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.

Anti-C1q

Evidence Summary

May help slow complement-mediated synaptic and neuronal loss in neurodegenerative diseases. Formulations with greater BBB penetrance are needed to mitigate risk for systemic infections.

Neuroprotective Benefit: C1q could be protective by promoting clearance of cell debris, or promote excessive synapse elimination and neurodegeneration. Anti-C1q could be protective in a high inflammation, high complement environment.

Aging and related health concerns: High C1q levels are associated with age-related muscle loss, vascular remodeling, glaucoma, and poor cancer prognosis. Anti-C1q therapy may be beneficial to mitigate pathology associated with elevated C1q.

Safety: May increase risk for autoimmunity and infection. Favorable safety profile in acute preclinical toxicology studies. Evidence for long-term safety and human data are needed.

Availability: In clinical trials	**Dose**: Not established 50-200 mg/kg IV expected based on preclinical studies	**Chemical formula:** N/A **MW**: 159kDa
Half-life: 50-106 hours (50 -200 mg/kg) based on preclinical studies	**BBB**: Minimal penetrance 0.1-0.2% (similar to other antibodies)	
Clinical trials: Phase 1 for anti-C1q mAbs: ANX005 (healthy volunteers) and ANX007 (glaucoma).	**Observational studies**: High serum C1q associated with some age-related diseases. High brain C1q associated with AD.	

What is it? C1q is a glycoprotein containing 18 polypeptide chains composed of 6 repeats of 3 polypeptides (C1qA, C1qB, C1qC) [1]. It is **the initiating protein of the classical complement cascade**. It is involved in the regulation of multiple cellular functions, including innate and adaptive immunity, through a variety of receptors. It has both complement cascade dependent and complement independent functions. C1q is synthesized and secreted locally, so its function in a given tissue is dependent on the microenvironment, such as the receptor milieu within a given tissue. Tissue damage in the context of autoimmune disease and some neurodegenerative diseases is associated with excessive levels of complement activation. Anti-C1q antibodies are being developed for the treatment of autoimmune and neurodegenerative diseases [2]. Annexon Biosciences has begun testing anti-C1q antibodies, ANX005 and ANX007, in Phase 1 clinical trials.

Neuroprotective Benefit: C1q could be protective by promoting clearance of cell debris, or promote excessive synapse elimination and neurodegeneration. Anti-C1q could be protective in a high inflammation, high complement environment.

Types of evidence:

- 1 genetic association complement CR1 with AD
- 6 observational studies (complement expression in AD or FTD brain)
- Numerous laboratory studies

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

No studies have directly tested whether anti-C1q therapy could prevent dementia or cognitive decline. However, observational studies suggest associations between C1q levels and brain aging. Levels of C1q have been found to increase in the human brain by as much as 300-fold in the course of normal aging [3]. Based on postmortem tissue analysis, it is localized near synapses, and is particularly enriched in regions known to be vulnerable to neurodegeneration, including the hippocampus**.**

A single nucleotide polymorphism (SNP) in the complement receptor CR1 gene (rs4844609 - Ser1610Thr) is associated with episodic memory decline (β (SE) = −0.034 (0.012), P = 0.005) [4]. This SNP alters the conformation of CR1 in a manner that may reduce its binding affinity for C1q, thereby reducing the efficiency of clearance of plaques/cellular debris. Indeed, it is also associated with increased susceptibility for Alzheimer's disease (AD) (Odds ratio (OR): 1.40, 95% CI: 1.02 to 1.94) and increased plaque burden (β (SE) = 0.244 (0.106), P = 0.021). This suggests that C1q dysregulation, where there is a loss of its protective role in promoting clearance of cellular debris, and increase in its destructive synapse eliminating activity, is involved in age-related cognitive decline, and may be related to changes in the inflammatory milieu.

