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The Successful Negotiator

CASE STUDY
AFFISURE

FOR PREVIEW PURPOSES ONLY

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March 2014

Case Study

Affisure

Introduction

Background

Pharmasur Inc. was founded by executives from several established pharma companies. The business plan was not new: buy old but still viable drugs from other companies, drugs that are no longer promoted either in advertisements or by detailing, and promote them with a skilled sales force and strong marketing. After obtaining venture capital, the executives were able to purchase a complete line of drugs from a pharma company in the process of a major reorganization. Astute marketing and detailing increased sales and the new company was profitable.

The second phase of the business plan was to develop line extensions to increase sales and profit and then sell the company. The portfolio of drugs included an old, DESI[1] drug as well as newer drugs.

Affisure (for the relief of moderate to severe acute pain due to muscle spasm), was found efficacious in the DESI review and was still marketed. However, with over 95% of the sales of Affisure going to generics, Pharmasur needed to do something to prop up sales.

John Hamilton, the CEO of Pharmasur, called a meeting of his Steering Committee to discuss ways of increasing Affisure sales. **Christine Applegate** MD, the VP of Clinical,

[1] Drug Efficacy Study Implementation: The 1962 Kefauver-Harris Drug Control Act required that all drugs must demonstrate efficacy in addition to safety. The DESI program was intended to review the 3,000+ drugs approved only on safety data (prior to 1962) and determine if they were effective, ineffective or needing further study. Those drugs determined to be efficacious as well as safe were allowed to continue to be marketed.

noted that **Paxamor**, a newer competing drug for a pain indication, was losing sales to generic competition and was re-introduced as a line extension at a lower dose and gained 3 years of marketing exclusivity before a generic copy could be marketed. Sales increased markedly.

This approach appealed to John and the Steering Committee. Because Affisure was approved without efficacy data, Pharmasur had no data from dose-ranging studies and could not be sure if a dose lower than the 1000 mg marketed dose would be effective or if the 1000 mg dose could be proven statistically significantly effective. Dr. Applegate's staff conducted a detailed literature search but were not able to find well designed clinical trials to help determine if a lower dose would be effective. Conducting dose-ranging studies could result in serious efficacy questions even for the marketed dose and the risk-benefit was heatedly discussed.

After much discussion, John decided to take the risk and conduct a dose-ranging study, hopefully targeting a dose not easily achieved by cutting a 1000 mg generic tablet and hopefully not showing lack of efficacy at the marketed dose. There was also thought that a lower dose would reduce or eliminate some of the already minimal side effects associated with Affisure while still maintaining acceptable efficacy, thus gaining support from FDA.

Alan Franks, VP of R&D, immediately began work formulating the new tablets and **George Pine**, VP of manufacturing, worked with marketing and R&D to design the new tablet, including possibly a new color and shape, and ordered tooling to fit their tablet presses.

Clinical and regulatory staff worked together to design a 3 dose, dose-ranging study and clinical efficacy program to assess the efficacy (and safety) of several lower doses with 650 mg the preferred dose. **Pete Higgins**, VP of Regulatory, argued that an IND was required even though Affisure was already marketed at a higher dose and the new studies would pose no new risks. Pete made this determination because the clinical trials would

be submitted to FDA to support new labeling and promotional activities and because Pete believes in getting FDA comment prior to initiating expensive clinical studies.

John Hamilton, Christine Applegate and Charley White, VP of Operations, opposed a new IND filing fearing extensive new requirements from the FDA review Division,

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Thirty days after the IND filing, **Elaine Short**, the FDA Project Manager, called Pete and told him the clinical team leader wanted the clinical trials extended to 4 weeks of treatment with pain end points at 14 and 21 days post treatment initiation. However, there was no clinical hold.

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Type B Meeting

Pete and Christine knew Kile Prescot was both difficult and opinionated and they anticipated a difficult meeting. Pete tried to get the Division Director to attend the meeting but he was unsuccessful. Elaine Short opened the meeting and Kile quickly took control and it was downhill from the beginning. Kile wanted to see 4 week data and was intransigent. The meeting was not a disaster, but close. Christine was sure that a 4 week trial would not show a statistically significant difference between doses of Affisure or Affisure and placebo at these end point times. The team could not get Kile to adequately explain his reason for the longer studies. It was just clear that was what he wanted.

Type A Dispute Resolution Meeting

After much internal debate, a Type A dispute resolution meeting was requested and granted by DPARP. The meeting was scheduled just 2 months before winter. In order not to lose the season if they prevailed, drug and placebo were shipped under quarantine

to the clinical sites. Pete knew that he needed **Fred Simmons** MD, the Division Director at the meeting or Kile would not change his position. Elaine Short tried several times to get Fred to attend the meeting but he did not plan to attend.

Since Type A meetings are supposed to have a higher level supervisor present, and since Fred was not going to attend, Pete was in a bind. Without an upper level supervisor he knew they would not get Kile to change his position. Pete was under tremendous pressure from John and knew that if could not get Kile's position changed, Pharmasur would be forced to cancel the study and drop the project. Pete was under a great deal of internal pressure to make this happen.

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In fact, Alan did attend the meeting by conference call. A speaker phone was placed in the center of the meeting table and Alan and other attendees were introduced. Pete orchestrated the meeting for Pharmasur and turned the meeting over to Christine to make the clinical presentation. There was animated discussion between Christine and Kile, moderated as much as possible by Pete, but nothing was resolved. Alan did not take part in the discussions. At the end of the meeting Pete summed up what had been discussed and that no decision had been reached. He then asked who would make the final decision and Alan Withers said it would be his decision.

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This is all Pete could think about over the weekend. Given the urgency, Pete decided to try to get to Alan Withers and convince him to sign the meeting notes. After closing his office door and mentally preparing himself, Pete called Jane on Monday morning in an attempt to reach Alan Withers. Unfortunately, Alan was attending an Advisory Committee meeting and was not reachable. Pete reviewed the situation with Jane, carefully explaining that they were now at day 31 and the clinical sites must begin enrolling immediately or another 6 months would be lost. He asked if Alan had a Blackberry and eventually convinced Jane to give him Alan's phone number, even though

Jane said Alan would not answer any calls during the Advisory Committee meeting. Pete sent an instant message to Alan's Blackberry titled "Urgent and Critical, for your attention only" in hopes of getting Alan to read the message right away.

Alan wrote back immediately saying the decision was made in Pharmasur's favor
This was quickly becoming a major disaster. Pete then mentioned the instant messages between himself and Alan Withers, confirming the acceptability of the end points. Burt stated that he had never known Alan to communicate directly with sponsors and never by instant message. Pete was severely insulted at being called a liar by an FDA Associate Director, but he held it together and offered to send Burt the instant messages and the telecom ended. The IM's were sent later that day.
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Prologue
The next morning Burt called and agreed the NDA was approvable pending some labeling issues. DPARP wanted fewer, more limited indications, a treatment period limited to 2 weeks and other negative changes to the package insert. John and marketing were appalled by the required changes and wanted to protest. Pete requested a brief period to discuss the changes and muted the phone. He counseled John that FDA needed to save face, that additional argument at this time could result in delays and, worst case, a second cycle review and John agreed to the changes. Marketing was very unhappy, especially with Pete, but finally agreed. The NDA was approved that afternoon, pending receipt of the labeling changes, and less than a year later Pharmasur was sold at a nice profit.