Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

TT-P34

Evidence Summary

TT-P34 is derived from SorCS2, which participates in BDNF signaling among other roles. Preclinical work suggests TT-P34 may enhance cellular function in disease models. Clinical studies are ongoing.

Neuroprotective Benefit: Preclinical work in different neurodegenerative disease models suggests that TT-P34 may improve markers of mitochondrial and lysosomal health; early-stage clinical trials in PD are ongoing.

Aging and related health concerns: TT-P34 has not been explored for use in any age-related diseases. TT-P34 is a derivative of a protein that is found in non-neurological tissues, but the effects of mimicking this protein in other tissue is not yet known.

Safety: An early trial of TT-P34 in healthy volunteers and PD patients reported that adverse events were not more common in the dosing group, and that all trial-related adverse events were mild, according to a conference presentation.

Availability: In clinical development	**Dose**: Dosing is still under investigation. Phase 1 trials have used doses ranging from 8.5 mg to 100 mg via once-weekly subcutaneous injection. The first clinical trial in PD patients used a 50 mg subcutaneous dose once-weekly.	**Chemical formula:** Peptide sequence not disclosed. **MW:** Not disclosed.
Half-life: Approximately 6 days.	**BBB**: Penetrant.	
Clinical trials: 67 individuals have received TT-P34 in early clinical trials.	**Observational studies**: N/A	

What is it?

The mammalian family of vacuolar protein sorting 10p (VPS10p)-domain receptors consists of five transmembrane receptor proteins: SorLA, sortilin, SorCs1, SorCS2, and SorCS3. These proteins play a role in signal transduction pathways as well as intracellular protein sorting and trafficking. They are highly expressed in the brain, though they are expressed in other tissues (Hermey 2009). In the brain, neurotrophins like NFG and BDNF bind to VPS10p-domain receptors. The VPS10p-domain receptors are then involved in subsequent signaling pathways (reviewed by Salasova et al., 2022). As neurotrophins are crucial for neuronal survival and function, it is perhaps not surprising that these receptors have been implicated in several neuropsychiatric conditions and neurodegenerative diseases, including Alzheimer's disease (Malik & Willnow, 2020).

SorCS2, one of the VPS10p-domain receptors that is predominantly expressed in neurons, is involved synaptogenesis, synaptic stability, and synaptic plasticity. Pro- and mature NGF and BDNF bind to SorCS2, and SorCS2 can also bind to TrkB and p75NTR, among other binding partners (Salasova et al., 2022).

TT-P34, generated and under development by Teitur Trophics, is an 11 amino acid macrocyclic peptide derived from SorCS2 that is conjugated to a diacid lipid. TT-P34 can mimic activated SorCS2 and

modulate downstream molecular pathways. Teitur Trophics posits that the end result of TT-P34 action is enhancement of critical cellular activities such as lysosomal and mitochondrial function (preprint by Dalby et al., 2025). Currently, this drug is in development for Parkinson's disease (PD). Teitur Trophics is also exploring its use in Huntington's disease (HD) and frontotemporal dementia (FTD) (Teitur Trophics), two other dementias, though TT-P34 may have broad efficacious potential across neurodegenerative diseases based on its mechanism of action. This is discussed further in the 'Mechanism of action for neuroprotection' section.

Neuroprotective Benefit: Preclinical work in different neurodegenerative disease models suggests that TT-P34 may improve markers of mitochondrial and lysosomal health; early stage clinical trials in PD are ongoing.

Types of evidence:

- 1 phase 1 clinical trial presented at a conference
- 3 genome-wide association studies
- 7 reviews
- Numerous laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

No studies have explored whether TT-P34 may improve cognitive function or prevent dementia or decline.

Human research to suggest benefits to patients with dementia:

The first trial of TT-P34 in patients with Parkinson's disease (PD) enrolled and started dosing patients in January 2026 (Teitur Trophics).

Teitur Trophics is currently developing TT-P34 for PD and is also exploring potential use in other neurodegenerative diseases such as Huntington's disease (HD) and frontotemporal dementia (FTD) (Teitur Trophics). TT-P34 also has potential for efficacy in AD, given that VPS10p-domain receptors, including SorCS2, have been linked to AD and that a drug that enhances lysosomal and/or mitochondrial

function would have theoretical utility in AD. This will be explored further in the 'Mechanism of action' section below.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

VPS10p-domain receptor proteins are involved in both signal transduction pathways and with sorting and trafficking of proteins between cellular compartments and the plasma membrane. These transmembrane proteins have an extracellular domain that interact with a variety of ligands including (but not limited to) neurotrophins, as well as intracellular domains that mediate interactions with adaptor molecules. By participating in cell signaling pathways and directing other proteins to specific subcellular localizations, VPS10p-domain receptor proteins are involved in an array of essential cellular activities. Changes in the genes coding for or activity of these receptors has been linked to a variety of neuropsychiatric and neurodegenerative including Alzheimer's disease and frontotemporal dementia (Malik & Willnow, 2020).