Human research to suggest benefits to patients with dementia: None

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

C1q appears to have both neuroprotective and neurodegeneration promoting properties in the CNS depending on conditions in the microenvironment. C1q has both complement-dependent and complement-independent functions, and the presence or absence of interacting partners necessary for mediating these processes can influence whether beneficial or deleterious processes dominate. **In the context of aging, there appears to be a shift toward conditions that promote the neurodegenerative activity of C1q.**

Age-related cognitive decline: Potential benefit (preclinical)

Similar to humans, levels of C1q increase in the mouse brain during aging. This age-related increase in hippocampal C1q was associated with age-related cognitive decline, and this decline could be prevented in absence of C1q [3]. Hippocampal increases in C1q were found to be higher in aged female mice, though it was significantly increased in both sexes [5]. Notably, females also had greater increases in inflammatory microglial-associated genes during aging, suggesting that the high inflammation neuro-

environment could promote pathological neurodegenerative processes, which contributes to an increased risk for dementia.

Alzheimer's disease: Potential benefit for treatment, but not prevention (preclinical)

C1q may play a protective role in preventing AD-associated pathology, however, this **protective role appears to be largely dependent on the functional state of astrocytes, particularly their phagocytic capacity.** The effect of C1q is partially dependent on ApoE, and the increased burden of AD-related pathology associated with the CR1 susceptibility allele was found to be dependent on an interaction with ApoE4.

C1q has been found to be upregulated in the context of neuronal injury and have neuroprotective effects *in vitro* by activating p-CREB and AP-1, which in turn activates LRP1B and GPR6 [6]. In young (2 month) 3xTg mice before the onset of symptoms, this neuroprotective pathway was found to be active. Under these conditions, C1q levels were increased, but other downstream complement components were not elevated. Meanwhile, complement was upregulated in older symptomatic mice when neuroprotection was lost. Neuron-associated C1q was also found to be elevated in the hippocampus and frontal cortex of a woman (age 47, ApoE2/4) with preclinical AD, which may have been a transient neuroprotective response to injury [7]. In later stages, C1q is localized to both plaques and neurons [7; 8]

Part of this neuroprotective response involves the clearance of Aβ and other cellular debris [9]. Astrocytes release both C1q and ApoE. **The interaction between C1q and ApoE is important for controlling astrocyte function and regulating inflammation.** Astrocytes are involved in eliminating damaged or unwanted synapses through C1q dependent phagocytosis [10]. ApoE2 expressing astrocytes have efficient phagocytic capacity, whereas ApoE4 astrocytes have reduced phagocytic capacity [11]. The phagocytic capacity of astrocytes was also found to be reduced in the context of aging, and in the 5XFAD model relative to wildtype mice [9]. This discrepancy is driven, in part, by a shift from less A2-like pro-phagocytic astrocytes to more A1-like pro-inflammatory astrocytes [12]. As a result of reduced clearance, there is a defect in synaptic turnover and debris removal, which can lead to an accumulation of C1q [11]. This defect in clearance can then promote the infiltration and activation of microglia, leading to inflammation and a loss of C1q tagged synapses and neurons.

The transition from a neuroprotective role for C1q to a neurodegenerative role appears to coincide with the upregulation of other complement components in the brain, such that its functions go from being primarily complement-independent to complement-dependent. The CNS is particularly vulnerable

to complement mediated toxicity because it has a very low level of complement regulatory/inhibitory proteins relative to other organ systems. Expression of complement proteins (C1 through C5) has been found to increase in the mouse brain during aging; similar increases have also been found in the human brain, especially C4 levels [13]. Complement accumulation is increased in AD mouse models [14], and in the human AD brain there is specific increase in proteins late in the complement cascade (C5b-9) that make up the membrane attack complex which facilitates complement-mediated cell death [13]. Astrocyte-derived exosomes from individuals that transitioned from preclinical to clinical AD contained higher levels of complement effectors and inflammatory proteins after the transition [12]. The use of an anti-C1q monoclonal antibody ANX-M1 (from Annexon) prevented A induced synapse loss in wildtype mice, and APP/PS1 transgenic mice lacking C3 did not experience deleterious microglial-driven synapse loss [15].

These studies suggest that blocking the classical complement cascade in the brain could potentially slow the progression of neurodegeneration in AD. While blocking the cascade at a late stage, such as with a C5 inhibitor, would be expected to be most effective for eliminating complement-mediated cytotoxicity, it would also pose a higher risk for increasing susceptibility to brain infections.

