Arvinas Announces Positive Phase 1 Data for ARV-102 Showing Greater Than 50% LRRK2 Degradation in the CSF of Patients with Parkinson's Disease Treated for 28 Days

March 18, 2026

– ARV-102 reduced endolysosomal and neuroinflammatory biomarkers implicated in Parkinson's disease and progressive supranuclear palsy –

– ARV-102 was well tolerated across all dose levels following 28 days of once-daily dosing –

– Data support further development of ARV-102 in additional neurodegenerative diseases characterized by lysosomal dysfunction, including progressive supranuclear palsy, a rapidly progressing and devastating tauopathy –

– Data presented during an oral session at the Alzheimer's and Parkinson's Diseases and Related Neurological Disorders Conference –

NEW HAVEN, Conn., March 18, 2026 (GLOBE NEWSWIRE) -- Arvinas, Inc. (Nasdaq: ARVN), a clinical-stage biotechnology company working to create a new class of drugs based on targeted protein degradation, today presented data from a Phase 1 clinical trial of ARV-102, an investigational PROteolysis TArgeting Chimera (PROTAC) degrader designed to specifically target and degrade leucine-rich repeat kinase 2 (LRRK2). In the trial, ARV-102 demonstrated approximately 50% or greater reduction of LRRK2 in cerebrospinal fluid (CSF) at all doses by day 14 and maintained the reduction through day 28 in patients with Parkinson's disease (PD). The Company targeted a 50% reduction based on data showing that patients with PD have a two-fold elevation of LRRK2. Results from the single-center, randomized, double-blind, placebo-controlled, multiple dose (MD) cohort of the Phase 1 clinical trial were shared in an oral presentation at the 2026 International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD™ 2026) in Copenhagen, Denmark.

The MD cohort of the Phase 1 clinical trial conducted in patients with PD evaluated ARV-102 oral doses ranging from 20 mg to 80 mg daily for 28 days. Key findings from the trial showed:

- ARV-102 exposure in CSF increased in a dose-dependent manner after multiple doses, indicating brain penetration.
- ARV-102 achieved approximately 50% or greater LRRK2 reduction in CSF at all doses by day 14 and maintained the reduction through day 28, indicating substantial central LRRK2 protein degradation.
- Treatment resulted in reduction of LRRK2 variant and expression-dependent endolysosomal and neuroinflammatory biomarkers (e.g., CD68, GPNMB) previously shown to be elevated in neurodegenerative diseases like PD and progressive supranuclear palsy (PSP).
- ARV-102 was generally safe and well tolerated with no serious adverse events (SAEs) reported after multiple doses.

ARV-102 is an investigational, orally bioavailable PROTAC designed to cross the blood-brain barrier and specifically target and degrade LRRK2. While LRRK2 is primarily known for its role in PD, emerging evidence suggests that it also plays a role in tauopathies, including PSP, and that LRRK2 dysfunction may contribute to the development and progression of both diseases.

"These data represent exciting progress in the Parkinson's disease treatment landscape," said Andrew Siderowf, M.D., Chair of the Parkinson Study Group. "Importantly, ARV-102's reduction of LRRK2 protein levels and other key biomarkers in patients with Parkinson's disease suggests that PROTACs may offer a path for future treatment approaches. I look forward to following the continued advancement of ARV-102 and what it could bring for patients."

"We are pleased to see compelling and consistent data that reinforce the continued development of ARV-102 as a potential treatment for neurodegenerative diseases like Parkinson's disease and progressive supranuclear palsy that profoundly impact millions of patients and their families worldwide," said Noah Berkowitz, M.D., Ph.D., Chief Medical Officer of Arvinas. "To our knowledge, this level of biomarker modulation has not previously been demonstrated by LRRK2 inhibitors, and we believe these data serve as the first of its kind. There is strong evidence that lysosomal dysfunction driven by increased LRRK2 in patients with PSP leads to significant declines in function over one year. Building on these results, and pending regulatory feedback, we intend to initiate a Phase 1b clinical trial in PSP in the second quarter of 2026, with the potential to initiate a registrational trial in late 2026, while we continue evaluating development options for ARV-102 in Parkinson's disease."

Data presented at AD/PD™ 2026
The ARV-102 Phase 1 clinical trial is designed to assess the safety, pharmacokinetics, and pharmacodynamics of orally administered ARV-102 in patients with PD. Data presented are from the MD cohort of the single-center, randomized, double-blind, placebo-controlled trial. In the MD cohort, patients were randomized to either placebo or multiple oral doses of ARV-102 (20 mg,

40 mg, or 80 mg) for 28 days with follow-up at day 42.

Safety Profile

- Multiple oral doses of ARV-102 (20 mg, 40 mg, or 80 mg once daily for 28 days) were well tolerated in participants with PD.
- All treatment-emergent adverse events and treatment-related adverse events were mild in severity, with no SAEs, discontinuations, or deaths reported.
- No significant changes in lung functions or respiratory symptoms were observed during the 28 days of treatment or during follow-up.

Pharmacokinetic and Pharmacodynamic Evaluation

- ARV-102 levels in CSF increased in a dose-dependent manner after multiple doses, indicating brain penetration.
- The area under the concentration-time curve (AUC_{0-24}) and the maximum plasma concentration (C_{max}) after daily dosing increased with dose with a mean terminal plasma half-life ($t_{1/2}$) of 68 hours.
- ARV-102 achieved peripheral LRRK2 degradation and dose-dependent degradation of LRRK2 in CSF, with approximately 50% or greater degradation observed at all doses by day 14 and maintained through day 28.
- Endolysosomal and neuroinflammatory pathway proteins that are elevated in LRRK2-related PD (e.g., CD68, GPNMB) were reduced with ARV-102.
- Pharmacology and changes in peripheral biomarkers in patients with PD were consistent with observations in healthy volunteers dosed with ARV-102.

