Essential CNS Drug Development

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Contents

List of contributors vi
Preface ix

1 History of CNS drug development 1
Sheldon Preskorn

2 Regulatory issues 14
Gwen L. Zornberg

3 Essential CNS drug development – pre-clinical development 31
Alan J. Cross and Frank D. Yocca

4 Phase I trials: from traditional to newer approaches 55
Matthew Macaluso, Michael Krams, and Sheldon Preskorn

5 Phase II development and the path to personalized medicine in CNS disease 70
Douglas E. Feltner and Kenneth R. Evans

6 CNS drug development – Phase III 92
Judith Dunn, Penny Randall, and Amir Kalali

7 Statistics issues relevant to CNS drug development 100
Craig H. Mallinckrodt, William R. Prucka, and Geert Molenberghs

8 Clinical trials management at company level 127
Nuala Murphy

9 Clinical trials management at the site level 148
Joseph Kwentus

10 Medical writing for CNS indications 156
Ginette Nachman

11 Dissemination of clinical trial information: multiple audiences, multiple formats 169
Leslie Citrome

12 The importance of treating cognition in schizophrenia and other severe mental illnesses: background, strategies, and findings to date 177
Philip D. Harvey and Richard S. E. Keefe

13 Leveraging disruptive technologies to drive innovation in CNS clinical drug development 192
Penny Randall, Judith Dunn, and Amir Kalali

Index 200

Color plates found between pages 118 and 119.
<table>
<thead>
<tr>
<th>List of contributors</th>
</tr>
</thead>
</table>
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Preface

It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of Light, it was the season of Darkness, it was the spring of hope, it was the winter of despair, we had everything before us, we had nothing before us, we were all going direct to heaven, we were all going direct the other way – in short, the period was so far like the present period, that some of its noisiest authorities insisted on its being received, for good or for evil, in the superlative degree of comparison only.

Charles Dickens
A Tale of Two Cities

Reminiscent of Dickens, the title of our book could also be "A Tale of Two Disciplines." That is, the discipline of clinical trials in the field of central nervous system disorders is now experiencing both the best of times and the worst of times.

The best of times are exemplified by the explosion of genomics and neuroimaging making possible the best translational neuroscience studies in the history of psychiatry and neurology. Findings from preclinical studies can be forward translated into novel, small population studies in well defined patient groups, utilizing powerful new technologies, and then these results backtranslated to inform better preclinical studies. Never before have the prospects been so great for gaining an understanding of the biological basis of psychiatric and neurological disorders. This might be our age of wisdom, our season of life, our epoch of belief and our spring of hope.

Alas, it is also the worst of times, as shown by the inflating placebo response rate worldwide, destroying our ability to prove the effectiveness of both new and old drugs. This has led first to increasing sample size and increasing site numbers to overpower dwindling drug placebo differences, then to transferring studies out of the US to the third world, and now to quitting the field by many in Pharma. Simultaneously our discipline is criticized for manufacturing psychiatric disorders for the sake of corporate profit, and hoodwinking everyone into thinking that our drugs work whereas these are really dangerous chemicals that do harm and are no more effective than placebo for corporate disease-mongering of illnesses that do not exist to be treated by drugs that do not work to the mutual enrichment of Pharma and their investigators. Thus, this might also be our age of foolishness, our epoch of incredulity, our season of darkness, and our winter of despair.

What went wrong? In part, this book is an answer to that question and a proposal for the way forward. As explained in the chapters here by the world’s leading experts, the solution is to combine the best methodologies, investigators, monitors, and, yes, new chemical entities. It requires understanding the science, the regulations, and the commercial imperatives of how this game of clinical trials is played and played to win.

We start with a background on the history of CNS drug development, and then an overview of regulatory issues, followed by a step-by-step progression through the clinical development process, from preclinical through approval. A unique aspect of our journey through CNS drug development is discussions of clinical trials management.
Although it is true that our discipline has a “worst of times” set of problems, we hope to show the way forward to deliver on the promise of new therapeutic agents for the CNS.

Stephen M. Stahl