Considerations for Commercial Development of a Topical Dermal Product

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Who we are

- Facility located in Research Triangle Park area, North Carolina
- ~26,000+ ft² state of the art facility
- 75+ Scientists/Staff
- Fully equipped laboratories (formulation, analytical, IVRT, skin biology and clinical supply-manufacturing)
- 150+ cell banks of IVRT and Skin Permeation cells
- cGMP Compliant Clinical Supply Manufacturing: Phase I / II / III
- FDA Inspected
- DEA Approved (Schedule II thru V)
- From Concept to Clinical

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Experts in Topical Product Development

- Full Contract Development Services
- Formulation, Development & Optimization
- Analytical Research & Development
- Skin Biology and Permeation Studies
- In Vitro Release Testing (IVRT)
- Clinical Supply Manufacturing GMP Phase I/II/III
- CMC logistics, Scale up and Tech transfer Consulting
Development Services

- Creams
- Lotions
- Ointments
- Gels
- Nail Lacquers
- Pastes
- Foams
- Suppositories
Tergus Collaboration

• **A one-stop shop to support**
  - NCE development incl. repurposing/repositioning
  - A generic equivalent of RLD
  - 2 men and a molecule
  - Post-approval (SUPAC), marketing claims support
  - M&A assistance
  - Building platforms / portfolios for companies

• **Begin with end in mind**
  - Next stage gate: tox / clinical / commercial
  - Type of dosage form / dossier
  - *In vitro* skin PoC or animal / disease models or straight to FIM / PoC
  - Clinical de-risking and reduce CMC surprises
    - Irritation / IID / Vehicle effect, permeation, scale-up, QbD, stability, phase-specific validations
  - Launch – ready products
Considerations for Commercial Development of a Topical Dermal Product

• Topics covered:
  • Innovations in dermatology
  • Commercial and business development aspects
  • Private-public partnership
  • IP / Legal matters
  • Navigating the global regulatory stream

• What you will learn:
  • Begin with end in mind
  • Protection of your asset
  • R&D and Business Junctures
  • Current State of:
    • Product launches
    • Regulations
    • Dermatology market
Innovations in dermatology

• Innovation vs. Excavation
• We are in the era of Targeted Therapies in Dermatology
• NCE is the new Black
• Janus Kinase (JAK) inhibitor & Tropomyosin receptor kinase A (TrkA) inhibitors
  • Alopecia Areata
  • Vitiligo
  • Inflammatory Skin Disorders
• Topical Angiotensin-converting enzyme (ACE) inhibitors
• Cyclooxygenase-2 (COX-2) inhibitors
Innovations in dermatology

- Topical ROR gamma inverse agonists
- Boron Chemistry Platform
  - Crisaborole – Targets PDE-4
  - Tavaborole – Anti fungal / Onychomycosis
- LXR Agonists
  - Atopic Dermatitis
- Topical Nitric Oxide platform
  - Acne
  - Molluskum
  - Warts (HPV)
Innovations in dermatology

- Topical Minocycline
- Brilacidin
- Sirolimus
- Doxycycline
- Oxymetazoline
- Dapsone

- Topical cannabinoids
Innovations in dermatology

- Combo products are still a rage
  - Acne

- New trend in converting age old DESI products

- Hormone Replacement Therapy (HRT) using topical and vaginal routes

- Novel anti-virals such as acyclic nucleoside phosphonate for cervical and anal indications
Innovations in dermatology

• Platform Technologies
  • Deuterated NCEs - Deuterium Chemistry
  • Liquidia – PRINT Technology
  • Confluence
  • Botanix – Permetrex Technology
  • Cage Bio – Ionic Liquids
  • Leon Nanodrugs – Nano Technology
  • Exicure – 3-D Spherical Nucleic Acid (SNA) Architecture

• Gold Nanoparticles
• Solid Lipid Nanoparticles (SLN)
Innovations in dermatology

• Excipients & Polymers
  • BASF
  • Gattefosse
  • Croda
  • Seppic

• Novel Skins
  • EpiSkin (pigmented, full thickness)
  • L’Oreal - Organovo 3-D Printing of human skin

• Pkg. innovations
  • Dual Chambers, novel applicators
Innovations in dermatology

• Novel Tools
  • Microdialysis
  • PBPK – PK/PD models
  • MALDI imaging

• Pharmaceutical tools
  • IVPT
  • Raman
  • Rheology / Texture Analyzer / Q3 Working group

• Innovative Pricing Model$
Commercial & Business Aspects

• New companies are coming into dermatology
  • Roivant - Dermavant
  • Sienna
  • Brickell Biotech
  • Dermira
  • Aclaris
  • Pfizer

• Few big players are exiting too

• Some companies stopped medical derm but continuing in aesthetic dermatology
Commercial & Business Aspects

• M&A Events
  • Mylan – DPT
  • Allergan – Kythera
  • Pfizer – Anacor
  • Aclaris – Confluence
  • Sienna - Creabilis
  • Valeant – Everyone else

• Incubators, Special Economic Zones
  • South Australia, Israel, Singapore, South Korea, Ireland
Commercial & Business Aspects

