Edition 02: December 2023

INVESTOR NEWSLETTER

Amplia THERAPEUTICS

Note from Dr Chris Burns
ATX CEO and MD

As we reflect on the last six months, our focus has been on diligent progression of the ACCENT clinical trial. This crucial phase of our journey saw the completion of dosing in the Phase 1b stage for narmafotinib (AMP945), combined with the chemotherapy agents gemcitabine and Abraxane®, targeting advanced pancreatic cancer. In total we dosed 14 patients across 3 dose levels, identifying a dose of narmafotinib that is safe and well tolerated, and that provides significant suppression of FAK activity over the dosing period.

The data emerging from the Phase 1b study is encouraging. Not only has narmafotinib proven to be safe and well-tolerated, but early indicators also suggest promising efficacy.

With patient recruitment to commence shortly for the Phase 2a portion of the trial, we remain optimistic about our approach. To amplify our efforts, we're expanding our horizons to South Korea, leveraging the country's exceptional clinical trial infrastructure. Our successful submission to Korean drug regulators, a pivotal step, is a testament to our meticulous preparation and international collaboration. I recently visited Korea to partake in detailed discussions with clinical trial sites and was heartened by the enthusiasm of the clinical teams in relation to the trial. We look forward to initiating recruitment in the New Year.

Our team's commitment to manufacturing excellence has resulted in the preparation of additional narmafotinib capsules to world's best standards by our U.S.-based manufacturer.

Our ambitions in ovarian cancer treatment have also been bolstered by promising preclinical data by our collaborators at the University of California, San Diego - reinforcing the the potential of FAK inhibitors, like ours, in combating this prevalent and challenging disease.

2024 looks set to be another significant year for Amplia, as we continue to explore the clinical possibilities offered by our FAK-inhibitors.

We are ever grateful to our valued shareholders, collaborators and partners, and look forward to continuing this journey with your support.

Dr Chris Burns
CEO & MD

ACCENT Milestone Reached with Completion of Phase 1b

In October, Amplia announced the completion of the Phase 1b portion of the ACCENT clinical trial in patients with advanced pancreatic cancer, marking a significant milestone in the clinical development of our lead FAK-inhibitor, narmafotinib. The trial focused on the safety and tolerability of narmafotinib in combination with standard chemotherapy agents, gemcitabine and nab-paclitaxel (Abraxane®).

The trial successfully identified a dose of narmafotinib that provides sufficient circulating drug levels to significantly block the activity of the FAK enzyme – which has been implicated in solid tumours such as pancreatic cancer. Notably, the dose was found to be both safe and well-tolerated, paving the way for recruitment to commence for the Phase 2a portion.

These findings highlight narmafotinib's potential in treating pancreatic cancer, and reinforce Amplia's commitment to advancing innovative treatment approaches for fibrotic cancers, using our FAK-inhibitors.

The next phase of the trial is eagerly anticipated, as it will provide more comprehensive efficacy data and bring us closer to realising narmafotinib's full therapeutic potential.

Recruitment for Phase 2a expands to Korea

As Amplia prepares to commence recruitment for the Phase 2a stage of the ACCENT trial, attention has turned overseas, with confirmation that the Korean Ministry of Food and Drug Safety (MFDS) has approved a clinical trial to test narmafotinib in combination with gemcitabine and Abraxane®, in advanced pancreatic cancer patients in Korea.

Korea has been chosen thanks to its excellent clinical trial capability and world-class cancer hospitals and physicians. This approval means that five preselected clinical trial sites in Korea can be opened shortly to commence enrolment of patients for the Phase 2a stage of the ACCENT clinical trial.

These sites will operate in addition to six existing sites across Australia.

Amplia CEO and MD, Dr Chris Burns, commented:

"The approval from the Korean MFDS comes after many months of hard work from the Amplia team, who have worked closely with the Korean regulators, to achieve this important approval. The Korean health system and clinical trial capabilities are world class, and recruitment into pancreatic cancer trials has been historically strong. We look forward to opening our planned sites in Korea and working with the excellent clinical groups, to further test the impact of our drug narmafotinib in the treatment of advanced pancreatic cancer."

New Data Reveals Promise in Ovarian Cancer

Data from preclinical studies in ovarian cancer have highlighted the clinical potential of FAK-inhibitor narmafotinib in the treatment of ovarian cancer, which currently claims over 1,000 Australian lives annually.

Professor Dwayne Stupack, a collaborator from the University of California, San Diego, presented the compelling evidence as part of a poster presentation at the American Association for Cancer Research (AACR) Special Conference In Cancer Research: Ovarian Cancer meeting held in Boston in October. This data, derived from a series of preclinical studies, demonstrates narmafotinib's superior efficacy compared to the current standard-of-care in models of chemotherapy-resistant high-grade serous ovarian cancer.

