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.

Nilotinib

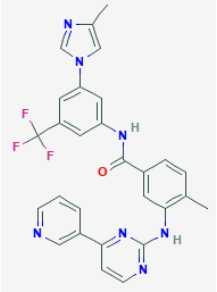
Evidence Summary

May be neuroprotective at low doses by promoting autophagic clearance of disease-associated proteins, but may also increase risks for cardiovascular disease, diabetes, and atherosclerosis.

Neuroprotective Benefit: Promotes the clearance of neurotoxic proteins via autophagy. May also protect mitochondria and synaptic function, and reduce neuroinflammation. Possible cognitive benefits seen in a small clinical study need to be validated.

Aging and related health concerns: May increase risk for cardiovascular disease, atherosclerosis, and diabetes in people with pre-existing risk factors. Changes to blood glucose and lipids are reversible and of unclear long-term clinical significance.

Safety: Confers a significant risk for QT prolongation. Primarily associated with myelosuppression, gastrointestinal events, rash, and fatigue. It is unclear whether lower doses also pose significant risks for adverse cardiovascular events.

Availability: Rx/Clinical trials	**Dose**: 300 or 400 mg 2X daily orally for chronic myeloid leukemia 150 and 300 mg 1X daily being tested for neurodegenerative diseases.	**Chemical formula:** $C_{28}H_{22}F_3N_7O$ **MW**: 529.527 g/mol  Source: PubChem
Half-life: 15-17 hours	**BBB**: Moderately penetrant	
Clinical trials: Primarily for chronic myeloid leukemia. Small pilot study in Parkinson's (n=12). Current trials for Parkinson's (n=75), Huntington's (n=10), and Alzheimer's (n=42).	**Observational studies**: Retrospective real-world studies in chronic myeloid leukemia patients show increased risks for vascular occlusive disease, diabetes, and atherosclerosis.	

What is it? Nilotinib (Tasigna®, AMN-107) is a second-generation **tyrosine kinase inhibitor** approved for Philadelphia chromosome positive chronic myeloid leukemia. It targets multiple kinases, but has high affinity for Abelson (Abl) and discoidan domain receptor tyrosine kinases. Abl is involved in the regulation of cell growth, motility, survival, and autophagy [1]. Nilotinib has modest blood brain barrier (BBB) penetrance and has been demonstrated to **promote the autophagic clearance of a variety of proteins associated with neurodegenerative diseases** including alpha-synuclein, tau, amyloid, and TDP-43 [2]. As a result, a group at Georgetown University has spearheaded an effort to repurpose nilotinib for use in neurodegenerative diseases, and clinical trials are ongoing for Parkinson's disease, Alzheimer's disease, and Huntington's disease.

Neuroprotective Benefit: Promotes the clearance of neurotoxic proteins via autophagy. May also protect mitochondria and synaptic function, and reduce neuroinflammation. Possible cognitive benefits seen in a small clinical study need to be validated.

Types of evidence:

- 1 open-label, non-controlled clinical trial in Parkinson's disease (n=12)
- Numerous laboratory studies

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

There have not been any observational studies indicating whether cancer patients chronically treated with nilotinib have a higher or lower incidence of dementia relative to patients treated with other therapies.

Human research to suggest benefits to patients with dementia: **Potential benefit**

The non-receptor tyrosine kinase Abl is activated under conditions of oxidative stress, and its activation can lead to subsequent mitochondrial dysfunction and cell death [2]. Both total (by 220%) and active phosphorylated forms (by 267%) of Abl have been found to be increased in the striatum of Parkinson's disease patients relative to age-matched controls based on postmortem tissue analysis [3]. Abl can phosphorylate alpha-synuclein and promote its aggregation [4].

As a tyrosine kinase inhibitor with high potency for Abl, nilotinib has been shown to be protective against the accumulation of alpha-synuclein and other aggregated proteins associated with neurodegeneration in preclinical models [2]. A small open-label, non-controlled proof-of-concept study for low dose nilotinib (150 or 300 mg) (n=12) in patients with advanced Parkinson's disease or Lewy body dementia showed possible evidence of both motor and cognitive improvements over the course of 24 weeks on its exploratory endpoints [5]. **Nilotinib was found to be brain penetrant, and the levels of phosphorylated Abl were reduced by 30% in the cerebrospinal fluid (CSF) following treatment**. Although levels of free nilotinib were not detectable in the CSF after 4 hours, inhibition of Abl in the CSF was maintained for up to 6 hours. This trial was not powered for clinical outcomes, but found that treatment with 150 or 300 mg nilotinib for 24 weeks led to average improvements on the Mini Mental State Examination (MMSE) of 3.85 and 3.5 points relative to baseline, and an average increase of 1.85 and 2 points on the Scales for Outcomes in Parkinson's disease-cognition (SCOPA-Cog) test. A placebo-controlled phase 2 RCT is currently underway to validate these findings in Parkinson's patients (NCT02954978).