The CNS increase in late complement components with aging and in AD may be related to changes in neurovascular integrity influenced by the C1q-ApoE interaction. C1q can bind to oxidized lipids and promote their uptake by macrophages [16]. These lipids can also serve as a surface for complement activation. Therefore, the **C1q binding to lipids accumulated at blood-CNS barriers can attract immune cells, drive their infiltration, and lead to breakdown of these neurovascular barriers** [17]. Influx of Ig across these weakened barriers can promote complement expression and signaling. Some of the Ig may bind to CNS proteins and activate complement-dependent cytotoxicity. The binding of ApoE to C1q prevents binding to the oxidized lipids, and associated complement activation and inflammation [17]. ApoE secretion by astrocytes was found to decrease during aging in mice, which may contribute to the age-related decline in neurovascular integrity [18]. Long-term aerobic exercise prevented deterioration of neurovascular structures during aging in mice by preventing the age-related decline in ApoE and increase in C1q. This suggests that therapies which reduce C1q levels may promote healthy aging.

Frontotemporal dementia: Potential benefit (preclinical)

Progranulin deficiency is associated with age-related increases in microglial activation, complement production, and microglia mediated synaptic loss. In brain tissue from FTD patients with progranulin mutations, microglial density was increased in association with C1q deposits [19]. Furthermore, levels of complement proteins C1q and C3 increased as cognitive function declined, based on the Mini-Mental

State Examination (MMSE). In the context of progranulin deficiency in mice, loss of C1q prevents synaptic loss and neurodegenerative phenotypes [19]. The neuronal damage following microglial driven phagocytosis of C1q tagged synapses exacerbated tau pathology in mouse models [20].

APOE4 interactions:

ApoE4 carriers would be expected to preferentially benefit from anti-C1q therapy, because the presence of ApoE4 reduces the phagocytic capacity of astrocytes and appears to mitigate the neuroprotective benefits of C1q, while potentiating its deleterious effects [11]. While all ApoE isoforms were found to have similar binding affinities to C1q, the increased lipid load associated with ApoE4 status may exceed the levels of the protective ApoE-C1q complex, especially as ApoE levels decline, and increase the vulnerability of neurovascular damage [17].

Aging and related health concerns: High C1q levels are associated with age-related muscle loss, vascular remodeling, glaucoma, and poor cancer prognosis. Anti-C1q therapy may be beneficial to mitigate pathology associated with elevated C1q.
Types of evidence:

- 9 observational studies (Serum C1q levels in association with age-related muscle loss, diabetes and atherosclerosis, obesity, coronary artery disease, aging; Tissue C1q in glaucoma and cancer)
- Numerous laboratory studies

Age-related muscle loss: High C1q levels associated with muscle loss

Levels of circulating C1q have been found to increase with age. In a cross-sectional study including subjects from 20 to 81 years of age (n=131), serum C1q levels were inversely correlated with age, thigh cross-sectional area, muscle mass, and muscle (knee) power, and were positively correlated with pro-inflammatory markers (IL-6, TNFα) [21]. Twelve weeks of (knee) resistance training reduced age-associated increases in C1q while increasing thigh cross-sectional area ($r = -0.703$; $P < 0.01$) in older men (n=11; age 60-81 years).

Preclinical studies in rodents suggest that the **age-related increase in C1q may play an active role in inhibiting muscle repair and regeneration**. In senescence accelerated SAMP1 aged mice (38 weeks old), 12 weeks of resistance training reduced circulating C1q levels which was associated with a reduction in muscle fibrosis ($r = 0.640$, $P < 0.05$) and increased muscle mass ($r = -0.375$, $P < 0.05$) [22]. Pre-administration of recombinant C1q prevented these protective effects and suppressed muscle

regeneration [22; 23]. Secreted C1q can bind to frizzled receptors which activates canonical Wnt signaling in satellite cells and fibroblasts, which in turn, promotes muscle fibrosis and inhibits regeneration [24]. This activity is independent of classical complement activation and instead involves C1q mediated, complement component 1s (C1s) dependent cleavage of the ectodomain of the Wnt co-receptor, LRP6.

These studies suggest that exercise protects against age-related muscle loss, in part, by reducing C1q. Therefore, anti-C1q therapy could potentially help protect against muscle loss and frailty with age. However, it is not clear what is driving the age-related increase in C1q or how it is reduced by exercise, so it is possible that other factors are required to see benefit.

