Author's response to reviews

Title: Drug discovery in ophthalmology: past success, present challenges, and future opportunities

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Dear Editor

Re: Drug discovery in ophthalmology: past success, present challenges, and future opportunities

Thank you for your comments, we have made the following changes as requested:'...' I have changed the format of the article from a research article to a debate as I feel this reflects the review style of this article.

1. No competing interests for any of us.

2. NG, RB, ME, AD carried out the literature searches, NG and AD conceived the study, all authors drafted the manuscript, read and approved the final manuscript.

3. Acknowledgements - None

4. Ethics - N/A

5. Consent - N/A

6. Abstract

Background: Drug discovery has undergone major transformations in the last century, progressing from the recognition and refinement of natural products with therapeutic benefit, to the systematic screening of molecular libraries on whole organisms or cell lines and more recently to a
more target-based approach driven by greater knowledge of the physiological and pathological pathways involved. Despite this evolution, increasing challenges within the drug discovery industry are causing escalating rates of failure of development pipelines.

Methods: Narrative review based on a search of articles relevant to drug discovery in ophthalmology from the medical and investment literature identified via pubmed and google, with hand-searching of relevant reference lists.

Results: We review the challenges facing the drug discovery industry, and discuss what attempts are being made to increase the productivity of drug development, including a refocusing on the study of the basic biology of the disease, and an embracing of the concept of ‘translational research’. We consider what ophthalmic drug discovery can learn from the sector in general and discuss strategies to overcome the present limitations. This includes advances in the understanding of the pathogenesis of disease; improvements in animal models of human disease; improvements in ophthalmic drug delivery and attempts at patient stratification within clinical trials.

Conclusions: As we look to the future, we argue that investment in ophthalmic drug development must continue to cover the whole translational spectrum (from ‘bench to bedside and back again’) with recognition that both biological discovery and clinical understanding will drive drug discovery, providing safe and effective therapies for ocular disease.

7. Manuscript

Rename Introduction —> Background

Methods: This is a narrative review based on a search of articles relevant to drug discovery in ophthalmology using search terms “Drug discovery” AND (“ophthalmic” OR “ophthalmology” OR “ocular”) from the medical literature via the search engine, Pubmed. Commercial and investment literature was identified using a similar strategy via Google. Relevant articles were assessed for content by a minimum of two authors with hand-searching of reference lists to identify additional articles not identified in the original searches.

Put a title of “Results:” above the rest of the manuscript but keeping all the headings (which effectively become subheadings) - could we please remove this ‘Results’ title at a later date?

8. Added line numbering

9. Added our emails

10. Affiliations:
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Yours faithfully

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