SorCS2 is one of the VPS10p-domain receptor protein family members. Like its family members, SorCS2 is involved in cellular signaling and trafficking. And, like its family members, genetic variations in SorCS2 have been associated with diseases such as AD (Salasova et al., 2022). Reitz et al., 2013 describes a study assessing the associations between single nucleotide polymorphisms (SNPs) in the VPS10p-domain receptor family and AD. The researchers used a Caucasian case control data set with 11,840 AD patients and 10,931 controls. In the single-marker analysis,18 SNPs in *SorCS2* were associated with AD, though they did not quite reach statistical significance after correction for multiple testing and taking linkage disequilibrium into account. The researchers then tested for epistatic effects between SNPs identified in the single-marker analysis and found that 34 pairs of SNPs had nominally significant epistatic effects, including several in *SorCS2*, though the p-values for epistatic effects were just under the significance threshold for multiple comparisons. Most of the identified SNPs were located in the gene regions that code for the VPS10p domain. Using six independent datasets of families with AD, Rogaeva et al., 2007 also identified one SNP in *SorCS2* that had a nominally significant association with AD. The SNPs identified in the two studies did not overlap.

SorCS2 binds to pro- and mature NGF and BDNF, among other ligands, and mediates cell signaling of axonal retraction and growth cone collapse (Dalby et al., 2025). SorCS2 is crucial for BDNF-induced synaptic plasticity in the hippocampus and for activity-dependent targeting of TrkB to the postsynaptic density and thus for long-term memory formation in mice (Glerup et al., 2016). Other studies show that

SorCS2 is involved in trafficking NMDA receptors to dendrites of medium spiny neurons, which is the most affected cell population in Huntington's disease (Ma et al., 2017). Laboratory studies show that SorCS2 helps protect neurons from oxidative stress, and that SorCS2 activities can mitigate oxidative damage and neuronal death in mouse models of epilepsy (Malik et al., 2019), among other roles (Malik & Willnow, 2020). Preclinical models that lack SorCS2 have memory deficits, increased neuronal loss, and neuropsychiatric phenotypes such as hyperactivity (Dalby et al., 2025a).

Dalby et al., 2025a describes preclinical work that found that a signaling motif in the intracellular domain of SorCS2 was able to induce neurotrophic effects independently of BDNF. The group then designed cell-penetrant peptides derived from this intracellular domain that mimicked the intracellular domain's activated, phosphorylated form. They then showed that these peptide mimics could activate downstream effects such as changes in trafficking and signaling pathways.

The researchers treated mouse primary hippocampal neuron cultures with their SorCS2 derived peptides and found that the treatment modulated recycling of TrkB. They then looked at changes in patterns of phosphorylated proteins in treated versus control treated neurons in order to assess pathway activations. They found that several proteins were differentially phosphorylated (after statistical correction), including several proteins in BDNF pathway. KEGG pathway analysis indicated that engagement of MAPK, ERBB, and neurotrophin signaling pathways were some of the most enriched pathways. KEGG analysis was also performed on RNA-seq data from the treated mouse hippocampal cultures. The analysis suggested that the peptides affected pathways involving mitochondrial energy processes and also neurogenerative diseases including PD, HD, and AD. Treatment of human iPSC-derived glutamatergic neurons with the SorCS2-derived peptides led to a significant increase in the transcription factor CREB.

CREB regulates the transcription of many important genes, including those that code for BDNF, PGC1α, and TFEB. BDNF levels are reduced in patients with various neurodegenerative diseases (Dalby et al., 2025b), including in AD. Increasing levels of BDNF is an area of active research in the AD field (Gao et al., 2022), as is modulating the BDNF/TrkB pathway (Dalby et al., 2025b).

In a not-yet peer-reviewed preprint, Dalby et al., 2025b describes the further optimization of a SorCS2-derived peptide from the earlier study; this optimization led to TT-P34, an 11 amino acid cyclized peptide conjugated to a C_{18} diacid lipid that is cell-permeable and blood-brain barrier penetrant. They tested TT-P34 in two animal models: the zQ175 mouse model of Huntington's disease (HD) and an MPTP

model of Parkinson's disease (PD). They tested TT-P34 in an animal model of HD because there is impairment in BDNF signaling and concomitant reduced activity of CREB in HD. SNPs in *SorCS2* have also been associated with HD (Chaves et al., 2019); interestingly, one SNP identified by this study was also identified as a SNP associated with AD by Reitz et al., 2013. In Dalby et al., 2025b, they found that TT-P34 rescued the motor behavioral phenotype of this animal model, though interestingly, TT-P34 did not mitigate the brain volume loss in the zQ175 mice compared to wild-type littermates. TT-P34 also upregulated levels of proteins associated with mitochondrial respiration, lysosomal proteins, and synaptic proteins. TT-P34 also reduced levels of mutant huntingtin protein in fibroblasts from patients compared to vehicle treatment. In an MPTP model of PD, dosing with TT-P34 protected against dopaminergic neuron loss in a dose-dependent manner and improved the motor phenotype of the model compared to control treatment. Based on these data, the group proceeded to a clinical trial in healthy volunteers and PD patients that is described in the preceding section.