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

Tyrosine kinase inhibitors, such as nilotinib, have been hypothesized to be beneficial for neurodegenerative diseases by promoting the clearance of aggregation-prone proteins through autophagy. Nilotinib has also been associated with other neuroprotective effects, including the enhancement of synaptic function and reduction of neuroinflammation.

Parkinson's disease: Potential benefit

Parkin is an E3 ubiquitin ligase which tags proteins with ubiquitin to direct their degradation via autophagy or the proteasome [6]. Auto-ubiquitination of parkin is important for its stability and activity [7], and the ubiquitin specific protease USP13, which removes ubiquitin from parkin, thus deactivating it, was found to be upregulated (>3.5 fold) in the midbrain of PD patients [8]. Parkin promotes the clearance of damaged mitochondria and various neurotoxic proteins, including alpha-synuclein, and mutations in the parkin gene play a causative role in some familial forms of PD [6]. Parkin is also implicated in sporadic forms of PD, as postmortem brain tissue indicates that PD patients have a shift toward decreased levels of active soluble forms and increased levels of inactive insoluble forms of parkin [9].

The **tyrosine kinase Abl is known to inhibit parkin E3 ligase activity**, and several Abl targeted tyrosine kinase inhibitors have been shown to promote parkin activation and stability. Preclinical studies indicate that **nilotinib can increase the levels of active ubiquitinated parkin** and promote its interaction with beclin-1, which facilitates autophagic processes [9; 10; 11]. **Nilotinib promotes autophagic flux** at the step of transferring cargo for degradation from autophagic vesicles to lysosomes [3; 9; 10; 12]. In rodent models of alpha-synuclein overexpression, nilotinib treatment (10 mg/kg i.p. 3 to 6 weeks) **reduced levels of alpha-synuclein and phosphorylated tau** by promoting autophagic clearance [3; 10; 13]. Nilotinib was also protective against dopaminergic loss and behavioral deficits in the MPTP model of PD [14; 15], suggesting that the oxidative stress mediated induction of Abl may drive some of the downstream neurological damage in this model. The pro-autophagic effects appear to be largely mediated through parkin, since they are attenuated in parkin knockout animals [10; 11]. Nilotinib has also been shown to modulate immune responses in disease models but not in wildtype mice, with different effects on peripheral and central immune compartments [13]. Since nilotinib targets multiple tyrosine kinases, its effects may vary depending on the tyrosine kinases expressed under different conditions within a given tissue.

Alzheimer's disease: Potential benefit (preclinical)

Similar to PD, nilotinib has been found to be beneficial in preclinical AD models by promoting autophagic protein clearance. In rodent AD models (Tg-APP or hippocampal Aß injection), nilotinib treatment (10 mg/kg i.p. daily for 3 weeks) decreased Abl activation and led to a shift toward more soluble ubiquitinated parkin and less insoluble parkin [9; 11]. This was accompanied by **a decrease in levels of soluble and insoluble Aß42 and a reduction in amyloid plaques**, and suggests that promoting parkin activation can enhance amyloid clearance. The efficacy of nilotinib may be reduced in the context of low

levels of functional tau, as one study found that tau is also important for autophagic flux and acts at a step in the pathway downstream of where nilotinib acts [12].

Nilotinib has been shown to **promote the clearance of tau and TDP-43**, and to ameliorate deficits in cellular metabolism and synaptic function by restoring astrocyte function in animals overexpressing these aggregation prone proteins [16; 17]. The effect on TDP-43 is mediated through parkin, since parkin ubiquitinates TDP-43 and promotes its translocation from the nucleus to the cytoplasm [18].

