

## CRITICAL REVIEW

# Complement-targeted therapeutics: An emerging field enabled by academic drug discovery

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### Abstract

Within a short few years, the number of complement inhibitors that are either approved for therapeutic application or evaluated in late-stage clinical trials has expanded remarkably. The sudden emergence of this target area in the pipelines of many biotech start-ups and even large pharmaceutical companies appears even more surprising when considering that the involvement of the complement system in various clinical conditions had long been recognized. In many aspects, however, the complement system is far from being a traditional drug target, which may explain the delayed breakthrough of this therapeutic strategy. While complement modulation is now considered an attractive “platform technology” with applications in a wide spectrum of disorders, the broad yet heterogeneous disease involvement of the complement system has long restricted its placement in traditional drug discovery programs. Concerns about the safety of complement-targeted interventions, the large number and high plasma concentrations of target proteins, and the complexity of the complement system's engagement in biological processes are among other factors that kept complement off the drug discovery radar for decades. Alongside technical advances and financial incentives, the innovation and persistence of academic and clinical researchers have been the critical driving force to navigate complement therapeutics out of the shadow into the spotlight. In this commentary, we document this remarkable development using select examples and aim to venture some predictions where this promising field may be headed to.

.....For over 20 years, Aegean Conferences, a non-profit educational organization run by the scientific community has been organizing highly targeted Complement Therapeutics meetings, a unique forum that brings together academic leaders and industrial innovators active in the field of complement drug discovery. Their cross-disciplinary nature has fostered scientific exchange among the complement community and the knowledge base shared in these highly interactive meetings has helped immensely in advancing new complement therapeutics to the clinical stage.<sup>56–62</sup> In many aspects, these conferences have been a unique hub for charting new frontiers in our renewed perception of complement biology and a true catalyst for the recent resurgence of clinical approvals of new complement-specific drugs.<sup>56–62</sup>

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