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Amplia Therapeutics (INNMF-OTCQB)

INNMF--Breakthrough Technology in the Fight Against Cancer

Research Note

Amplia Therapeutics (OTCQB:INNMF) is a clinical stage drug development company that has a compelling oncology story centered on a differentiated scientific approach and a focused clinical strategy targeting some of the most difficult-to-treat cancers, including pancreatic cancer and ovarian cancer. The company's pipeline is built around its lead asset, narmafotinib (AMP945), a highly selective inhibitor of focal adhesion kinase (FAK), an enzyme that plays a critical role in tumor growth, metastasis, and the dense stromal environment that makes cancers such as pancreatic tumors particularly resistant to treatment. By inhibiting FAK, narmafotinib is designed to disrupt tumor cell signaling while also modifying the tumor microenvironment, potentially making cancers more responsive to chemotherapy and improving patient outcomes.

The company's strategy is focused at the present time on two key studies, ACCENT and PRROSE, the first focused on advanced pancreatic cancer, and the second on ovarian cancer, both diseases with historically poor survival rates. The ACCENT trial represents the most encouraging near-term value driver. In this study, narmafotinib is combined with the chemotherapy combination of gemcitabine and nab-paclitaxel (Abraxane), a regimen widely viewed as more tolerable than other combinations. Data from the trial have demonstrated response rates and progression-free survival outcomes that compare favorably to historical benchmarks for chemotherapy alone, suggesting that the addition of a FAK inhibitor may enhance treatment efficacy without introducing significant additional toxicity (see below Figure). This balance of improved efficacy and manageable safety is particularly important in pancreatic cancer, where patient tolerability often limits treatment intensity, and positions narmafotinib as a potentially meaningful advancement in the standard of care if results continue to mature positively.

FAK levels are elevated in pancreatic cancer

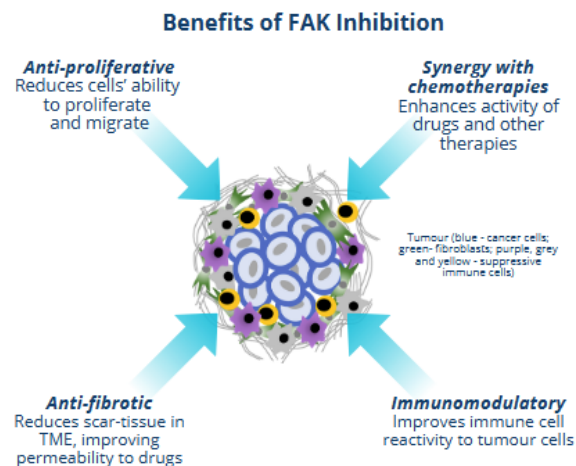
- Correlate with worse patient outcome

FAK inhibition blocks processes that support:

- Tumour growth
- Metastasis
- Treatment resistance

FAK over-activity in both cancer cells and surrounding cells

- Cause fibrosis *and* immune suppression



Source: Ampliatx.com

The PRROSE trial is investigating narmafotinib in combination with standard chemotherapy agents carboplatin and paclitaxel in women with high-grade serous ovarian cancer who have not responded adequately to initial platinum-based chemotherapy before surgery.

Beyond pancreatic and ovarian cancer, Amplia's FAK inhibitor platform has broader potential applications in other fibrotic tumors and even non-oncology indications such as idiopathic pulmonary fibrosis, reflecting the central role of FAK signaling in both cancer progression and fibrotic disease and demonstrating the large potential upside Amplia has.

The ACCENT Trial

The ACCENT trial is the primary clinical program for Amplia Therapeutics and represents a structured, multi-stage effort to validate its lead drug, narmafotinib, in one of the most difficult oncology settings—advanced pancreatic cancer. It is best understood as a combined Phase 1b/2a study designed to first establish the optimal dose and then expand into a broader efficacy evaluation, all within a real-world first-line treatment framework.