Nilotinib **may also promote synaptic function** via additional mechanisms. Nilotinib was identified in a screen as an inhibitor of the tyrosine kinase EphA4 [19], which is involved in the formation of neural circuits and is dysregulated in AD. In human embryonic stem cell derived neurons expressing the mutation in presenilin associated with AD, nilotinib treatment was able to recover expression of synaptic proteins (Rab3A and SV2B) and restore synaptic function, via an unknown mechanism [20].

These additional targets may be critical for mediating the *in vivo* neuroprotective effects of nilotinib. In a comparative study including second and third generation Abl targeted tyrosine kinase inhibitors, nilotinib was found to be more effective at clearing Aß and tau than later generation drugs with higher specificity for Abl despite having lower BBB penetrance [21]. This suggests that the **inhibition of multiple tyrosine kinases may be necessary for therapeutic benefits**.

APOE4 interactions:

How ApoE status affects the safety and efficacy of nilotinib is not known, but since ApoE4 carriers often have higher baseline levels of cholesterol, they may be at higher risk for nilotinib-induced hyperlipidemia.

Aging and related health concerns: May increase risk for cardiovascular disease, atherosclerosis, and diabetes in people with pre-existing risk factors. Changes to blood glucose and lipids are reversible and of unclear long-term clinical significance.

Types of evidence:

- 6 meta-analyses of studies for tyrosine kinase inhibitors in chronic myeloid leukemia (n=12 RCTs including 4270 patients; n=29 RCTs and cohort studies including 15,760 patients; n=13 RCTs including 3155 patients; n=10 RCTs including 3043 patients; n=17 RCTs including 7127 patients; n=13 RCTs including 5079 patients)

- 3 clinical studies for blood profile changes with nilotinib treatment (n=27, n=36, n=168)
- 6 Real world observational studies on risk for adverse events (Diabetes n=51, n=2004; hyperlipidemia n=1280; Cardiovascular disease n= 25, n=63, n=82)
- Numerous laboratory studies

Cancer (Chronic myeloid leukemia): Effective as Treatment

Tyrosine kinase inhibitors are the standard of care for patients with Philadelphia chromosome positive chronic myeloid leukemia, and nilotinib is FDA approved for this indication. The Philadelphia chromosome is a translocation between chromosomes 9 and 22 resulting in the formation of the fusion gene BCR-ABL, which forms an oncogenic constitutively active tyrosine kinase (ACS).

Imatinib (Gleevec®) is the first-generation tyrosine kinase inhibitor, while nilotinib, dasatinib, and bosutinib are second generation, and ponatinib and radotinib are the third-generation inhibitors [22]. The newer generation inhibitors have higher potency and/or specificity for Abl than the earlier inhibitors. For example, nilotinib has 20 to 50-fold higher potency and selectivity for Abl relative to imatinib. However, they are all multi-kinase inhibitors, thus the safety and efficacy profile of each drug is related to the particular kinases that they target with highest affinity.

A recent network meta-analysis of these tyrosine kinase inhibitors found that nilotinib was the most effective for chronic myeloid leukemia in terms of the number of patients who achieved cytogenic and molecular responses, although improvements to overall survival were similar to imatinib [22]. Furthermore, a separate meta-analysis found that nilotinib was associated with the lowest incidence of hematological adverse events, such as anemia, leukopenia, and neutropenia [23]. Nilotinib is typically used as a second-line treatment in patients refractory to imatinib, but its superior safety and efficacy suggest that nilotinib could be considered as a first-line treatment for chronic myeloid leukemia.

Diabetes: Increased risk

In preclinical models, tyrosine kinase inhibitors have been shown to improve glucose levels and reduce insulin resistance [24]. As a result, several tyrosine kinase inhibitors are thought to be suitable for repurposing as anti-diabetic agents. However, nilotinib often exerts the opposite effect, and **induces hyperglycemia in a subset of patients** [25].

