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INVESTOR NEWSLETTER

Amplia THERAPEUTICS

Note from Dr Chris Burns
ATX CEO and MD

The progress over this calendar year has been highly significant for the company, with major clinical and regulatory achievements. Our primary focus is the ACCENT clinical trial in pancreatic cancer where we are investigating the combination of our lead drug narmafotinib with standard-of-care chemotherapy. We recruited the first patients in the Phase 2a stage of the trial in January this year and in just over six months had enrolled 26 patients.

Recruitment has been paused at present whilst we conduct an interim assessment of activity. Based on analyses of historic data we have determined that six (6) or more patients showing a confirmed partial or complete response (see next page for a detailed description on response criteria) will be considered a sufficiently robust response rate to support recruitment of a further 24 patients. Thus, in total, we will recruit a cohort of 50 patients, which will allow us to generate statistically robust data to compare with that obtained from other pancreatic cancer clinical trials.

At this time we have recorded five confirmed partial responses and are waiting on data from additional patients in the trial to record an additional confirmed response.

This year we also announced that we received clearance of our Investigational New Drug (IND) application from the U.S. Food and Drug Administration (FDA). Clearance of the IND allows us to undertake a clinical trial of narmafotinib in the U.S. and comes after FDA review of the full drug dossier, amounting to over 10,000 pages! The clinical trial planned in the U.S. combines narmafotinib with a different standard-of-care therapy, called FOLFIRINOX, widely used in the U.S. and parts of Europe. **Our U.S. trial of narmafotinib is in advanced planning stages, and we've convened a Clinical Advisory Board comprised of renowned pancreatic cancer experts from North America and Australia to assist in its development.**

In addition to these trial related activities, we have been working closely with our collaborators in Australia and the U.S., exploring the potential of narmafotinib in the treatment of ovarian cancer at various disease stages. Narmafotinib blocks the activity of the cancer-associated protein FAK, and the role of FAK in ovarian cancer disease progression has been widely demonstrated. Our collaborators and potential partners are reviewing the promising preclinical and clinical data already obtained for narmafotinib to identify the best clinical trial opportunities for the drug in this aggressive and challenging disease.

Dr Chris Burns
CEO & MD

ACCENT Trial Update

Amplia's ACCENT clinical trial is examining the combination of Amplia's best-in-class FAK inhibitor narmafotinib in combination with standard-of-care chemotherapy in first-line patients with advanced pancreatic cancer. Following the successful completion of the Phase 1b portion of the trial in late 2023, the Company is now progressing the Phase 2a portion of the trial at six sites in Melbourne, Sydney and Brisbane and five sites across Korea.

Completion of Phase 1b

In November 2023, Amplia announced the completion of the Phase 1b portion of the ACCENT trial, which evaluated narmafotinib in combination with standard of care chemotherapy for advanced pancreatic cancer. The trial successfully identified a safe and well-tolerated dose of narmafotinib (400 mg once daily) which achieved levels of drug in patients that aligned with significant and efficacy in FAK inhibition seen in preclinical studies.

Initial results were promising, with seven out of 14 patients remaining on the trial for over six months, and three patients having stayed on trial for more than 10 months. This is notable considering the median progression-free survival for this type of cancer with standard treatment is 5.5 months. Additionally, six patients showed a partial response, and eight demonstrated stable disease, surpassing historical response rates for chemotherapy alone.

Objective Response Rate is categorised* as:

Complete Response (CR)
Disappearance of all tumour lesions; no new lesions

Partial response (PR)
>30% decrease in tumour lesions; no new lesions

Stable Disease (SD)
Tumour lesions have reduced in size by less than 30% or have shown either no growth or minimal growth (<20%)

Progressive Disease (PD)
At least a 20% increase in tumour lesions; or new lesions

** Following the clinical standard criteria (RECIST 1.1) - European Journal of Cancer 2009, vol. 45, pg 228–247.*

ACCENT Trial Update

Commencement of Phase 2a

In January, Amplia announced that the first patient in the Phase 2a portion of the ACCENT trial had commenced dosing. The Phase 2a stage of the of the trial will assess the efficacy of narmafotinib in combination with gemcitabine and Abraxane, along with continued assessment of safety and tolerability. The primary endpoints are Objective Response Rate (ORR) and Duration on Trial (DOT) with additional endpoints being Progression Free Survival (PFS), Overall Survival (OS) and Biomarkers.

The Phase 2a trial employs a Simon's Two-Stage design, which allows for an interim analysis after the first 26 patients. The trial will proceed to enrol an additional 24 patients once six patients exhibit a confirmed partial or complete response.

In early July, Amplia announced that it had successfully completed the enrolment of the first 26 patients in the Phase 2a stage of the ACCENT clinical trial. To date, the study has observed five (5) confirmed partial responses among patients assessed at four months from enrolment. A 'confirmed partial response' means in these patients there is at least a 30% decrease in the overall size of tumour lesions, with no new tumour lesions, sustained over a two-month period, while a confirmed complete response refers to a total absence of tumour lesions over a two-month period.

Early efficacy signals from the Phase 2a trial appear promising and align with the positive data observed in the Phase 1b stage. The Company anticipates reporting the interim analysis results around the beginning of Q4 2024.

