AAPS Advances in the Pharmaceutical Sciences Series 60

Bhavishya Mittal

Sustainable Global Health Systems and Pharmaceutical Development

aaps®

Springer

AAPS Advances in the Pharmaceutical Sciences Series

Volume 60

AAPS and Springer Nature Seek New Editor Advances in Pharmaceutical Sciences Book Series

Springer Nature, the American Association of Pharmaceutical Scientists, are pleased to announce an exciting opportunity for an exceptional candidate to serve Editor for the Advances in Pharmaceutical Sciences Book series.

Interested candidates should provide a statement of why they are interested in this position and what their vision would be for the editorship of this series, along with two or three references and/or letters of recommendation from knowledgeable colleagues and a current CV to Publications Manager, Matt Baughman (BaughmanM@aaps,org).

Review the job description (PDF) before applying.

Applications Due: May 1, 2024

Volunteer Opportunities - American Association of Pharmaceutical Scientists (aaps.org)

Bhavishya Mittal

Sustainable Global Health Systems and Pharmaceutical Development

Springer

aaps®

Bhavishya Mittal
Vice President, Product Development
and Manufacturing
BioDuro-Sundia
Irvine, CA, USA

ISSN 2210-7371 ISSN 2210-738X (electronic)
AAPS Advances in the Pharmaceutical Sciences Series
ISBN 978-3-031-50414-3 ISBN 978-3-031-50415-0 (eBook)
https://doi.org/10.1007/978-3-031-50415-0

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

बड़ा हुआ तो क्या हुआ जैसे पेड़ खजूर |
पंथी को छाया नहीं फल लागे अति दूर ||
– कबीर

Humility is the solid foundation of all virtues
– Confucius

Preface

> If there is any one secret to success, it lies in the ability to get the other person's point of view and see things from his angle and your own. (Henry Ford)

The importance of the pharmaceutical industry for human society was never in question. However, the clear and present danger of the COVID-19 pandemic brought our industry into sharp focus. The world recovered from the pandemic due to the significant efforts of numerous research institutes, pharmaceutical companies, regulatory agencies, government institutions, and many other healthcare agencies. Such a recovery effort has never happened in human history. However, the post-pandemic years have also presented unique opportunities to discuss how society can capitalize on this innovative industry to deliver the safest and most cost-effective medicines for the myriad of diseases.

For me personally, it all started with a seemingly benign question from a close family member, "Why do pharmaceutical products cost so much?". I knew the answer and tried to frame it in the context of the high costs of innovation and risks associated with product development. However, the second question was more profound for me: "What is being done to reduce the costs of pharmaceutical products?". The answer to this question was not as simple and did require me to reflect on the question a lot more. It made me wonder how the public perceives the innovation potential of the pharmaceutical industry and why all conversations around pharmaceuticals revolve around the costs. I also realized that being a member of the pharmaceutical industry for 21+ years may have insulated me from the perception of the industry in the general public.

There is no doubt that the pharmaceutical industry has done so much good for the world (and continues to do so). But as a responsible member of the industry, I also believe that it is my solemn duty to understand and appreciate the perspectives of the numerous stakeholders and patients for whom we are developing these products in the first place. Such introspective exercises help build empathy and create safe-space conversations aiming to appreciate other people's viewpoints. The quest to answer these questions led to reviewing numerous topics on global health inequality, healthcare technology assessment, stakeholder analysis, pharmaceutical

sciences, and the latest trends, such as Industrial Revolution 4.0. The results of this research are amalgamated in this book.

More than 750 companies are listed as either biotechnology or major pharmaceutical companies on the NYSE and NASDAQ combined. These companies cover a whole spectrum of business-operating models all the way from fully integrated research companies with thousands of employees to completely virtual entities that operate with minimal permanent staff. No matter what their *modus operandi* may be, all these companies are developing new drug products for a vast number of therapeutic indications. From a societal viewpoint, with the amazing number of resources spent on each new drug candidate, the total costs start to add up quickly! This further necessitates that any efforts that can help to lower the development time and costs should be carefully reviewed and, if possible, integrated into the product development strategy.