ACCENT is a multicenter, open-label, single-arm study evaluating narmafotinib in combination with standard-of-care chemotherapy—specifically gemcitabine and nab-paclitaxel (Abraxane). Narmafotinib is administered orally alongside these agents in patients with metastatic or unresectable pancreatic ductal adenocarcinoma. The trial is being conducted across multiple sites in Australia and South Korea, reflecting both geographic diversity and a coordinated international development strategy.

The study is deliberately divided into two stages. The Phase 1b portion focused on dose escalation, testing multiple dose levels of narmafotinib to evaluate safety, tolerability, pharmacokinetics, and preliminary signs of efficacy. This stage successfully identified 400 mg as the recommended dose for further study. The Phase 2a portion then expanded enrollment at this selected dose to assess clinical effectiveness more rigorously, with an initial cohort followed by expansion to approximately 50–60 patients total.

The Phase 1b dose-escalation stage was completed in 2023, followed by initiation of the Phase 2a expansion in early 2024. Interim data began emerging through 2024 and 2025, with increasingly mature datasets reported into 2026. The trial is ongoing, with completion of the current dataset anticipated around the second half of 2026, alongside regulatory discussions for a potential registrational study. The results to date have been the most compelling aspect of the study and should be the primary focus of investors. Across 64 patients treated at the 400 mg dose, the trial has demonstrated a confirmed objective response rate (ORR) of 35.9%, which compares favorably to historical benchmarks of roughly 20–25% for chemotherapy alone. Particularly notable is the emergence of complete responses—five

confirmed cases, representing 7.8% of patients, which is widely described as unprecedented in first-line metastatic pancreatic cancer.

Survival outcomes also reinforce this signal of clinical benefit. Median overall survival has reached 11.1 months, representing an improvement of roughly two months versus historical data for gemcitabine and nab-paclitaxel alone. Progression-free survival and durability metrics have likewise compared favorably to prior studies, with some patients remaining on therapy for extended periods, including patients approaching two years.

Equally important is the safety and tolerability profile, which has remained consistent with chemotherapy alone, indicating that narmafotinib does not appear to add meaningful toxicity burden. This is a critical factor in pancreatic cancer, where treatment intensity is often limited by patient condition.

Mechanistically, the results align with the drug's intended biological role. As a FAK inhibitor, narmafotinib is believed to "prime" tumors by reducing stromal density and altering the tumor microenvironment, thereby improving chemotherapy penetration and effectiveness. In simpler terms, doctors have described pancreatic cancer cells as having a cover like "solid wood" that makes it extremely difficult to penetrate, narmafotinib weakens that structure, allowing more medicine to get to the actual cancer cells. The clinical outcomes seen in ACCENT, particularly the depth of responses and occasional complete tumor clearance, provide early validation of this approach in human patients.

This trial's combination of strong response rates, unprecedented complete responses, improved survival metrics, and favorable tolerability positions it as a potentially important step toward a registrational pathway for narmafotinib in pancreatic cancer.

A critical element of the clinical studies in pancreatic cancer is the regulatory positioning with the FDA. The company has an open Investigational New Drug (IND) application, which allows Amplia to run clinical trials in the United States and engage directly with the FDA on development strategy. This is a foundational regulatory step that enables access to the world's largest pharmaceutical market and provides a pathway toward eventual drug approval. The FDA has also granted narmafotinib Orphan Drug Designation and Fast Track Designation for pancreatic cancer.

Equally important is the trial's alignment with the FDA's Project Optimus initiative, a relatively new regulatory framework aimed at improving dose optimization in oncology drug development. By explicitly incorporating dose-finding and dose-comparison stages, ACCENT and a small follow-up study recently announced position narmafotinib in line with FDA expectations for more precise dosing strategies, rather than the historically more empirical approaches used in earlier oncology trials. This alignment is strategically beneficial because it increases the likelihood that future data packages will meet regulatory standards without requiring extensive additional studies, potentially accelerating the path to later-stage trials and approval.