Based on the positive outcomes of the Phase 1 clinical trial, Arvinas plans to continue investigation of ARV-102 in neurodegenerative diseases associated with LRRK2 and endolysosomal dysfunction.

Additional detail on the ARV-102 data presentation at AD/PD™ 2026 follows below:

Presentation Title: Safety, Pharmacokinetics, and Pharmacodynamics of Multiple Doses of ARV-102, a PROTAC LRRK2 Degrader, in Participants with Parkinson's Disease
Session Title: Modulating Neuroinflammation, A-Synuclein, LRRK2, and Dopaminergic Repair: Early Human Data
Session Type: Symposium
Session Location: Hall 180-181

Date: March 18, 2026
Lecture Time: 3:30-3:45 PM CET

About ARV-102

ARV-102 is an investigational, orally bioavailable PROTAC designed to cross the blood-brain barrier and specifically target and degrade leucine-rich repeat kinase 2 (LRRK2), a large, multidomain scaffolding kinase with GTPase activity. Increased activity and overexpression of LRRK2 have been implicated in the pathogenesis of neurological diseases, including Parkinson's disease and progressive supranuclear palsy (PSP). ARV-102 is currently being evaluated in a Phase 1 clinical trial in patients with Parkinson's disease and Arvinas plans to initiate a Phase 1b clinical trial with ARV-102 in patients with PSP, pending regulatory feedback, in the second quarter of 2026.

About Parkinson's Disease
Parkinson's disease is a progressive brain disease that damages dopamine-producing neurons, leading to progression of symptoms including motor-related symptoms like tremors and limb stiffness, as well as non-motor symptoms including depression, sleep disorders, cognitive decline, and more. LRRK2 activity is abnormally increased in Parkinson's—and experimental studies strongly suggest that blocking LRRK2 may be neuroprotective.

About Progressive Supranuclear Palsy
Progressive supranuclear palsy (PSP) is a rare, rapidly progressing neurodegenerative disease that affects brain cells that control balance and coordination, eye movement, speech, swallowing, and thinking. Symptoms may start as early as a patient's 40s. PSP is characterized by widespread tau pathology. LRRK2 influences tau pathology by directly modifying it and indirectly by disrupting cellular processes (actin, mitochondria, endocytosis) crucial for tau's normal function and clearance, promoting its toxic accumulation and spread.

About Arvinas
Arvinas (Nasdaq: ARVN) is a clinical-stage biotechnology company dedicated to improving the lives of patients suffering from debilitating and life-threatening diseases. Through its PROteolysis TArgeting Chimera (PROTAC) protein degrader platform, Arvinas is pioneering the development of protein degradation therapies designed to harness the body's natural protein disposal system to selectively and efficiently degrade and remove disease-causing proteins. Arvinas is currently progressing multiple investigational drugs through clinical development programs, including ARV-102, targeting LRRK2 for neurodegenerative diseases; ARV-806, targeting KRAS G12D for mutated cancers, including pancreatic, colorectal, and non-small cell lung cancers; ARV-393, targeting BCL6 for relapsed/refractory non-Hodgkin Lymphoma; ARV-027, targeting the polyglutamine-expanded androgen receptor, or polyQ-AR, in skeletal muscle; and vepdegestrant, targeting the estrogen receptor for patients with locally advanced or

metastatic ER+/HER2- breast cancer. Arvinas is headquartered in New Haven, Connecticut. For more information about Arvinas, visit **www.arvinas.com** and connect on **LinkedIn** and **X**.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties, including statements regarding: the potential of ARV-102, including its degradation of leucine-rich repeat kinase 2 ("LRRK2"), and potential future benefit to patients; the potential of PROteolysis TArgeting Chimeras; Arvinas' belief that the data presented related to the level of biomarker modulation has not previously been demonstrated by LRRK2 inhibitors and serves as the first of its kind; Arvinas' plans with respect to ARV-102, including its development and, pending regulatory feedback, the initiation of a Phase 1b clinical trial of ARV-102 in patients with progressive supranuclear palsy, and the initiation of a registrational trial, and the timings thereof; Arvinas' potential development plans with respect to ARV-102 in Parkinson's disease; and whether LRRK2 dysfunction contributes to the development and progression Parkinson's disease and progressive supranuclear palsy. All statements, other than statements of historical fact, contained in this press release, including statements regarding Arvinas' strategy, development plans, future operations, prospects, plans and objectives of management and the statements identified in the prior paragraph, are forward-looking statements. The words "ability," "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "potential," "target," "goal," "potential," "whether," "will," "would," "could," "reliance," "should," "look forward," "seek," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Arvinas may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on such forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements Arvinas makes as a result of various risks and uncertainties, including but not limited to: whether Arvinas will be able to successfully conduct and complete development for its product candidates, including ARV-102, on its current timelines or at all; risks related to clinical trial results and the interpretation thereof, including with respect to ARV-102; Arvinas' ability to protect its intellectual property portfolio; Arvinas' reliance on third parties; whether Arvinas will be able to raise capital when needed; whether Arvinas' cash and cash equivalents will be sufficient to fund its foreseeable and unforeseeable operating expenses and capital expenditure requirements; and other important factors discussed in the "Risk Factors" section of Arvinas' Annual Report on Form 10-K for the year ended December 31, 2025 and subsequent other reports filed with the U.S. Securities and Exchange Commission. The forward-looking statements contained in this press release reflect Arvinas' current views with respect to future events, and Arvinas assumes no obligation to update any forward-looking statements, except as required by applicable law. These forward-looking statements should not be relied upon as representing Arvinas' views as of any date subsequent to the date of this release.

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