If you’ve been keeping an eye on recent headlines for ophthalmology clinical studies and research focusing on age-related macular degeneration (AMD), the news has not been optimistic:

September 30, 2016:
Failed Eylea® Combo Trial Throws a Wrench in Regeneron’s Expansion Effort
– FiercePharma

December 16, 2016:
Ophthotech Plunges on Eye-Drug-Study Failure
– The Street

February 24, 2017:
Struggling Ohr Shutters Lab After Halting Enrollment for PhIII Wet AMD Study
– Endpoint News

Today, Regeneron is taking a wait-and-see approach for rinucumab co-therapy with final results from the CAPELLA study still to come; Ophthotech is terminating its Fovista® combination and expansion programs to free capital for in-licensing of new compounds and Ohr is making cost-cutting maneuvers as it continues to seek an investment partner. All three stocks have been battered on Wall Street of late, though Regeneron looks to be rebounding on solid 2016 Eylea sales and a strong, diversified asset portfolio. To add to the hedging, Clearside Biomedical announced a “strategic realignment” at the end of February shelving an early-stage AMD drug to devote resources to their promising diabetic macular edema program.

Fear in the AMD R&D space is reducing new funding to a trickle, particularly for combination therapies, which have proven elusive thus far. And with safe, efficacious anti-VEGF therapies readily available, it is easy to understand how wet AMD patients, investigators and researchers may feel deflated by the prospects for the next advancement in AMD treatment.
Right now, there is an open window of opportunity for neovascular AMD developers. There are three key reasons for this:

1. First, there is tremendous commercial opportunity. An aging global population, expected to reach nearly 300 million AMD sufferers by 2040, has brought a sales bonanza, with Eylea reporting over $5 billion in 2016 global sales on 32 percent year-over-year growth and over $3 billion earned for Lucentis® in 2016. Penetrating even a fraction of this expanding market may equate to blockbuster status. Note: Eylea and Lucentis are also approved for multiple age-related retina diseases, including diabetic macular edema and retinal vein occlusion; sales figures include all indications.

2. Secondly, though existing anti-VEGF therapies are safe and efficacious for the majority of wet AMD patients, these come with a high treatment burden from repeated intravitreal injections that must continue as often as monthly for life to prevent further vision degradation. And the $8,000 to $16,000 annual price tag is cost-prohibitive for many, particularly those in nations lacking government subsidies or progressive private insurance. So despite the success of current drugs, there is a continuing high demand for less burdensome, less costly standards of care.

3. And finally, with the completion, termination or delay of several clinical programs, there is far less competition for new wet AMD clinical trial patients now than would have been predicted even just a year ago. There are some enrolling Phase II and III global multicenter studies – namely from Allergan, Bayer, Ophthotech, Roche/Genentech and Regeneron – but from at least mid-2016 through early 2017, the neovascular AMD clinical trial space is ripe for the taking.

So what can we expect from this great window of opportunity? Here are some likely approaches:

1. With written guidance in place from the FDA and EMA, there are now four biosimilars approved in the U.S. and 31 in Europe across all therapy areas. Lucentis patents will expire in 2020 in the U.S. and 2022 in Europe. Eylea patents last through 2020 and 2021, respectively. The race is on to fill the void when patent exclusivity ends, and there are no fewer than eight companies developing ranibizumab biosimilars, the first of which, Intas’ Razumab™, has already been marketed in India for nearly two years. Biosimilars will remain a significant development area for the next several years with patients eager for the price relief and developers aiming to claim a piece of an $8 billion pie.

2. Anything that can improve the long-term effects or reduce treatment burden will be well-received by AMD patients and ophthalmologists. Though the adjunct therapy route is looking questionable, there are still new anti-VEGF therapies in development that may offer less frequent dosing, as well as new approaches underway. For example, Allegro Ophthalmics’ Luminate acts on both anti-angiogenesis and vitreolysis mechanisms; Gene Signal is aiming to develop a topical eye drop with its Aganirsen antisense DNA oligonucleotide; the Roche/Genentech AVENUE and LADDER studies are testing a one-of-a-kind port delivery system for repeated intravitreal dosing through a semipermanent surface implant; and still others are evaluating cell therapy, subcutaneous injections and novel biochemical pathways.

Syneos Health has conducted 16 AMD studies since 2011 in every global region, and our team members have worked on trials for nearly every AMD drug brought to market so far (as well as many others that weren’t). Right now, we are seeing many new protocols taking one or more of the tracks mentioned – biosimilar, novel treatment pathway, less burdensome regimen and/or improved delivery approach. It has been a bumpy few months for AMD drug developers, but we think now is a great time to conduct an AMD study, and we’re excited for the companies that can take advantage of this rare window of opportunity.

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References


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