

I. Client's Objective

- Therapeutic program strategy team at an international pharmaceutical company sought to develop aspirational neuropathic pain (NP) target product profiles (TPPs) and evaluate two potential early stage assets

II. Lumleian's Perspective

- Successful entry into a complex therapeutic area such as that for NP requires an acute understanding of the market. Lumleian's expert scientist-consultants can synthesize secondary research for a comprehensive audit of the scientific, clinical, and commercial NP space
- To supplement the current market overview, a combination of targeted KOL focus groups and physician interviews can help our team identify unmet needs and understand clinical trends to develop target product profiles that will be successful in the future NP market.

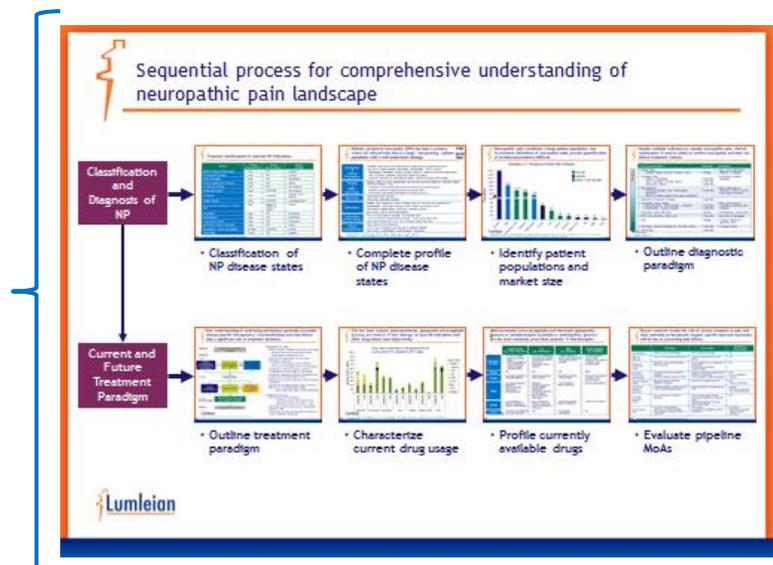
III. Client Result

- **Data-driven market analysis:** Client was not only presented with therapeutic area overview, but also a complete analysis of 20 distinct NP disease states so it could consider the advantages and challenges associated with each subdivision of the market
- **Actionable deliverable:** Client was armed with multi-scenario asset forecasts and a strong grasp of future market trends to design a forward-thinking clinical development strategy for one asset and recognize the hurdles they need to overcome with another potential asset

IV. Engagement Summary

Evaluate Clinical Landscape

- Classified and profiled 20 disease states within the NP therapeutic space:
 - Clinical presentation & pathophysiology
 - Current diagnostic paradigm
 - Market size & disease burden
 - Current treatment options & unmet need
 - Patient population characteristics



IV. Engagement Summary

Characterize Current and Pipeline Therapeutics

- All mechanisms of action currently being explored for treatment of NP were analyzed based on:
 - Scientific merit
 - Development challenges
 - Competition
 - Physician perception

Current drugs are generally systemic and non-specific; defining characteristics of NP therapeutics may provide for phenotype specific matching to NP disease.

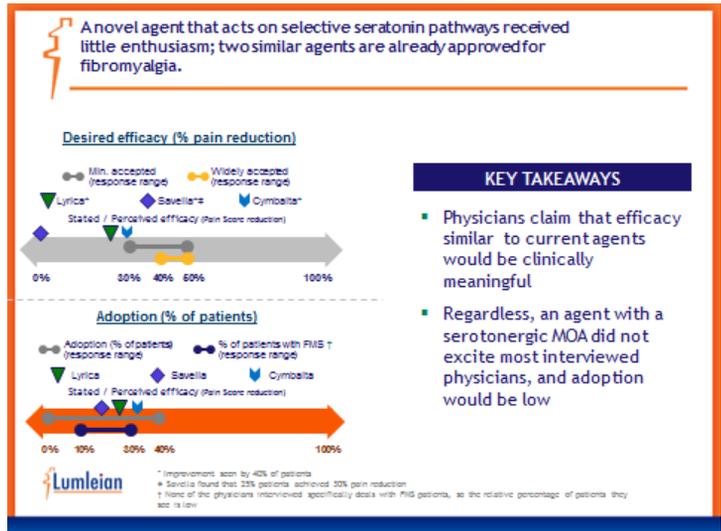
Drug Target	Advantages	Disadvantages	Specificity & Clinical Utility
Sodium channels (non-specific)	• Recent advances in understanding of role of channel subtypes in NP	• Blocks sodium channel nonselectively, thus all sensation • Activity required for normal signaling	• CNS • Regulatory approval in TGN
Sodium Channel (Nav1.3)	• Only upregulated after neuronal injury	• Still a novel target	• Primarily CNS
Sodium Channel (Nav1.7)	• Genetic mutations in Nav1.7 associated with pain syndromes • Only present in peripheral sympathetic neurons • Increased understanding of role of p38 and ERK1/2 MAPK in Nav1.7 activity, offering additional targets	• Only upregulated after inflammatory models • Still a novel target	• Small fibers: PHS • Painful neuromas
Sodium Channel (Nav1.8)	• Downregulated in NP • Selectively expressed in PHS, mainly in nociceptive sensory neurons	• Not restricted to neuropathic pain states • Redundancy with other sodium channels • Still a novel target	• Dorsal root ganglion injury in PHS • Neuromas
Sodium channels (Topical)	• Topical application to specific area of lesion	• Blocks sodium channel nonselectively, thus all sensation	• PHS • Regulatory approval in PHN
Calcium channels (Cav 2.1, 2.2, 2.3)	• Neuron-specific channels • May target other receptors associated with pain (e.g. P2X3)	• Side effects	• CNS
Calcium channel subunits (α2δ1)	• Regulatory approval for DPN, PHN, TGN, and central NP	• Often poor tolerability, especially in elderly • Effective only in mechanical and diabetic neuropathies?	• PHS/CNS • Effective in peripheral NP

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Source: #28, #25, #30, #40, #3, #73, #103, #73, #53, #21, #77

KOL Focus Groups and Physician Interviews

- Three geographically diverse KOL focus groups and interviews with neurologists and pain specialists provided information about the need for and potential adoption of novel therapies
- Insights gleaned from physician interviews guided development of four target product profiles



Market Forecasting

- High-level financial analysis and forecasting of each TPP and the client's portfolio as a whole under multiple scenarios provided client with knowledge needed for confident go/no-go decisions