- Dermatology is adopting the big PhRMA model
  - Internal R&D
  - Collaborative R&D (early phase)
  - Acquisition & further develop (late stage)
  - Life Cycle Management
- Repurposing Big Pharma’s leftovers
- Specialty Generics
- Orphan drugs
- Rare diseases
Commercial & Business Aspects

• Aesthetic Dermatology is still lucrative
• Novel alternatives to fillers & toxins in development
• Emerging markets are targets for premium products
Commercial & Business Aspects

• How to you make sure R&D and Business junctures are hand-in-hand?
  • Koke model
  • Pipeline competition
  • Business Development input early on and throughout clinical phases
  • Avoid late input of commercial & clinical teams

• Packaging is often ignored in the beginning but becomes a nightmare later on

• PAI approval-readiness
Commercial & Business Aspects

- Commercial bottlenecks
  - Launch readiness
  - Last minute negotiation of label
  - Not realizing the market capitalization
  - Under estimating the cost of development
  - Surprise regulatory burdens
  - Pricing models
  - Market risks
  - Competition

- Market size, generic intrusion, citizens backlash, loss of exclusivity, tribal patents
Commercial & Business Aspects

• Portfolio Decisions
  • Group thinking
  • Poor translation of early PoC clinical data
  • Forcing a molecule with open IND into skin without understanding the nuances of skin
  • One formulation for many indications
  • One molecule for many indications

• Influence of Investors, VCs, Business partners and markets

• Lack of knowledge for dermal assets at University Tech transfer Offices
Public-Private Partnerships (PPP)

- US FDA – CROs – Academia initiatives
- New BA/BE guidances
- New Q3 technologies

- Dermatopharmaceutics Focus Group
- NIH/R01/SBIR grants
- Department of Defense (DoD) funding
Public-Private Partnerships (PPP)

• Foundations – General
  • US AID
  • C | O | N | R | A | D
  • FHI360
  • Gates Foundation
  • Wellcome Trust

• Foundations – Dermatology
  • Derm Foundation
  • Rosacea, Itch, Psoriasis foundations
Public-Private Partnerships (PPP)

• Apple Watch / Fitbits / Smart Phones

• IBM / Watson – Big data analytics

• University Collaborations
• Multi- stakeholder PPP
• Charities
• Regulatory agencies
Global Regulations

• API
  • Multiple monographs
  • Impurities – known vs. unknown
  • Early tox assessment requirements
  • Export / Import
  • Stability - zones

• Excipients
  • Q3 influence
  • JP/USP/EP issues
  • Branded excipients with hidden ingredients
  • Global sourcing
Global Regulations

• Packaging
  • Types of DMFs
  • Extractables & Leachables
  • Stability – zones
  • Requirements for penetration enhancers absorption
  • Sprays, measured vs. metered
  • Applicators
  • Combo devices – Drug-Device Combos
  • Kits with applicators vs. two different products
Global Regulations

• Manufacturing
• Marketing Claims
• Pharmacoeconomic vs. Approval criteria
  • Me too vs. best in class
  • Comparator studies vs. non-inferior studies
  • Price controls
• BA / BE waivers
  • US & EU harmonization?
• OTC in EU but Rx in USA?  *vice versa*
• Devices (510k and PMA) vs CE mark
• FDA Inspections vs. QP audits
IP / Legal Considerations

- Why?
  - Intellectual Property Protection
  - Regulatory Exclusivity
  - Secure Investments
  - Strategic Partnerships
  - In and Out Licensing

- Protect & Commercialize the IP assets while minimizing the risk of liability
- M&A acquisition of privately held companies purely depends on the IP protection
IP / Legal Considerations

• In addition to patents, companies should:
  • Trademarks
  • Copyrights
  • Trade Secrets
  • Unfair Competition
  • Privacy
  • Confidentiality
  • Tech Transfer

• Ability to litigate & dispute the patents in front of International Trade Commission
IP / Legal Considerations

- Freedom to Operate (FTO) or Analysis of Market
  - Sizing the competition
  - Locating relevant players in the space
  - Examining the 3rd party blocking patents
  - Weighing the risk of infringement & potential injunction
  - Infringement Analysis with proper search terms
  - Licensing and assignment agreements
  - Settlement agreements

- Ancillary patents – PLEs, polymorphs, salts, formulations, prodrugs, delivery devices, new indications
IP / Legal Considerations

• Few Regulatory associated concerns
  • Application review period – Patent term extension
  • Multiple patent term extensions for a single product
  • Paragraph I through IV certifications
  • Non-Infringement vs. Invalidation for a generic product
  • Exclusivity for 505(b)1, (b)2 and Orphans
  • Deuterated drugs are NCEs?

• Listing in Orange Book for
  • Molecule
  • Methods of use
  • Formulation
  • Patent extension
Final Thoughts

• Begin with end in mind
• Know your molecule and the drug product
• Protect the IP and mitigate the legal risks
• Thorough understanding of the regulatory changes in the global arena is important
• Have an appreciation for commercial and clinical inputs much early on
• Interact with business folks to understand what is happening with the competition
• Pay attention to industry’s events & innovations
Questions

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