Members of Teitur Trophics have presented other preclinical data on TT-P34 at conferences. These data showed that TT-P34 activates CREB and CREB target genes such as PGC1α and TFEB in human iPSC-derived neurons, and that leads to increases in mitochondrial and lysosomal genes, including glucocerebrosidase (GCase), and increased brain glucose metabolism in healthy rats. They also reported that in pre-formed fibril models of PD, treatment with TT-P34 reduced levels of pathological alpha-synuclein and reduced dopaminergic cell loss as measured by DAT scan (AD/PD 2025; AD/PD 2026 presentation, ID 1758).

While the clinical studies thus far have been in healthy volunteers or PD patients and preclinical work has been in animal models of PD or HD, there is potential for utility in other neurodegenerative diseases. Progranulin is associated with frontotemporal dementia (FTD). Mutations in progranulin are thought to be causative in 10-15% of all FTD cases; many of these mutations are loss of function mutations (Salzano et al., 2025). A 2023 paper reported that SorCS2 is also a receptor for progranulin and modulates trafficking and secretion of progranulin as well as progranulin signaling in murine cortical and motor neurons. The researchers found that neurons lacking *SorCS2* had increased secretion of progranulin, and that overexpression of *SorCS2* increased intracellular progranulin, and hypothesized that SorCS2 could be a candidate target for FTD and motor neuron disease (Thomasen et al., 2023)

While Teitur Trophics has not published or presented any data on this compound in AD, the association of SorCS2 with AD (Salasova et al., 2022), the known deficits of BDNF signaling in AD and the potential for TT-P34 to enhance BDNF signaling (Gao et al., 2022), and the pleiotropic effects of increasing

mitochondrial and lysosomal function in a neurodegenerative disease all suggest that TT-P34 has theoretical utility in AD as well.

APOE4 interactions:
It is not known whether TT-P34 may interact with APOE status.

Aging and related health concerns: TT-P34 has not been explored for use in any age-related diseases. TT-P34 is a derivative of a protein that is found in non-neurological tissues, but the effects of mimicking this protein in other tissue is not yet known.

Types of evidence:

- 2 laboratory studies with ex-vivo human tissue and mouse models

TT-P34 has not been tested or explored for use for non-neurodegenerative age-related diseases, and a bulk of the work on SorCS2 has focused on its role in the nervous system.

SorCS2 is expressed in in other tissues such as the pancreas where it may be involved in insulin release (Kalnytska et al., 2023). Some studies have suggested that SorCS2 may be a prognostic marker in some cancer types and may act as a tumor suppressor in ovarian cancer (Qiu et al., 2025). It is theoretically possible that a peptide that mimics some of SorCS2 molecular roles could have effects in other tissues and/or in age-related diseases. However, this is purely speculative given the very early stage of research of both SorCS2 outside the nervous system and TT-P34.

Safety: An early trial of TT-P34 in healthy volunteers and PD patients reported that adverse events were not more common in the dosing group, and that all trial-related adverse events were mild, according to a conference presentation.

Types of evidence:

- 1 phase 1 clinical trial presented at a conference

TT-P34 has been tested in Phase I studies in both healthy volunteers and patients with Parkinson's disease (PD); the results have not yet been published in peer-reviewed journals as of April 2026.

Drug interactions:

The drug interactions of TT-P34 are not yet known.

Research underway:

There are no currently ongoing trials of TT-P34 that are registered on clinicaltrials.gov or the EU clinical trial register.

A phase 1 study including healthy volunteers and PD patients began in 2026; the first PD patients were enrolled initiated in January 2026 at the Centre for Human Drug Research (CHDR). The study is a randomized double-blinded placebo-controlled study with both single and multiple ascending doses. The trial aims to evaluate safety, tolerability, and pharmacokinetics. The company announced that enrollment had been completed and dosing had been initiated in all patients as of April 2026 (Teitur Trophics news releases).

Search terms:
Pubmed, Google: TT-P34

- SorCS2, Alzheimer's disease, Parkinson's disease, Huntington's disease, frontotemporal dementia, APOE4

Websites visited for TT-P34:

- Clinicaltrials.gov (0)
- Examine.com (0)
- PubChem (0)
- DrugBank.ca (0)
- Cafepharma (0)

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