While specific expedited designations such as Fast Track have been associated more prominently with Amplia's broader narmafotinib program, the ACCENT trial itself benefits indirectly from this regulatory engagement. The combination of an active IND, ongoing FDA dialogue, and adherence to Project Optimus principles enhances the company's credibility with regulators and investors alike. It also allows for more efficient trial design, clearer guidance on endpoints, and faster progression into registrational Phase 2b study which was recently announced. The Phase 2b trial is especially important because it is intended to be "registration-enabling." That phrase matters tremendously. It means the trial is being designed in consultation with the FDA as part of a pathway that could ultimately support drug approval if the results are strong enough. Amplia disclosed that the FDA provided positive feedback regarding the company's proposed trial structure and dose optimization strategy during a formal Type D meeting. The FDA also endorsed Amplia's proposed two-dose comparison design for the Phase 2b component that would precede a pivotal Phase 3 stage.

From an investment and strategic perspective, these FDA-related elements are highly valuable. They reduce regulatory uncertainty, improve the probability of successful trial design, and can shorten development timelines—factors that directly influence both capital efficiency and ultimate valuation. In a competitive oncology landscape, demonstrating early and proactive alignment with FDA priorities is often a differentiating factor for smaller biotechnology companies.

The PRROSE Trial

Amplia Therapeutics is expanding its lead drug narmafotinib beyond pancreatic cancer and into ovarian cancer because the company believes ovarian tumors may be especially dependent on FAK. Ovarian cancer, particularly high-grade serous ovarian cancer, is often highly fibrotic and aggressive, and many tumors express elevated levels of FAK. Amplia's strategy is built around the idea that inhibiting FAK may weaken the tumor's ability to survive chemotherapy, spread, and resist immune attack.

The company recently announced a collaboration with the Australia New Zealand Gynaecological Oncology Group to launch a new ovarian cancer study called the PRROSE trial. This study will investigate narmafotinib in combination with standard chemotherapy agents carboplatin and paclitaxel in women with high-grade serous ovarian cancer who have not responded adequately to initial platinum-based chemotherapy before surgery.

This is an important patient population because approximately one in five ovarian cancer patients fail to respond sufficiently to initial chemotherapy, which can prevent surgeons from successfully removing the tumor. In ovarian cancer, the ability to perform successful "debulking" surgery is one of the major determinants of long-term outcome and survival. Amplia is attempting to use narmafotinib to make tumors more sensitive to chemotherapy and potentially improve the likelihood that surgery can effectively remove the disease.

The ovarian cancer program is also important because it broadens the potential commercial opportunity for narmafotinib. Up to now, most of Amplia's clinical focus has been on pancreatic cancer, where the drug has shown encouraging efficacy signals in the ACCENT trial when combined with gemcitabine and Abraxane. Those results helped support the rationale for moving into other difficult fibrotic cancers such as ovarian cancer.

Importantly, the PRROSE trial is not only evaluating safety and tolerability, but it will also collect extensive tissue and blood biomarkers. That means Amplia is trying to better understand exactly how narmafotinib changes the tumor environment and whether certain biomarkers can predict which patients benefit most. This could eventually help the company position narmafotinib as a precision oncology therapy rather than simply another chemotherapy add-on.

Future Prospects

The science behind narmafotinib means that it has the potential to be a part of other cancers and their treatments. For example, former U.S. Senator Ben Sasse has been diagnosed with Stage 4 pancreatic cancer and has been in the news recently and noted he is taking an experimental pancreatic cancer drug called daraxonrasib, also known as RMC-6236. The drug is being developed by Revolution Medicines and is currently in late-stage clinical trials for metastatic pancreatic cancer.

Beyond daraxonrasib, several other KRAS inhibitors are emerging in late-stage or advanced clinical development, and together they are creating what many now view as an entirely new era in precision oncology for RAS-driven cancers, which narmafotinib could be a critical component of.