A real-world retrospective study (n=2004) comparing patients treated with nilotinib and dasatinib found that there was a higher incidence of patients developing Type 2 diabetes following treatment with nilotinib (Hazard ratio HR: 2.77, 95% CI 1.58 to 4.86) [26]. A separate real-world study comparing

patients taking nilotinib, imatinib, and dasatinib (n=168) found that nilotinib treated patients have **significantly higher levels of fasting glucose, insulin, c-peptide, and insulin resistance**, although the rates for developing diabetes or metabolic syndrome were around 30-40% for all treatment groups, and not significantly higher for people taking nilotinib [27]. Nilotinib also reduces endogenous insulin production [28]. Nilotinib associated hyperglycemia is reversible with drug cessation, and it is still **unclear whether it is clinically meaningful** [26]. The glucometabolic changes are most likely to occur in those already predisposed to developing diabetes. One study developed a predictive genetic risk score (including the genes: IRS1, GRB14, ARL15, PPARG, PEPD, ANKRD55/MAP3K1, PDGFC, LYPLAL1, RSPO3, and FAM13A1) and found that higher genetic risk scores were associated with a higher risk for nilotinib associated diabetes/prediabetes (HR: 1.42, 95% CI 1.04 to 1.94) [25].

Cardiovascular disease: Increased risk

Nilotinib is associated with several adverse cardiovascular events in clinical trials and real-world use. These effects are most common in patients that already have preexisting risk factors for cardiovascular disease, suggesting that nilotinib augments these risk factors to push subclinical disease over the threshold to being clinically relevant.

QT prolongation: Nilotinib has a **black box warning for QT prolongation**, which can induce tachycardia, and led to to sudden cardiac death in 0.3% of patients in early clinical trials (Tasigna® product insert). Patients with a history of QT prolongation or myocardial infarction were excluded in subsequent trials, but a subset of patients have continued to experience this adverse event.

Vascular occlusive events: In a meta-analysis of 10 RCTs for chronic myeloid leukemia patients taking tyrosine kinase inhibitors, nilotinib (odds ratio OR: 3.42; 95% CI 2.07 to 5.63), dasatinib, and ponatinib were all found to have higher risk for vascular occlusive events relative to imatinib [29]. A separate meta-analysis of 12 RCTs in the same population found that the effect is driven by an increased risk for arterial occlusive events (nilotinib OR: 3.69; 95%CI 2.29 to 5.95), with no significantly increased risk for venous occlusive events [30]. Notably, the **increased risk for arterial events with nilotinib** was consistent across trials, whereas there was more variability for the other drugs where risk was driven primarily by a small number of trials. In another meta-analysis of both RCTs and cohort studies (n=29), nilotinib was associated with a significantly increased risk for major arterial events (Risk ratio RR 5.3; 95% CI 3.0 to 9.3, $p < 0.001$) and a higher risk for peripheral arterial occlusive disease (RR: 5.5; 95% CI 2.6 to 11.8) [31]. The incidence for peripheral arterial occlusive disease in patients with chronic myeloid leukemia is 0.3 per 100 patient-years (95% CI 0.2 to 0.4; $I^2 = 73.2\%$), which is increased to a rate of 1.3 per 100 patient-years (95% CI 0.8 to 1.8; $I^2 = 73.2\%$) for nilotinib treated patients.

The risk for vascular events appears to be highest in the subset of patients already at high risk for cardiovascular disease. A real-world analysis of the French Pharmacovigilance Database found that the majority of cases of peripheral arterial occlusive disease occurred in people over the age of 60 (84%) and in people with two or more preexisting cardiovascular risk factors (88%) [32].

Atherosclerosis: Nilotinib has been found to alter the plasma lipid profile in chronic myeloid leukemia patients in a manner that promotes atherosclerosis. There are ongoing lawsuits filed against Novartis regarding the link between use of nilotinib (Tasigna®) and the development of atherosclerotic related adverse events (Biospace.com). The product label was updated to include a warning for atherosclerosis in Canada, but not in the US.

A real-world retrospective study (n=1280) found that relative to dasatinib, nilotinib is **associated with a higher incidence of hyperlipidemia** (HR: 1.75; 95% CI 1.07 to 2.87) [26], and patients taking nilotinib were also found to have higher levels of total cholesterol and LDL-c in a separate comparative study [27]. In a small prospective study (n=27), nilotinib treatment significantly increased total cholesterol (from 1.80 g/L ± 0.38 to 2.24 g/L ± 0.47, $P<0.0001$), LDL-c (from 1.13 g/L ± 0.30 to 1.46 g/L ± 0.38, $P<0.0001$), and HDL-c (from 0.44 g/L ± 0.1 to 0.58 g/L ± 0.18, $P<0.0001$) within the first 3 months [33]. The proportion of patients with low levels of HDL-c (<0.4 g/L) decreased from 40.7% to 7.4% within 12 months. Although higher levels of HDL-c are generally associated with lower risk for cardiovascular disease, any potential benefits appear to be outweighed by the concomitant increase in LDL-c. The **proportion of patients with non-optimal LDL-c increased from 48.1% to 88.9%**, and 22.2% of patients had to initiate a cholesterol-lowering drug intervention during this period.