Cardiovascular: C1q dysregulation associated with CVD risk; context dependent

The longitudinal CODAM (Cohort on Diabetes and Atherosclerosis Maastricht) study (n=574, 60±7 years, 61% men) examined the 7-year incidence of cardiovascular disease (CVD) and found that cardiovascular health was associated with serum C1q levels in the middle tertile [25]. High or low C1q levels were associated with 2 to 2.5-fold higher risk [T_{low} vs T_{middle} odds ratio (OR): 2.38 (95% confidence interval, 1.14 to 4.95]; T_{high} vs T_{middle} OR: 1.96 (95% CI, 0.94 to 4.07)]. This suggests that there may be an optimal level of C1q with respect to CVD.

Coronary artery disease (CAD): Men (n=159) with diabetes and suspected CAD who had low levels of serum C1q (≤179 ug/ml) were found to have a higher rate of all-cause mortality (65.4%) than those with high levels of serum C1q (46.8%) (adjusted hazard ratio, HR: 0.66, 95% CI 0.52 to 0.84, P = 0.0006) [26].

C1q can bind and interact with a variety of different proteins and form protein-complexes. The levels of C1q bound in these complexes could be important for regulating its activity, thus altered complex formation could potentially play a role in age-related diseases. Adiponectin is an adipokine secreted by adipose tissue that exerts beneficial effects on insulin sensitivity and glucose homeostasis. One study (n=153) found that having a high ratio of C1q complexed with adiponectin relative to total adiponectin levels was associated with more severe coronary stenosis (OR: 2.09, 95% CI 1.12 to 3.91) [27]. Similar associations were found with respect to atherosclerosis and CAD risk [28]. High levels of adiponectin complexed C1q relative to total C1q was also associated with aging (r=0.09, p=0.03) in Japanese men (n=509, age 30-100) [29]. The biological role of the complex is not known, but it may prevent C1q from activating the complement cascade, however, as a side effect may prevent adiponectin from performing other beneficial functions.

Based on a twin study, having higher levels of adipose tissue leads to decreased levels of adiponectin and an upregulation of early complement components, including C1q, in adipose tissue [30]. The increase in C1q in the context of obesity may be a compensatory response to increased inflammation and play a role in the clearance of lipids and apoptotic debris. Anti-C1q therapy is expected to target free C1q, but spare complexed C1q. It is not known how this would influence CVD.

Atherosclerosis: In the vasculature, C1q plays a role in the opsonization of modified lipids, and has a similar profile to the opsonin Mfge8 (see Mfge8 report) in terms of preventing plaque formation/promoting clearance while also promoting arterial wall thickening. The **beneficial effect on lipoprotein clearance involves the ability of C1q to modify macrophage polarization** [31]. C1q opsonizes oxidized or acetylated LDL, and uptake of these C1q studded lipid particles alters the transcriptional profile of the macrophages to a state that is anti-inflammatory, anti-apoptotic and promotes efferocytic activity [32; 33]. C1q can also bind to advanced glycation end products (AGEs) and facilitate their removal [34]. This suggests that C1q may be protective against early atherosclerosis, which is further supported by evidence of increased lesion size and apoptotic cell accumulation in the vessels of C1q deficient mice.

However, similar to the CNS, these protective effects are likely to be dependent on the local environment, with respect to which prospective binding partners are present, and whether other downstream components of the complement pathway are upregulated in a given tissue. In a high complement environment, high C1q may instead promote inflammation and plaque buildup**. C1q can also adversely affect arterial remodeling** in a complement-independent manner that involves Wnt activation [35], similar to what is seen in skeletal muscle. This process is stimulated by Angiotensin II, suggesting that Angiotensin inhibitors may exert some of their beneficial effects by reducing C1q [23; 36]. Therefore, anti-C1q therapy could potentially promote atherosclerosis in young healthy people, but is likely to be beneficial in older individuals with ongoing vascular inflammation and plaque buildup.