The data clearly demonstrates that narmafotinib is active in mouse models of chemotherapy-resistant ovarian cancer, with improved tumour growth inhibition activity and tolerability compared to the current standard-of-care agent for this chemotherapy-resistant patient population. Moreover, narmafotinib showed promising activity in a model where the standard-of-care therapy was ineffective.

These results build on previous research by Professor Stupack and his collaborators showing that activity of the FAK enzyme is upregulated in chemotherapy-resistant ovarian cancer and that FAK inhibition sensitises the cancer to standard-of-care chemotherapy and immunotherapy as well.

In light of this data, plans are now underway to work with local and international ovarian cancer specialists to initiate a clinical trial of narmafotinib in ovarian cancer patients.

> *PARP inhibitors are now widely used in the treatment of high-grade serous ovarian cancer (HGSOC) and work well in a subset of patients with what's known as homologous recombinant deficient (HRD) HGSOC – at least until drug resistance occurs. We have shown in our preclinical models that narmafotinib has better activity across the non-HRD disease, and importantly works in PARP inhibitor-resistant disease as well. Moreover, it appears to be very well tolerated, which is important for a drug that will be taken daily."*
>
> **- Prof Dwayne Stupack, Lead Researcher, University of California, San Diego.**

Q&A with CMC Project Manager, Adrian Sulistio

Maintaining high standards of production and distribution are necessary to meet the rigorous quality and regulatory benchmarks in drug development. As Amplia's CMC Project Manager, Dr Adrian Sulistio, leads the complex processes of manufacturing and ensuring the reliable supply chain for narmafotinib – which are critical for Amplia's ACCENT clinical trial.

Q. What is CMC, and why is it so important to the drug development process?

CMC, which stands for Chemistry, Manufacturing, and Controls, ensures the safety, effectiveness, and quality of the produced drugs so that we can trust the results of clinical trials. CMC activities span the entire drug development spectrum, from the preclinical stage where we produce small amounts of drug, all the way to commercial manufacturing which is at very large scales.

The **Chemistry** component of CMC focuses on the characterisation and synthesis of the drug substance and the formulated drug product. In our case, narmafotinib is added to excipients to create a capsule formulation that is: (a) suitable for administration; (b) has suitable stability (shelf-life); and, (c) provides maximum absorption of drug into the body.

The **Manufacturing** component focuses on the development and implementation of manufacturing processes for the drug substance and the drug product under the Good Manufacturing Practices (GMP) system.

The **Controls** component focuses on the development and implementation of quality control procedures to ensure the consistent production of safe and effective drug products.

The CMC process runs in tandem with the drug development process. As the drug development process progresses from preclinical (small scale), clinical development, regulatory submission to commercialisation (large scale), so does the CMC process.

Q. What are the key CMC milestones that Amplia has achieved to date with narmafotinib?

Continued next page

Q&A with CMC Project Manager, Adrian Sulistio

Narmafotinib API Production: Significant Scale-Up and Optimisation

We have achieved significant progress in narmafotinib API production, successfully scaling up from 1 kg to 6 kg. This significant increase in production capacity is crucial for meeting growing demands as we advance through clinical development. We are working with our contract manufacturing organisation to optimise the synthesis route, which is expected to enhance product quality and cost-effectiveness, and streamline our production to scale up to 20 kg to meet future demand.

Drug Product Development: Capsule Formulation and Scale-Up

On the drug product development front, we have successfully developed multiple capsule forms for our drug development, with one in current oncology trials and another for future studies. We have also scaled up production from 3,000 to 25,000 capsules to meet clinical trial needs and ensure a smooth transition to commercial manufacturing post-approval.

How do regulatory agencies influence the CMC process?

CMC plays a critical role in the regulatory approval process for drugs. Regulatory bodies, such as the FDA, mandate comprehensive CMC data to validate the safety, efficacy, and consistency of drug products before granting marketing authorisation.

CMC is a complex and challenging area of pharmaceutical development, but it is essential for the successful development of safe and effective drugs.

Q. What achievements are you most proud of to date?

Amplia is dedicated to developing innovative cancer treatments that offer hope and improve patient outcomes. Being part of this endeavour is a privilege, knowing that every success that we accomplish brings us closer to improving treatment options for patients.

Since joining Amplia, I have overseen the production of the clinical trial material to supply our current pancreatic cancer ACCENT trial. Recently, we successfully completed the Phase 1b stage of the ACCENT trial, and the encouraging results have paved the way for commencement of Phase 2a, marking a crucial step forward in our pancreatic cancer treatment development.

In addition to my clinical supply oversight responsibilities, I took the lead on the regulatory submission process for ACCENT in Korea. We have received regulatory approval to initiate clinical trials in Korea, marking a significant milestone in our journey to combat pancreatic cancer. This regulatory approval also provides strong external validation on the importance of our work and its potential impact in this field.