Patients with preexisting risk factors for cardiovascular disease are the ones most likely to develop atherosclerosis in response to nilotinib treatment. A retrospective real-world study found that the Systematic coronary risk evaluation (SCORE) chart, which was developed by the European school of cardiology, can be used to stratify patients according to atherosclerotic risk [34]. In their small study (n=82), none of the low risk stratified patients had atherosclerotic events, while 29% of the high-risk patients did.

In a preclinical study, nilotinib was found to upregulate pro-atherosclerotic adhesion proteins (ICAM-1, E-selection, VCAM-1) on human endothelial cells, and suppress their proliferation and migration [35]. These effects stemmed from the inhibition of a set of kinases that are relevant to angiogenesis and atherosclerosis (TEK, ABL-2, JAK1, MAPK). Furthermore, nilotinib promoted lipid plaque accumulation in the aortic wall of high fat diet fed mice. This work provides mechanistic support for the ability of nilotinib to promote atherosclerosis in patients.

Safety: Confers a significant risk for QT prolongation. Primarily associated with myelosuppression, gastrointestinal events, rash, and fatigue. It is unclear whether lower doses also pose significant risks for adverse cardiovascular events.

Types of evidence:

- 6 meta-analyses of studies for tyrosine kinase inhibitors in chronic myeloid leukemia (n=12 RCTs including 4270 patients; n=29 RCTs and cohort studies including 15,760 patients; n=13 RCTs including 3155 patients; n=10 RCTs including 3043 patients; n=17 RCTs including 7127 patients; n=13 RCTs including 5079 patients)
- 1 clinical trial for dose reduction of tyrosine kinase inhibitors in chronic myeloid leukemia patients (n=174)
- 2 Systematic reviews for tyrosine kinase inhibitors (Cardiovascular toxicities, Safety and efficacy in elderly patients)
- 5 clinical studies for non-cancer indications (Parkinson's disease n=12, n=75; chronic cerebellar ataxia n=12; systemic sclerosis n=10; spondylarthritis n=28)
- Retrospective of RCTs with tyrosine kinase inhibitors for acute kidney disease (n=468 patients)
- 6 Real world observational studies on risk for adverse events (Diabetes n=51, n=2004; hyperlipidemia n=1280; Cardiovascular disease n= 25, n=63, n=82)
- Numerous laboratory studies

The majority of safety information related to nilotinib treatment comes from patients with chronic myeloid leukemia. Nilotinib contains a black box warning for QT prolongation and patients are supposed to undergo electrocardiogram (ECG) monitoring prior to starting treatment, 7 days after initiation, and then periodically throughout the treatment period [36]. It is **contraindicated in anyone with hypokalemia, hypomagnesemia, or long QT syndrome** (Tasigna product insert). It also has a warning for myelosuppression including neutropenia, thrombocytopenia, and anemia. The most common non-hematological side effects are skin rash, pruritus, headache, nausea, and fatigue.

Nilotinib is also associated with **increased risks for arterial occlusive disease, atherosclerosis, and diabetes**, especially in patients who are already at high risk for developing these conditions [26; 30; 35]. Various screening tools have been developed to stratify patients according to baseline risk factors [25; 32; 34]. However, one study found that the risk for developing cardiovascular adverse events may increase with treatment duration [35], and/or that clinical trials may have underestimated the drug-associated incidence of cardiovascular toxicities since these kinds of events can be delayed for years after starting treatment [37]. In chronic myeloid leukemia patients, the safety and efficacy of nilotinib

does not appear to significantly differ in elderly patients (>65 years old) relative to younger patients [38].

Nilotinib is generally well-tolerated in chronic myeloid leukemia patients, and has a relatively favorable safety profile in comparison to other tyrosine kinase inhibitors used in this population [22]. Each tyrosine kinase inhibitor has a distinct toxicity profile based on its specificity for different classes of tyrosine kinases. Imatinib is considered the safest, but is also least efficacious and is not BBB penetrant [22], and is associated with a higher incidence of acute kidney injury [39]. Ponatinib has a black box warning for heart failure and is associated with a high risk for hypertension [36]. Dasatinib has the highest risk for pulmonary toxicities, and increases risk for bleeding, heart failure, and acute kidney injury [36; 39].

