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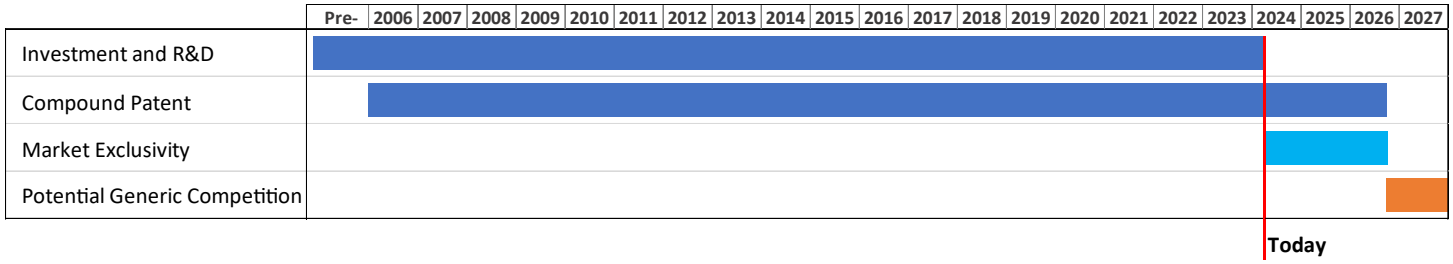
Patent Analysis of Resmetirom

Extending Market Exclusivity for First-in-Class NASH Treatment

On March 14, 2024, Madrigal Pharmaceuticals announced FDA approval of Resmetirom (Redzdiffra). This is a monumental advancement in the treatment of Non-Alcoholic Steatohepatitis (NASH), a condition lacking specific pharmacological interventions since its identification in 1980.

This pivotal milestone underscores the critical importance of innovative therapies in addressing longstanding medical challenges.

However, amidst the celebration of this achievement lies a pressing concern: **the need to safeguard Resmetirom's market exclusivity** against looming patent expirations and potential generic competition.



With the core compound patent set to expire in 2026, Madrigal Pharmaceuticals needed to implement strategic patent management initiatives to extend market exclusivity beyond this critical juncture.

Contained in this paper:

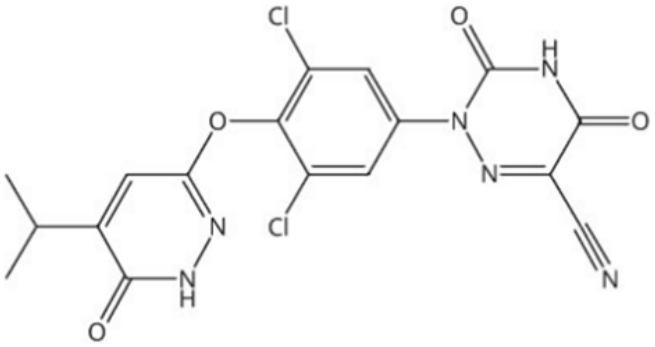
- **The need for novel treatments**
- **Patent strategies used by Madrigal Pharmaceuticals**
- **The importance of IP protection for the benefit of global patient populations**

Disease Overview

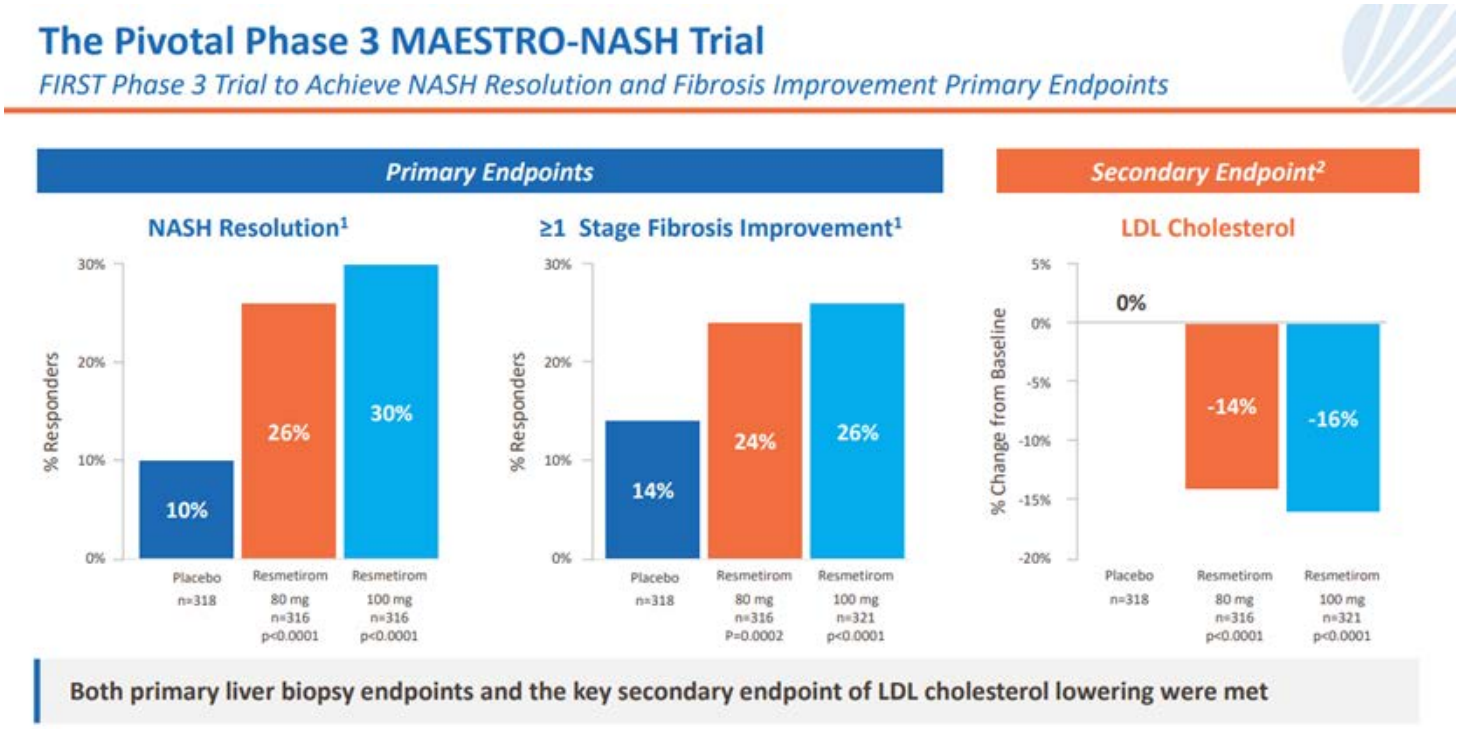
Nonalcoholic Fatty Liver Disease (NAFLD) encompasses a spectrum of hepatic disorders, with Nonalcoholic Steatohepatitis (NASH) representing a severe manifestation characterized by inflammation and fibrosis. The prevalence of NASH is staggering, affecting millions worldwide and posing significant health risks, including cirrhosis and hepatocellular carcinoma. Given the dire consequences of untreated NASH, the development of effective therapies is paramount.