Pharmaceutical innovation without integrating economics into product design is an inherently futile and non-sustainable proposition. Therefore, the time to discuss how the development of robust and productive healthcare options can be achieved economically has now come, for, after all, no industry is immune to the laws of economics. With this premise, this book hopes to spur a conversation that aims to integrate drug development, economics, and efficient manufacturing in a fashion that improves the accessibility of drugs to patients. Such conversations allow pharmaceutical scientists to get a step closer to building an "empathetic bridge" and be more aware of the patient's needs.

As the eminent economist Milton Friedman once said, "Only a crisis—actual or perceived—produces real change. When that crisis occurs, the actions taken depend on the ideas lying around." In that spirit, ideas to improve healthcare systems are regularly discussed in the literature. However, this book hopes to integrate the opportunities within pharmaceutical R&D with the sustainability of healthcare systems. Therefore, all this book is doing is collating those ideas and thus offering a perspective that summates economics, manufacturing sciences, and pharmaceutical R&D together. It is my sincere hope that the readers find that this book is thoroughly researched, its approach well-thought-out, and is a manuscript worthy of their time and consideration.

Irvine, CA, USA Bhavishya Mittal

Acknowledgments

I would like to thank my mentors, Dr. Michael Levin and Dr. Ajaz Hussain, for listening to my ideas and guiding me toward various critical source materials. I also sincerely thank the Acquisitions, Editorial Project Management, and Publishing teams at Springer. In particular, I appreciate the help from Ms. Merry Stuber and Ms. Charlotte Nunes that made this project come to fruition.

I am also thankful to my parents (Dr. J.P. Mittal and Madhu Mittal), who have positively influenced my life and have always provided their unbridled support, blessings, and encouragement. I am incredibly thankful to my loving wife, Shalini, for her unconditional love, positive attitude, and constant reassurance, which helped me to complete this project on time. I thank my son, Kern, for patiently proofreading this manuscript and providing critical input. I am also thankful to my daughter, Ariana, for their perennial encouragement and understanding while I worked on this book.

Contents

List of Figures

List of Tables

About the Author

Bhavishya Mittal is the Vice President of Product Development and Manufacturing at BioDuro-Sundia (Irvine, CA), where he leads the strategy and operations for drug product development of client-owned assets within the portfolio. Before BioDuro-Sundia, Bhavi worked at Kronos Bio (San Mateo, CA), AbbVie (Irvine, CA), US FDA (Silver Spring, MD), Takeda Pharmaceuticals (Cambridge, MA), and Astellas Pharmaceuticals (Norman, OK). Bhavi is also an adjunct faculty at the Keck Graduate Institute's Henry E. Riggs School of Applied Life Sciences (Claremont, CA). He has a PhD in Materials Engineering from the Pennsylvania State University and a BS in Chemical and Bio Engineering from the National Institute of Technology, Jalandhar (India).

Bhavi has 21+ years of industrial experience in the formulation design, process development, and project management of numerous drug products of small therapeutic molecules (oncology, inflammation, GI, and CNS indications) aimed for NDA and ANDA filings. His expertise includes product development strategy, project management, outsourcing management, phase-appropriate formulation design (immediate and modified release), process engineering, statistical process control, QbD implementation, FMEA/risk mapping, data analytics, and process modeling/simulation of unit operations for solid oral dosages.

An avid sports enthusiast and a history buff, Bhavi is a passionate supporter of continuing education and firmly believes in the noble tradition of passing-on knowledge to younger generations. He loves to travel, learn about various cultures, and spend time with his family.

Abbreviations

AAC	Actual Acquisition Cost
AAM	Association for Accessible Medicines
ADC	Antibody Drug Conjugate
ADME	Absorption, Distribution, Metabolism and Excretion
AHRQ	Agency for Healthcare Research and Quality
AI	Artificial Intelligence
AIDS	Acquired Immune Deficiency Syndrome
AM	Additive Manufacturing
AMP	Average Manufacturer Price
AMR	Antimicrobial Resistance
ANDA	Abbreviated New Drug Application
ARV	Antiretrovirals
ASQ	American Society for Quality
ATMP	Advanced Therapy Medicinal Products
AWP	Average Wholesale Price
BCS	Biopharmaceutical Classification System
BEA	Bureau of Economic Analysis
BLA	Biologics License Application
BPCIA	Biologics Price Competition and Innovation Act
CDER	Center for Drug Evaluation and Research
CET	Cost-Effectiveness Threshold
CHE	Current Health Expenditure
CHIP	Children's Health Insurance Program
CHO	Chinese Hamster Ovary
CL	Compulsory Licenses
CM	Continuous Manufacturing
CMC	Chemistry, Manufacturing, and Control
CMS	Centers for Medicare and Medicaid Services
COG	Cost of Good
COPQ	Cost of Poor Quality
CPP	Critical Process Parameter