Bosutinib also has a favorable safety profile with the primary adverse events being gastrointestinal and myelosuppression [40]. Notably, bosutinib was found to be similar or superior to nilotinib in promoting autophagic clearance in several animal models of neurodegenerative disease [10; 11; 13; 16; 17; 18; 21; 41].

There have been a few clinical trials performed in non-cancer patient populations, including systemic sclerosis, spondylarthritis, and an analysis of off-label use for chronic cerebellar ataxia at standard doses (600 to 800 mg) [42; 43; 44]. The adverse events were largely similar to those seen in clinical trials for chronic myeloid leukemia, including the risk for QT prolongation. In most cases adverse events were mild or transient, and could be mitigated through dose reduction.

The safety profile for nilotinib when used at lower doses (150 to 300 mg) has not been well-established. In the DESTINY trial, chronic myeloid leukemia patients transitioned from standard to half-dose (200 mg 2X daily) for 12 months [45]. In these patients, adverse events including gastrointestinal events, rash, and fatigue improved within the first 3 months, however 21% of patients also developed new grade 1 or 2 musculoskeletal symptoms during the study. In the non-controlled trial in patients with Parkinson's disease (n=12), one patient withdrew from the trial due to myocardial infarct and 2 patients experienced transient QT prolongation [5]. Other adverse events included gastrointestinal events, mild infections, headache, skin irritation, and transient liver enzyme elevations. This suggests that lower doses of nilotinib are associated with the same types of adverse events as standard doses, but that the severity may be reduced. It is not yet clear whether the lower doses also lead to metabolic changes that increase the risk for diabetes and hyperlipidemia.

According to Drugs.com, there are 305 major drug interactions with nilotinib, and one major food interaction with grapefruit. Nilotinib is an inhibitor of the cytochrome P450 enzyme CYP3A4, and has interactions with other drugs that are inhibitors or inducers of this enzyme. Nilotinib also has disease interactions with QT prolongation, pancreatitis, cardiovascular disease, fluid retention, bone marrow suppression, electrolyte abnormalities, hepatic impairment, and lactose intolerance.

Sources and dosing:

Nilotinib is marketed under the trade name Tasigna® by Novartis Pharmaceutical. It is available in 150 mg or 200 mg oral capsules. The standard dosage for patients with chronic myeloid leukemia is 300 mg or 400 mg 2X daily with doses taken 12 hours apart, but adjustments down to half the standard dose (200 mg 2X daily) can be used to mitigate adverse events. It is necessary to fast two hours before and 1 hour after taking each dose of nilotinib, and high fat foods have a significant effect on drug bioavailability.

The optimal dose for efficacy in neurodegenerative diseases has not been established, but a recent pharmacokinetic/pharmacodynamic study in Parkinson's patients suggests that 200 mg 1X daily may be the optimal dose [46]. They found that this level was sufficient to increase levels of dopamine metabolites, reduce levels of alpha-synuclein, and increase TREM2 levels on myeloid cells in the CSF [46].

Research underway:

According to Clinicaltrials.gov there are currently 75 active clinical trials for nilotinib. The vast majority are for patients with chronic myeloid leukemia or other types of cancer, however, there are several trials for patients with neurodegenerative diseases.

A Phase 2 trial is testing doses of 150 or 300 mg for 12 months in patients with Parkinson's disease for safety, tolerability, pharmacokinetics, and biomarkers (NCT02954978).

A Phase 1 trial is testing a dose of 150 mg for 3 months in patients with Huntington's disease for safety, tolerability, and biomarkers (NCT03764215).

A Phase 2 dose escalation trial of 150 mg and 300 mg for 12 months in patients with Alzheimer's disease is testing safety, biomarkers and clinical outcomes (NCT02947893).

Search terms:

Pubmed, Google: Nilotinib +

- Alzheimer's disease, Parkinson's disease, neurodegeneration, autophagy, cancer, aging, cardiovascular, diabetes, safety, clinical trials, meta-analysis

Websites visited for Nilotinib:

- Clinicaltrials.gov
- Drugs.com
- WebMD.com
- PubChem
- DrugBank.ca

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