COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Pharmaceutical Sciences Seminar Series
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2548 NUB or Zoom

"Characterization of Exparel®, Understanding of Critical Manufacturing Process Parameters and Investigation of Drug Release Mechanisms *in vitro* and *in vivo*"

Presented by:

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Abstract: Liposomes are some of the most popular drug carriers used for sustained drug release. Traditional liposomes, such as unilamellar vesicles (ULVs) and multilamellar vesicles (MVLs), have been studied extensively and are approved as the carriers for many drug products. A relatively novel type of liposome, known as a multivesicular liposome (MVL), recently sparked interest in the drug delivery community due to its unique structure and drug release characteristics. The unique pomegranate-like structure of multivesicular liposomes (MVLs) is attributed to the assembly of numerous nonconcentric liposomes within MVLs. The formation of MVLs is based on the DepoFoam® technology, which enables the encapsulation of active ingredients into MVLs and provides a sustained drug release.

Exparel® (Pacira Pharmaceuticals, Inc.) is one of the FDA approved MVLs formulations utilizing the DepoFoam® technology. Exparel® is a bupivacaine multivesicular liposomal injectable suspension indicated for post-surgical local pain management. Encapsulating bupivacaine via this DepoFoam® technology allowed for local analgesia to last up to several days, depending on patients' conditions.

Currently priced at $344 for a single dose of 260 mg/20mL, Exparel® has gained great success in the market. Its high price per dose, market success and impending loss of exclusivity make Exparel® an appealing drug for generic developers to manufacture. However, there is very limited literature describing the characterization and manufacturing process of Exparel®, which poses a challenge not only to the generic drug product developers but also to regulatory authorities.

The purpose of this research is to bridge the current gaps in Exparel®'s generic version development. The studies we propose will clarify the Exparel® formulation, its manufacturing process, and its release kinetics. Based on our results, we can establish Q1/Q2 equivalent formulations of Exparel® for further IVIVC analysis. This research is also aimed to elucidate both the *in vitro* and *in vivo* release mechanisms using an optimized cage model developed by Dr. Steve Schwendeman's lab. The results of this research will provide more information about the Exparel® and other MVL formulations, which will help both generic product developers and regulators better understand and characterize related drug products.