CQA	Critical Quality Attribute
CSDH	Commission on Social Determinants of Health
DAH	Development Assistance for Health
DALY	Disability-Adjusted Life Year
DCS	Developability Classification System
DDD	Daily Defined Dose
DMPK	Drug Metabolism and Pharmacokinetics
EM	Essential Medicines
FDA	US Food and Drug Administration
FDC	Fixed-Dose Combination
FDCA	Food, Drug, and Cosmetic Act
GATT	General Agreement on Tariffs and Trade
GDP	Gross Domestic Product
GHG	Global Health Governance
GHO	Global Health Observatory
HAQ	Healthcare Access and Quality
ICER	Incremental Cost-Effectiveness Ratio
IGO	Inter-Governmental Organization
IHI	Institute for Healthcare Improvement
IHME	Institute for Health Metrics and Evaluation
IND	Investigational New Drug
IP	Intellectual Property
IPCC	Intergovernmental Panel on Climate Change
LCM	Life-Cycle Management
M&S	Modeling and Simulation
mAb	Monoclonal Antibody
MCB	Master Cell Bank
MDG	Millennium Development Goal
NCE	New Chemical Entity
NDA	New Drug Application
NDC	National Drug Code
NGO	Non-Governmental Organization
NTD	Neglected Tropical Diseases
OBA	Outcomes-Based Agreement
OBD	Optimal Biological Dose
OECD	Organization for Economic Co-operation and Development
OTC	Over-the-Counter
P&R	Pricing and Reimbursement
PAT	Process Analytical Technology
PBM	Pharmacy Benefit Manager
PCE	Personal Consumption Expenditures
PDM	Product Design Management
PDP	Prescription Drug Plan
PDUFA	Prescription Drug User Fee Act
PFDD	Patient-Focused Drug Development

PhRMA	Pharmaceutical Research and Manufacturers of America
PHSA	Public Health Services Act
PPF	Production Possibilities Frontier
PPP	Public-Private Partnerships
PROM	Patient-Reported Outcome Measure
PSO	Patient Safety Organization
QALY	Quality-Adjusted Life Year
QbD	Quality by Design
QbED	Quality by Efficient Design
QTPP	Quality Target Product Profile
R&D	Research and Development
SDG	Sustainable Development Goals
SOC	Standard of Care
SPP	Special Patient Populations
THE	Total Health Expenditure
TPP	Target Product Profile
TRIPS	Trade-Related Aspects of Intellectual Property Rights
TTM	Time-to-Market
UN	United Nations
UNICEF	United Nations Children's Fund
USAID	US Agency for International Development
USPTO	United States Patent and Trademark Office
VA	Department of Veterans Affairs
VBP	Value-Based Pricing
WCB	Working Cell Bank
WHO	World Health Organization
WAC	Wholesale Acquisition Cost
WTO	World Trade Organization

Chapter 1
The Need to Introspect

No institution should expect to be free from the scrutiny of those who give it their loyalty and support.

Queen Elizabeth II

Contents

Abstract Global health inequity is a significant crisis facing humankind and is a gaping hole in our efforts to achieve a just and equal global society. Significant efforts have been taken by numerous political leaders, visionaries, and international organizations over many generations to outline the various actions, approaches, and recommendations that aspire to close the health inequity gap. Unfortunately, despite of well-intentioned efforts from stakeholders, access to medicines remains a vexing issue. Potential solutions include responsible governance, positive cultural shifts, balanced socioeconomics, infrastructure growth, and increased public awareness. Another approach could be to improve the efficiency of the pharmaceutical development process. From a for-profit company's perspective, substantial financial risk must be undertaken without any assurance of economic reward as pharmaceutical research is complicated, time-consuming, attritive, and costly, with estimated

B. Mittal, *Sustainable Global Health Systems and Pharmaceutical Development*,
AAPS Advances in the Pharmaceutical Sciences Series 60,
https://doi.org/10.1007/978-3-031-50415-0_1