The most advanced approved KRAS inhibitors are Lumakras from Amgen and Krazati from Bristol Myers Squibb. Both target the KRAS G12C mutation and are already approved for certain non-small cell lung cancer patients. However, resistance and durability issues have driven the development of newer agents with improved potency and broader mutation coverage.

One of the most important next-generation competitors is divarasinib from Roche/Genentech. Divarasinib is another KRAS G12C inhibitor, but it appears significantly more potent and selective than first-generation agents like adagrasib and sotorasib. Early studies demonstrated response rates approaching 60% in KRAS G12C lung cancer patients, along with relatively long progression-free survival durations. The drug has advanced into the Phase 3 KRASCENDO-1 trial directly comparing it against adagrasib and sotorasib, which is notable because head-to-head oncology trials are relatively uncommon. Another important late-stage candidate is olomorasib from Eli Lilly. Olomorasib is considered a second-generation KRAS G12C inhibitor and has shown promising activity across lung, colorectal, and other solid tumors.

Within Revolution Medicines itself, there are several additional KRAS-focused compounds beyond daraxonrasib. Zoldonrasib (RMC-9805) is especially important because it targets KRAS G12D, one of the most common KRAS mutations in pancreatic cancer and a mutation that historically had no targeted therapy options. Early pancreatic cancer data showed encouraging response rates and disease control, leading the FDA to grant Breakthrough Therapy Designation earlier this year. Revolution Medicines is also developing elironrasib (RMC-6291), a KRAS G12C-selective RAS(ON) inhibitor, and RMC-5127 targeting KRAS G12V mutations. These programs are important because they demonstrate the company's broader "RAS(ON)" platform strategy — targeting active RAS signaling rather than only inactive KRAS conformations.

Daraxonrasib or the various other KRASi and narmafotinib could potentially work very well together in pancreatic cancer because they attack two highly interconnected survival systems used by KRAS-driven tumors. The Company has presented preclinical data reinforcing this. Daraxonrasib is designed to directly inhibit active RAS signaling, which is the primary engine driving most pancreatic cancers. In pancreatic ductal adenocarcinoma, KRAS mutations are present in more than 90% of tumors, and drugs like daraxonrasib aim to shut down the downstream growth pathways that KRAS controls, including MAPK and PI3K signaling.

The problem is that pancreatic cancers are extremely adaptive. Even when KRAS signaling is suppressed, tumors often activate escape pathways involving cell adhesion, stromal interactions, fibrosis, and survival signaling through focal adhesion kinase (FAK). This is where narmafotinib becomes interesting. Narmafotinib inhibits FAK, a protein heavily involved in tumor microenvironment signaling, metastatic behavior, fibrosis, immune suppression, and resistance mechanisms in pancreatic cancer. Mechanistically, the combination could create a "double blockade." The RAS inhibitor would suppress the primary oncogenic KRAS signaling, while narmafotinib could prevent the tumor from rerouting survival signals through survival and stromal resistance pathways. There is already substantial preclinical evidence suggesting FAK inhibition can synergize with KRAS inhibition. Academic research has shown that combining KRAS inhibitors with FAK inhibitors can produce stronger anticancer effects than either approach alone.

Importantly, Amplia has stated that its ongoing preclinical work is specifically investigating combinations of narmafotinib with KRAS inhibitors in pancreatic cancer models. The company reported that narmafotinib appeared to block resistance pathways emerging during KRAS inhibitor treatment, potentially enhancing both efficacy and durability of response.

This concept makes biological sense in pancreatic cancer because the disease is not driven solely by KRAS mutations. Pancreatic tumors are also characterized by a dense fibrotic stroma and highly immunosuppressive microenvironment. FAK signaling contributes heavily to both. By inhibiting FAK, narmafotinib may help "soften" the tumor microenvironment, reduce fibrosis, improve drug penetration, and potentially make KRAS inhibition more durable and effective.