Glaucoma: High C1q in early disease pathology; Potential benefit for anti-C1q

C1q mRNA and protein have been found to be elevated in the retina from glaucoma patients, as well as in monkey and rodent glaucoma models [37]. The upregulation of C1q is indicative of the loss of dendrites and synapses, and precedes retinal ganglion cell loss, suggesting that it is an early stage in the degenerative process. Mice lacking C1q were protected from synapse loss in the DBA/2J mouse model of glaucoma, and a C1 esterase inhibitor was neuroprotective in a rat model [38].

ANX-007, an ophthalmic formulation of an anti-C1q Fab fragment has been tested in a Phase 1 open-label trial (NCT03488550) in 9 participants with primary open-angle glaucoma. The antibody is administered into the eye via intravitreal injection. The trial concluded in August 2018, and the results on safety, tolerability, pharmacokinetics, and immunogenicity are expected later in 2019.

Cancer: High C1q associated with metastasis and worse prognosis

C1q expression is associated with tumor growth and aggressiveness. In breast cancer patients, high levels of C1q was found to be associated with poor prognosis [39]. **C1q may play a role in modifying the tumor microenvironment in a manner that promotes tumor growth** and spread in a complement-independent manner. In tumor-associated tissue (melanoma, colon lung, breast, and pancreatic adenocarcinoma n=6 for each type), C1q was found to be primarily expressed in vascular endothelial and fibroblast cells and in infiltrating monocytes, and was associated with tumor invasion [40]. The ability to promote the proliferation and migration of endothelial cells promotes tumor angiogenesis and metastasis. C1q binds to a variety of ligands in the extracellular matrix, including hyaluronic acid [41]. In mesothelioma cells, C1q enhanced cell adhesion, migration, and proliferation through activation of ERK1/2, JNK, and p38 signaling pathways.

However, C1q has been shown to either promote or inhibit cancer growth in different preclinical cancer models, suggesting that tumor type and microenvironment conditions may be critical for determining whether a given patient may benefit from anti-C1q therapy [42].

Safety: May increase risk for autoimmunity and infection. Favorable safety profile in acute preclinical toxicology studies. Evidence for long-term safety and human data are needed.
Types of evidence:

- Numerous studies on role of complement cascade in immunity
- Several observational studies on association of C1q with lupus
- 1 Preclinical toxicology study for ANX005

Preclinical studies suggest that the recombinant humanized IgG4 anti-C1q monoclonal antibody (mAb), **ANX005, does not induce overt toxicity in rats or monkeys at doses up to 200 mg/kg** [43]. There were no significant sex differences in the pharmacokinetics, although the half-life was slightly different. In monkeys the Cmax in the serum was 2 hours (peak levels 2000 ug/ml at 100 mg/kg). Low doses (15 mg/kg) were cleared within 5 days, while the high doses (100 mg/kg) took 20 days to clear. CSF levels

were 0.04 to 0.11% of levels in the serum for high doses, and undetectable at low doses (≤50 mg/kg). At doses of 100-200 mg/kg the levels of ANX005 antibody was found to be sufficient to fully occupy C1q in the CSF. ANX005 CSF levels were in the range of 100-200 ng/ml, while in humans, C1q levels are normally in the 20-200 ng/ml range, suggesting that doses of 50-200 mg/kg should be sufficient to neutralize C1q in humans. However, at these levels, ANX005 also reduced free C1q in the serum to undetectable levels, suggesting that **ANX005 would exert significant effects on complement activity in the periphery at levels necessary to have therapeutic benefit in the brain.** Additionally, anti-drug antibodies were detected in the animals treated at high doses, and these antibodies negatively impacted the drug response. The modification of the anti-C1q mAb to include a BBB molecular Trojan horse could potentially increase BBB penetration and allow for a lower systemic therapeutic dose [44], but there is currently no evidence that efforts are being made to enhance the BBB penetration of ANX005.

ANX005 was tested in a Phase 1 RCT (NCT03010046) in healthy volunteers (n=27) as a monotherapy or in combination with IVIg in a single ascending dose intravenous infusion. According to Clinicaltrials.gov, ANX005 was well-tolerated at the doses used in the study, but the trial has been terminated by the sponsor (Annexon), in order to initiate a trial in the relevant patient population (Alzheimer's disease or Guillain-Barre Syndrome). Results from a completed Phase 1 open-label trial (n=9) (NCT03488550) using an ophthalmic formulation of anti-C1q, ANX007, for patients with open-angle glaucoma are expected in 2019. Since ANX007 is injected directly into the eye, it is expected to have less systemic effects and a more favorable therapeutic profile. Information about the safety and pharmacokinetics of anti-C1q mAbs in humans is not yet available.

