Pharmaceuticals, Inc., paid expenses for travel to an FDA statistics meeting. Lia Donahue is employed by the sponsor, Biohaven Pharmaceuticals, Inc. Irfan A. Qureshi is employed by the sponsor, Biohaven Pharmaceuticals, Inc., and is a shareholder in the company. Howard H. Feldman reports grants to UCSD from Biohaven Pharmaceuticals, Annovis (QR Pharma), AC Immune, Vivoryon (Probiodrug), and LuMind. He also reports service agreements through UCSD for consulting with Novo Nordisk, Merck Pharmaceuticals, Samus Therapeutics, Arkuda Therapeutics, Samumed, and Axon Neurosciences. He reports serving on a DMC and DSMB for Roche/Genentech Pharmaceuticals and Janssen Research & Development LLC with service agreements through UCSD, as well as serving on the Scientific Advisory Board for the Tau Consortium. He reports travel expenses to UCSD from World Events Forum (ADDF), Samus, Samumed, Axon, and Novo Nordisk. He reports personal funds received for Detecting and Treating Dementia Serial Number 12/3-2691 U.S. Patent No. PCT/US2007/07008, Washington DC, U.S. Patent and Trademark Office. Andrea Z. LaCroix reports receiving grant funding through University of California, San Diego from the National Institute on Aging and National Heart, Lung, and Blood Institute for research studies related to aging; receiving consulting fees from the Fred Hutchinson Cancer Research Center for working on grants funded by NIH; and receiving a payment for giving a lecture at the University of Utah. She serves on two Data and Safety Monitoring Boards for the National Institute on Aging. Ronald G. Thomas reports receiving a payment for board membership from Syneos Health. Aladdin H. Shadyab, Genevieve Matthews, Daniel Bennett, Alexandre A. Shadyab, Donna Tan, Jennifer Mason, Alex Lopez, Brianna Askew, and Branko Huisa have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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APPENDIX OF COLLABORATORS

T2 Protect AD group information

The Alzheimer's Disease Cooperative Study T2 Protect AD Study Group members are as follows: *Protocol Committee*: Thomas Obisesan, MD, MPH; Amanda Smith, MD; Judith Heidebrink, MD, MS; and Jacobo Mintzer, MD. *Site Principal Investigators*: Thomas Ala, MD, Southern Illinois University; Aimee Pierce, MD, Oregon Health and Science University; Lon Schneider, MD, University of Southern California; Gabriel Leger, MD CM, University of California, San Diego; Judith Heidebrink, MD, MS, University of Michigan, Ann Arbor; Karen Bell, MD, Columbia University Medical Center; Milap Nowrangi, MD, MBE, Johns Hopkins University; Amanda Smith, MD, University of South Florida Health Byrd Alzheimer's Institute; Gregory Jicha, MD, PhD, University of Kentucky; Oscar Lopez, MD, University of Pittsburgh; Anton Porsteinsson, MD, University of Rochester Medical Center; Angela Jefferson, PhD, Vanderbilt Memory & Alzheimer's Disease Center; Martin Farlow, MD, Indiana University; Christopher Van Dyck, MD, Yale University School of Medicine; Ian Grant, MD, Northwestern University; Alan Siegal, MD, Geriatric and Adult Psychiatry; Alireza Atri, MD, PhD, Banner Sun Health Research Institute; Alan Lerner, MD, Case Western Reserve University; Douglas Scharre, MD, Ohio State University; Del D. Miller, PharmD, MD, University of Iowa; Elaine Peskind, MD, University of Washington; Jonathan Drake, MD, Rhode Island Hospital; Ralph Richter, MD, Central States Research; Aaron Ritter, MD, Cleveland Clinic Lou Ruvo Center for Brain Health; Charles Bernick, MD, Cleveland Clinic Lou Ruvo Center for Brain Health; Ralph Richter, MD, Central States Research; Michael Karathanos, MD, Central States Research; Olga Brawman-Mintzer, MD, Clinical Biotechnology Research Institute at Roper St. Francis Hospital; Jacobo Mintzer, MD, MBA, Clinical Biotechnology Research Institute at Roper St. Francis Hospital; Bernard Baumel, MD, University of Miami; Jeffrey Keller, MD, Pennington Biomedical Research Center; Andrea Bozoki, MD, Michigan State University; Sharon Brangman, MD, SUNY Upstate Medical University Center of Excellence for Alzheimer's Disease; Olga Tchikindas, MD, Princeton Medical Institute; Kiran Bath, MD, Neurology Center of North Orange County; David Weisman, MD, Abington Neurological Associates; Clifford Singer, MD, Northern Light Acadia Hospital; Maya Lichtenstein, MD, Geisinger Medical Clinic; Mary Sano, PhD, James J. Peters VA Medical Center; Alexander Beyzer, MD, Galen Research Center; Farzad Qureshi, MD, Galen Research Center; Richard Shubin, MD, SC3 Research Group; Peter McCallister, MD, New England Institute for Clinical Research; Stephen Flitman, MD, Xenoscience, Inc.; Cherian Verghese, MD, Keystone Clinical Studies; Sudha Seshadri, MD, Glenn Biggs Institute for Alzheimer's & Neurodegenerative Diseases - UTHSC San Antonio; Anna Burke, MD, Barrow Neurological Institute; Jeffrey Ross, MD, Great Lakes Clinical Trials; and Mark Brody, MD, Brain Matters Research.