Another important aspect is tolerability. Based on current clinical data, narmafotinib appears to have a relatively manageable safety profile when combined with chemotherapy, which raises the possibility that it could potentially be paired with targeted therapies like KRAS inhibitors without excessive overlapping toxicity.

If KRAS inhibitors like daraxonrasib become foundational therapies in pancreatic cancer, then drugs that can improve durability of response and overcome resistance mechanisms could become highly valuable combination partners. Amplia's recent collaborations and preclinical work suggest the company is positioning narmafotinib specifically for that role.

Financial Outlook

Amplia Therapeutics should be looked at from the perspective of a classic clinical-stage biotechnology company, where value is driven not by current revenues but by pipeline advancement, clinical data, and capital efficiency.

The company has recently strengthened its balance sheet. As of the December 2025 quarter, Amplia reported approximately A\$27.9 million in cash, an increase from the prior quarter, supported in part by government grants and incentives. This level of liquidity is meaningful relative to its size and reflects disciplined cost management, with quarterly cash outflows largely tied to research and development and clinical trial execution rather than overhead. Historically, annual operating cash burn has been in the range of roughly \$5–7 million, consistent with a focused, early-stage biotech platform.

The company's cash runway and funding outlook are relatively favorable compared to many peers. Following recent capital raising efforts, management has indicated that Amplia is funded well into 2027, providing a multi-year window to advance its clinical programs without immediate financing pressure. This is a critical strategic advantage, as it allows the company to generate additional clinical data before needing to return to capital markets, potentially improving valuation and reducing dilution for existing shareholders.

Amplia remains a pre-revenue enterprise, with no commercial products and ongoing net losses, which is typical for companies at this stage. The absence of revenue, however, is offset by relatively low leverage—its balance sheet shows minimal debt and a capital structure primarily funded through equity. This clean balance sheet provides flexibility for future financing options, including additional equity raises, strategic partnerships, or non-dilutive funding such as grants or licensing agreements.

Looking forward, the company's capital needs will be driven primarily by clinical progression. Advancing narmafotinib into later-stage trials—particularly a potential Phase 2b/3 registrational study—will require a significant step-up in spending. These trials are substantially more expensive due to larger patient populations, global site expansion, and regulatory requirements. As a result, while current funding covers near-term milestones, Amplia will almost certainly require additional capital to fully commercialize its lead asset.

Encouragingly, the company is already positioning itself for this next phase through strategic and financial initiatives. These include expanding its investor base via its uplisting to the U.S. OTCQB market, strengthening intellectual property protection with patents extending into the 2040 timeframe, and maintaining active engagement with regulators such as the FDA. These steps are not merely operational, they are designed to enhance the company's attractiveness to potential partners or institutional investors, which could provide funding through collaborations rather than solely through equity issuance. Another important aspect of Amplia's financial strategy is its use of non-dilutive funding sources, particularly government grants and tax incentives, which have already contributed meaningful cash inflows. This reduces reliance on capital markets and improves overall capital efficiency, an important differentiator for smaller biotech firms.

Amplia Therapeutics presents a financially disciplined early-stage biotech profile with a solid cash position, manageable burn rate, and funding visibility into 2027. While future capital raises are inevitable as the company advances into later-stage trials, its current strategy—combining strong clinical momentum, regulatory engagement, and diversified funding sources—positions it well to access capital on increasingly favorable terms as its data continues to mature.

With an estimated 53,000 people expected to die from pancreatic cancer in 2026 in the US alone, the need for better and more effective treatments is urgent and Amplia Therapeutics is giving hope to patients that the number of deaths may start to decrease. Doctors have described the process of finding a “cure” for pancreatic cancer as similar to attacking a large dam with pickaxes, with multiple pickaxes working on various parts of the wall. When the right pickaxes come together, the dam will break and a “cure” will be available—we believe that narmafotinib is one of those axes. With prospects like that, we believe INNMF is worth a look for investors with a longer time horizon and higher risk tolerance, with encouraging test results and solid management practices boding well for the future.



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