

Characterization and Optimization of a Novel VEGFR-2 Receptor Antagonist

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NON-CONFIDENTIAL SUMMARY

Angiogenesis, the process of new blood vessel growth, is vital throughout life for the development of new body tissues and the maintenance or healing of existing tissues. It is required for many physiological processes and is precisely controlled by many molecules, including both positive and negative regulators of angiogenesis. The breakdown of this dynamic balance between these positive and negative regulators of angiogenesis leads to many pathological conditions. For example, the lack of angiogenesis results in the failure of wound repair processes; and tissues die due to lack of oxygen, as occurs in heart disease. However, inappropriate angiogenesis can also be detrimental and contributes to a variety of diseases including cancer, rheumatoid arthritis (RA) and loss of vision in old age (age-related macular degeneration, AMD). In the case of RA, angiogenesis plays a crucial role in the formation and maintenance of the pannus, which provides nutrients to the hyperplastic synovial cells. However, regardless of the vital role of angiogenesis in RA, the major treatments remain focussed on targeting the inflammatory response of the disease. We have identified a compound (P1) that acts as an anti-angiogenic agent. P1 has shown significant inhibitory effects *in vitro* in a series of standard cell-based functional assays and it also effectively reduces RA symptoms *in vivo* in a mouse model. This result gives P1 potential to become an effective novel RA treatment agent. A patent application is now underway. The future direction of this project will be to synthesize modified versions of the compound with increased half-life and test these in mouse model.