AGMON with TULCHINSKY

Responding to Disappointing Clinical Trial Results

Client Update – August 2026

Dear Clients,

Clinical development is inherently uncertain. Even well designed late stage studies may fail to meet their primary endpoints, or interim data may not support continuation of a development program on its original path. For Israeli life sciences companies, many of which operate with lean teams, rely on cross-border clinical operations and depend on successive financing rounds, strategic partners and global market access, such outcomes can have immediate consequences for valuation, financing, partnering discussions, manufacturing commitments and overall development strategy.

A disappointing clinical result does not, however, necessarily require abandonment of the relevant asset (i.e., the relevant product candidate, technology, or development program). Recent developments in the life sciences sector illustrate several possible strategic responses: identifying a more responsive patient population, continuing development in other indications, modifying the clinical development plan, or reallocating resources to higher priority programs.

For Israeli biotechnology, pharmaceutical and medical device companies, the key challenge is to respond promptly and credibly, while maintaining scientific discipline and avoiding decisions driven solely by short term market pressure.

Assessing whether a defined patient population may still benefit

A missed primary endpoint may conceal clinically relevant outcomes in a distinct patient population. Tenax Therapeutics recently reported a Phase III trial failure, while indicating that patients with more severe disease showed more meaningful benefit. The company has stated that it plans to submit the data to the FDA and EMA (click here to read Tenax Therapeutics' announcement) .

This type of outcome may justify further analysis, but it requires particular care. A company should distinguish between findings that were prespecified in the protocol or statistical analysis plan and those identified after the data became available. The latter may still inform future development, but will often need to be confirmed in a dedicated study.

Where a subgroup signal appears promising, the company may need to reconsider patient selection criteria, endpoint selection, sample size assumptions and the overall target product profile. It may also need to evaluate whether the commercial opportunity for a narrower population remains sufficient to support further investment.

From a business perspective, a subgroup based strategy may affect development budgets, investor communications, partnering discussions, manufacturing forecasts and market-access planning. Agreements with collaborators, licensors, CROs and manufacturers should therefore allow sufficient flexibility to accommodate a revised development focus.

Continuing development in other indications

An asset may fail in one indication without undermining its potential in others. Novo Nordisk’s monoclonal antibody ziltivekimab did not succeed in a Phase III study focused on reducing the risk of major cardiovascular events. Novo Nordisk is nevertheless continuing to investigate the product in studies involving heart failure and patients who have experienced an acute heart attack (click here to read Novo Nordisk's announcement).

This approach reflects the importance of considering each indication on its own scientific, clinical and commercial merits. Different patient populations, disease settings,

comparators and endpoints may lead to materially different outcomes, even where the investigational product and its underlying mechanism remain the same.

Companies should therefore avoid treating a negative result in one program as conclusive for the entire asset. At the same time, continued development should be supported by a clear rationale, an updated assessment of benefit and risk, and a realistic evaluation of the resources required to pursue the remaining programs.

A diversified clinical portfolio can provide important strategic optionality. However, companies should ensure that their development, financing and partnering arrangements do not create unnecessary constraints if a lead indication fails and the company seeks to prioritize another program - an important consideration for Israeli companies pursuing global development and commercialization pathways.

Adapting the development plan following interim data

A third response may be to adjust the design or scope of an ongoing study. Moderna recently added a new cohort to a Phase III vaccine study after interim data did not support the original plan, while continuing the study in a blinded manner (click here to read Moderna's announcement).

Changes to an ongoing program may help preserve valuable development options, but require careful scientific, statistical, operational and regulatory planning. Depending on the circumstances, a revised approach may involve adding a cohort, modifying enrollment criteria, refining endpoints, collecting additional data or developing a follow on study designed to address the questions raised by the initial result.

Any adjustment should be supported by a robust rationale and implemented in a manner that protects the integrity of the study. Companies should also consider the practical implications for clinical sites, patient recruitment, investigational product supply, budget, timelines and communications with investors and commercial partners.

The possibility that a development program may need to evolve should be reflected in the company's contractual arrangements. Agreements with CROs, clinical sites, data providers

and manufacturers should address change control, additional work, data access, ownership of study materials, transition support and termination rights.

Reallocating resources when continued development is not justified

In some cases, the appropriate response will be to discontinue the program. Soligenix recently decided to stop developing a topical lymphoma asset following a Phase III failure and to focus instead on its rare disease pipeline candidate and vaccine platform (click here to read Soligenix's announcement).

A disciplined decision to discontinue a program can preserve resources for assets with a stronger clinical, regulatory or commercial rationale. It may also improve a company's ability to communicate a focused strategy to investors and prospective partners.

Before discontinuing a program, companies should consider the consequences for existing contractual commitments, intellectual property strategy, clinical data access and ongoing obligations to investigators, patients, regulators, suppliers and partners. They should also assess whether the data or the underlying technology may retain value for a different indication, a licensing transaction or a future research collaboration.

Practical considerations for life sciences companies

Disappointing trial results should be anticipated as part of clinical development planning, rather than treated as an unexpected crisis. Companies should consider the following:

1. Develop alternative scenarios before key data readouts, including potential next steps if a study succeeds, produces mixed data or fails to meet its primary endpoint.

2. Ensure that clinical, regulatory, commercial and financing teams are aligned on the decision criteria for continuing, modifying or discontinuing a program.

3. Build sufficient flexibility into CRO, manufacturing, supply, licensing and collaboration arrangements to support changes in study design, patient population, indication or development priorities.

4. Preserve access to clinical data, study materials, regulatory correspondence and other assets that may be needed for a follow on study or a revised development strategy.

5. Review disclosure, investor communication and confidentiality considerations before public release of material clinical results.

6. Consider whether a negative result changes the company's patent strategy, freedom to operate analysis, manufacturing footprint or partnering priorities.

7. Assess whether AI-enabled analytical tools can help identify factors contributing to the outcome, generate hypotheses and improve the design of future development programs, while ensuring appropriate scientific oversight, data governance and validation.

Looking ahead

A disappointing clinical result can be a significant setback, particularly in late stage development. It does not necessarily determine the future of the underlying technology or asset. The appropriate response will depend on the quality and nature of the data, the strength of any remaining scientific rationale, the availability of alternative indications or patient populations, and the company's financial and operational capacity. For Israeli companies, that assessment should also account for the practical demands of managing international trials, regulatory pathways, financing and strategic relationships.

For companies that plan early, maintain contractual flexibility, use available analytical capabilities responsibly and evaluate outcomes with scientific and commercial discipline, a negative result may lead to a more focused and sustainable development strategy.

The information provided in this client update is for general informational purposes only and should not be construed as legal advice or a substitute for professional legal counsel.

As always, the team at Agmon with Tulchinsky remains at your disposal.

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