Resmetirom Overview

Resmetirom, a thyroid hormone receptor beta (THR-β) agonist, has emerged as a promising therapeutic option for NASH. Clinical trials have demonstrated its efficacy in resolving NASH and ameliorating fibrosis, offering hope to patients and healthcare providers alike. However, the imminent expiration of its core compound patent in 2026 necessitates strategic measures to safeguard its market position.



Resmetirom Structure



Patent Status

Patents play a crucial role in the lifecycle of a pharmaceutical product. To extend the patent protection period of a drug, innovators typically proceed to file patents related to polymorphs, formulations, and uses after the initial core compound patent submission. Peripheral patenting is particularly vital for drugs whose compound patents expire early.

Resmetirom has an early expiration for its core compound patent, set to lapse in 2026. With the compound set to expire only two years post-market launch, Madrigal Pharmaceuticals has implemented an extensive patent strategy for Resmetirom, particularly with regard to polymorphs, securing multiple crystal forms in 2013 and 2019.

In the United States, Madrigal has not only secured patents for the marketed crystalline Form I and all its hydrates, including mono- and dihydrates, but also conducted a second round of systematic crystalline form screening and research. This effort led to the protection of additional newly identified crystalline forms, encompassing over twenty anhydrous forms, numerous salt forms, and co-crystal forms, as well as amorphous solid dispersions.

The objective of the robust patent framework is to construct formidable barriers against strategies that might circumvent crystalline form patents. Generic and competitor companies often try to develop market alternatives as soon as possible by adopting new crystalline forms or altering salts. This initiative is expected to extend the patent protection period for the drug until 2033 or beyond.

Patent	Patent Expiration Date
	2026 | 2027 | 2028 | 2029 | 2030 | 2031 | 2032 | 2033 | 2034 | 2035 | 2036 | 2037 | 2038
Compound	Patent No. US7452882
Polymorph (Form I)	Patent No. US9266861
Polymorph (hydrate, monohydrate, dihydrate)	Patent No. US10376517
Polymorph (Form I and two solvate forms)	Patent No. US11564926
Use	Patent No. US9968612
Use	Patent No. US11090308
Use	Patent No. US11806353
Polymorph (Free form B/C/D/E/F/G/H/I/K/L/S+T/S/U/V/W/X/Y/Z/α/β/χ/δ/ε/Φ/η/λ; some salt crystal forms, co-crystal forms, amorphous solid dispersion)	Patent No. US20210122740 - *Patent under examination*

Conclusion

The approval of Resmetirom marks a watershed moment 44 years into the fight against NASH, offering hope to millions of patients worldwide. Novel pharmacological treatments like Resmetirom require significant investment to push projects from discovery to market.

Madrigal Pharmaceuticals' strategic patent management exemplifies a proactive approach to extending market exclusivity. Approaches like this ensure companies and investors can find prolonged success in the market after investing many years and millions of dollars towards development of groundbreaking therapies.

Crystal Pharmatech Expertise

Comprehensive screening ensures market exclusivity, and the smallest mistake can open the door for competitors. Our comprehensive suite of services, including crystal form screening, developability assessment, and polymorph patent filing, ensures that clients have the necessary tools to navigate the complexities of solid-state research and development.

With our deep expertise and commitment to excellence, we empower companies to safeguard their innovations and propel the future of pharmaceuticals forward.

Drug development stage	Polymorph patent strategy analysis	Patentability assessment	Polymorph patent application research scheme	Polymorph patent application	Patent reply support	Formulation of non-infringement strategy	Formulation of defense strategy
Pre-Tox	√	√	√	√			
Pre-IND	√	√	√	√			
Phase I	√	√	√	√			
Phase II	√	√	√	√	√	√	√
Phase III	√	√	√	√	√	√	√
NDA	√	√	√	√	√	√	√
Post Marketing	√	√	√	√	√	√	√

References

1. https://ir.madrigalpharma.com/node/15401/pdf
2. Guidelines of prevention and treatment of nonalcoholic fatty liver disease (2018, China)
3. https://www.pfizer.com/disease-and-conditions/nash
4. Madrigal pharmaceuticals corporate presentation in January 2024