Risk for autoimmunity: C1q deficiency is associated with increased risk for the autoimmune disease systemic lupus erythematosus [45], and the presence of serum anti-C1q antibodies can be part of the diagnosis for lupus, particularly in patients with renal pathology [46]. Apoptotic cell debris is considered a source of autoantigens for lupus. C1q can facilitate the phagocytic uptake of apoptotic cells in a complement-independent manner, thus C1q deficiency can hamper clearance [42; 47]. C1q is also involved in preventing autoimmunity by polarizing phagocytic cells to regulate effector immune cell activation. This suggests that a **severe depletion of C1q could potentially lead to an increased risk for lupus**, but further safety testing is needed to determine if the level of C1q reduction associated with therapeutic doses of anti-C1q antibody therapy would significantly increase the risk for an autoimmune disease.

While it may increase risk, anti-C1q therapy is expected to mitigate rather than exacerbate disease severity in individuals with pre-existing autoimmune diseases. C1q facilitates the clearance of antibody-

antigen immune complexes. In autoimmune diseases, deposition of autoantibody-antigen complexes on healthy cells can drive complement-mediated cytotoxicity, leading to extensive tissue damage. In preclinical studies, anti-C1q treatment was able to reduce complement-mediated damage in rodent models of Guillain-Barre Syndrome and Neuromyelitis Optica [48; 49].

Risk for infection: The complement pathway is part of the innate immune system and is important for regulating components of both the innate and adaptive immune systems. C1q has a recognition motif for the Fc part of IgM and IgG antibodies and **initiates the antibody-mediated killing of pathogens through activation of the downstream complement cascade** [42]. **Loss of this system is associated with an increased risk for infection**, particularly by bacteria. C1q is the initiating component of the classical complement system, but is not involved in the lectin or alternative pathways, which also converge on downstream complement components. Therefore, targeting C1q is expected to specifically affect the classical complement system, while sparing the others, and thus have a lower risk for infection than therapeutic agents targeted to downstream components. The C5 inhibitor, eculizumab, contains boxed warnings for fungal, meningococcal, and streptococcal infections, and is contraindicated in people unvaccinated against Neisseria meningitis (PDR.net).

Drug interactions: The extent of drug interactions with anti-C1q is not yet known, but is expected to overlap with that of other complement component inhibitors, such as the C5 inhibitor eculizumab.

Sources and dosing:

Anti-C1q antibodies are being developed for therapeutic use for neurodegenerative diseases by Annexon Biosciences, and are currently being tested in clinical trials. ANX-005 is recombinant humanized IgG4 anti-C1q mAb used in an IV formulation and ANX-007 is an antigen binding (Fab) fragment that targets C1q used in an ophthalmic formulation administered via intravitreal injection. They are currently only available for human use in clinical trials.

Preclinical studies have shown that angiotensin II inhibitors can reduce levels of C1q, and its deleterious effects on vascular remodeling and skeletal muscle repair [23; 36]. Exercise has also been shown to reverse the age-related increases in C1q [18; 21; 22].

Research underway:

The Phase1b clinical trial for ANX-007 in open angle glaucoma concluded in 2018 (NCT03488550), and results are expected later in 2019. The Phase 1 trial for ANX-005 in healthy elderly volunteers was terminated (NCT03010046), and the sponsor (Annexon) is planning a new Phase 1 safety trial in AD

and/or Guillain-Barre patients. In December 2019, Annexon announced that they had closed a $75M Series C financing led by Bain Capital Life Sciences (Press release). The financing will support future clinical development of ANX005 and ANX007.

Search terms:

Pubmed, Google: C1q, Anti-C1q, ANX005, ANX007 +

- Alzheimer's disease, neurodegeneration, aging, cardiovascular, diabetes, inflammation, autoimmunity, cancer, glaucoma, safety, pharmacokinetics, clinical trials

Websites visited for Anti-C1q:

- Clinicaltrials.gov
- Annexonbio.com

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