Navigating Regulatory Milestones

The path to drug approval is complex and not simply a linear progression through clinical trial phases. The process is a dynamic one, which involves continuous learning and demands flexibility and adaptation. New data can lead to unexpected findings, requiring adjustments to the development plan. As such, regulatory milestones serve as critical checkpoints on the journey to bring a new drug to market.

Regulatory frameworks for drug approvals – both in Australia, and overseas – are very structured, with good reason. The process is designed to protect the public from potentially harmful medications, while making sure that new drugs meet stringent safety and efficacy standards. This balance of safety and innovation is critical to the advancement of pharmaceutical assets.

Trial Approval

Approval to conduct a clinical trial varies in different countries.

In Australia

In Australia, approval to conduct a clinical trial is provided via the Australian Clinical Trials Notification (CTN) framework. Initiation of a trial is subject to the approval of an independent Human Research Ethics Committee (HREC), which reviews the scientific validity of the trial design, the balance of risk versus harm of the therapeutic good, the ethical acceptability of the trial process, and approves the trial protocol.

In the U.S.

U.S. based clinical trials must receive IND Approval. The Investigational New Drug (IND) application marks the transition from preclinical to clinical research. It signifies that the U.S. regulator, the U.S. Food and Drug Administration (FDA) has reviewed the available data and deemed the drug safe enough to be tested in humans.

In South Korea

Clinical trials conducted in South Korea must be approved by the Korean Ministry of Food and Drug Safety (MFDS). To obtain approval, companies must go through the clinical trials authorization (CTA) process, and all documentation must be provided in Korean.

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Navigating Regulatory Milestones

Key Regulatory Milestones

Several key regulatory milestones mark the progress of drug development. These include:

Phase II Proof of Concept

This milestone demonstrates that the drug has the potential to work in its intended patient population. It's a critical step in validating the drug's efficacy.

Registration Studies

These late-phase trials, typically Phase III, provide the robust data needed to support a marketing application. Success in these studies is crucial for obtaining regulatory approval.

Regulatory Designations: Accelerating the Path

For drugs targeting serious or life-threatening diseases, certain regulatory designations can expedite the development process. The FDA has developed four distinct approaches:

Fast Track Designation

This designation is available for drugs that show potential to address unmet needs in serious conditions. It offers increased interaction with the FDA and eligibility for other expedited programs. Fast Track Designation is a special status granted by the FDA to drugs that show promise in treating serious conditions and address unmet medical needs. It provides the opportunity for more frequent and direct communication with the FDA, which can help streamline the development process and potentially get drugs to patients faster.

Breakthrough Therapy Designation

This designation is for drugs demonstrating substantial improvement over existing therapies. It provides intensive FDA guidance and support, potentially accelerating the approval process.

Accelerated Approval

These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint.

Priority Review

A Priority Review designation means FDA's goal is to take action on an application within six months (compared to 10 months under standard review).

Orphan Drug Designation: This designation is granted to drugs for rare diseases affecting fewer than 200,000 people in the U.S. It provides benefits such as fee exemptions and market exclusivity, incentivising development in areas of unmet medical need. Amplia has already secured Orphan Drug Designation for its pancreatic cancer treatment, narmafotinib.

In Conversation with Charlotte Mulder
Director of Early Clinical Development

As Director of Early Clinical Development at Amplia, Charlotte Mulder works at the intersection of science, strategy and patient outcomes. Her role involves guiding Amplia's potential drug candidates through critical early phases of clinical development, ensuring rigorous scientific standards are met while keeping the focus on the needs of patients who may benefit from these therapies.

Q: Can you describe your role as Director of Early Clinical Development at Amplia?

My role at Amplia is essentially to guide our drug candidates through the critical early stages of clinical development. It's a dynamic role that requires me to wear many hats. I'm involved in everything from development planning and data analysis to coordinating across different functional areas like CMC*, preclinical, and clinical. The goal is to ensure we're making informed decisions that move our assets forward towards registration, always keeping the commercial viability and scientific validity in mind.

Q. What do you enjoy most about your role, and why?

The most rewarding part is knowing that our work has the potential to make a real difference in the lives of patients. It's incredibly motivating to be part of a team that's pushing the boundaries of science to develop new and better treatment options. The constant influx of new data and the opportunity to explore new therapeutic areas also keep things exciting. It's never boring!

Q. What are some of the biggest challenges you face?

The aggressive nature of pancreatic cancer demands urgency. We are constantly working to deliver quality data in a timely and cost-efficient manner, all while remaining adaptable as the science evolves. Each new insight about our drug is an opportunity to deepen our understanding, and refine our approach. It's a dynamic process, but one that fuels our commitment to making a real difference for patients battling this devastating disease.

** Chemistry, Manufacturing, and Controls*

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In Conversation with Charlotte Mulder
Director of Early Clinical Development

Q. How important is it to be agile when you're working in drug development?

Agility is critical in the dynamic world of drug development. In this field, we're constantly learning and generating new data that can challenge existing assumptions or reveal unforeseen opportunities. It allows us to mitigate risks and avoid costly delays or setbacks. As we move through the development process, we need to be able to quickly interpret this new information and adapt our strategies accordingly.

Q: What are some of the significant milestones ahead for you and the team?

We have several exciting milestones on the horizon. A major focus is getting our next study in pancreatic cancer off the ground in the U.S. We're also excited about exploring the potential of our drug in ovarian cancer and are actively engaging with experts in the field to design the best possible trial.