## 510(k) Application Submitted to U.S. FDA for Regulatory Clearance for HepaFat-AI

Resonance Health Ltd (ASX: RHT) ("Resonance Health" or "Company") announces that its 510(k) application for regulatory clearance by the United States Food and Drug Administration ("FDA") for the Company's newly developed AI solution, HepaFat-AI, has been submitted to the FDA.

HepaFat-AI is a fully automated artificial intelligence (AI) software tool that measures a patient's volumetric liver fat fraction (liver fat). HepaFat-AI can be deployed in the cloud or on premises and can be integrated directly into existing radiology workflows. HepaFat-AI may be suitable to aid in a patient's management of several conditions, including fatty liver disease (see Annex A), monitoring the liver-fat content in patients undergoing weight loss management, and aiding in the assessment and screening of living donors for liver transplants.

Picture below shows sample HepaFat-AI patient images: The top row shows the MRI images analysed, and the bottom image shows a HepaFat-AI Liver Fat Distribution Map.
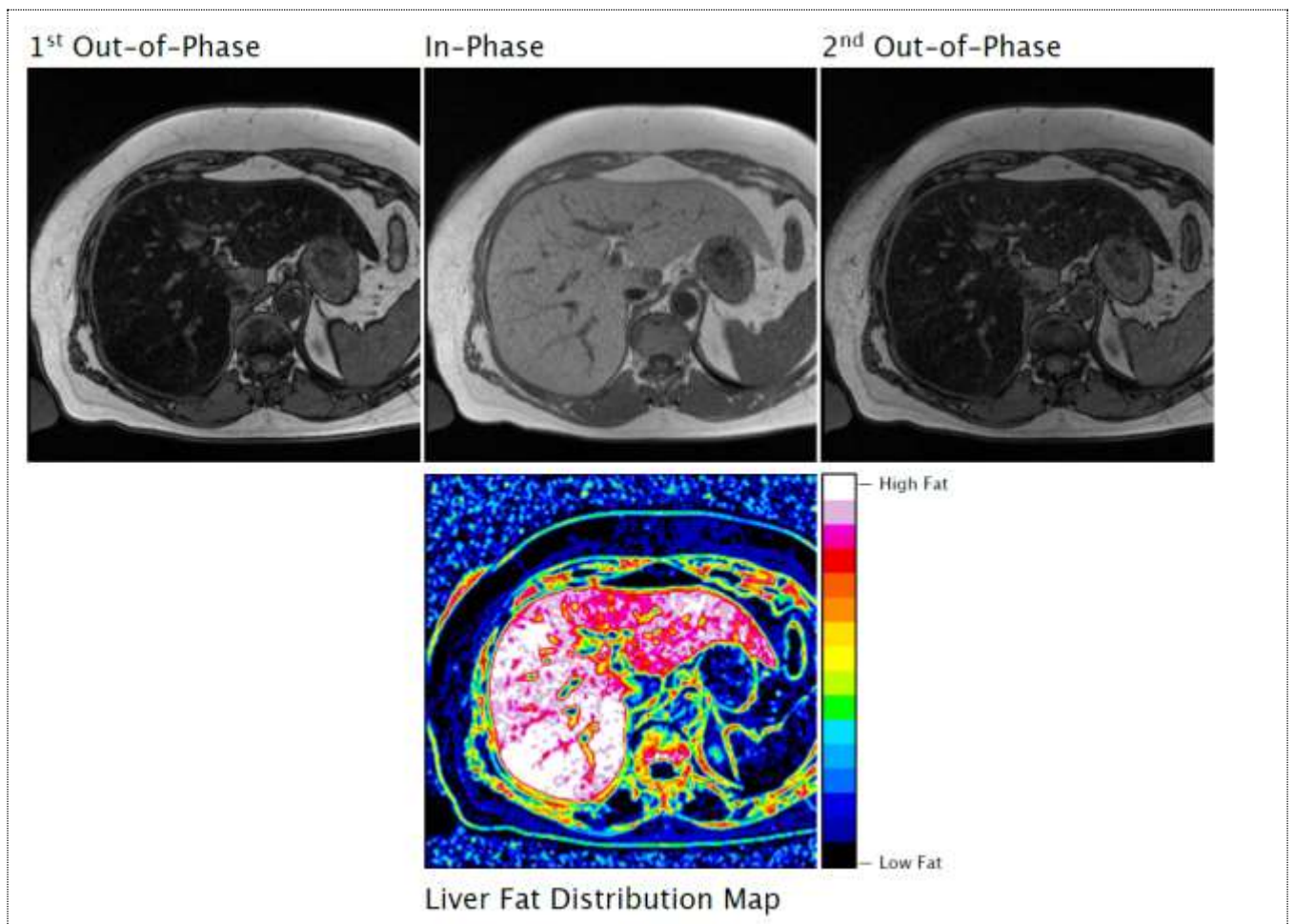
The Company intends to now proceed with work required for Australian TGA and European CE Mark regulatory clearances.

Further work is in progress to apply AI to other organs and disease conditions, with the Company focusing on developing and deploying efficient solutions for clinicians and radiologists globally to aid in the diagnosis, monitoring, and management of patients.

Authorised by:

This announcement has been authorised for release in accordance with the delegated authority of the Board of Directors of Resonance Health Limited.

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Annex A

What are Fatty Liver Diseases and Disorders

Fatty liver disorders refer to a group of conditions characterised by the accumulation of fat in hepatic cells via a process known as steatosis, or the abnormal retention of lipids within a cell. Fatty liver disorders can be related to significant alcohol intake (alcoholic liver disease, ALD) or occur in people who consume minimal or no alcohol (non-alcoholic fatty liver disease, NAFLD). Significant alcohol intake is defined as an average of > 21 standard drinks per week for men and >14 for women[1].

Non-Alcoholic Fatty Liver Disease (NAFLD)

The current definition of non-alcoholic fatty liver disease (NAFLD) requires that: (a) there is evidence of hepatic steatosis, either by imaging or by histology; and (b) there are no other causes of secondary hepatic fat accumulation such as significant alcohol consumption, chronic Hepatitis C virus infection, medication use or hereditary disorders. NAFLD encompasses the entire histological spectrum from simple steatosis, to steatohepatitis and cirrhosis.

NAFLD can be further characterised histologically into non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). NAFL is defined as the presence of hepatic steatosis with no evidence of hepatocellular injury in the form of ballooning of the hepatocytes. NASH is defined as the presence of hepatic steatosis and inflammation with hepatocyte injury (ballooning) with or without fibrosis (**Figure 1**).

Risk factors for NAFLD include age, male gender, obesity, hypothyroidism, hypopituitarism, hypogonadism, sleep apnoea and polycystic ovary syndrome.
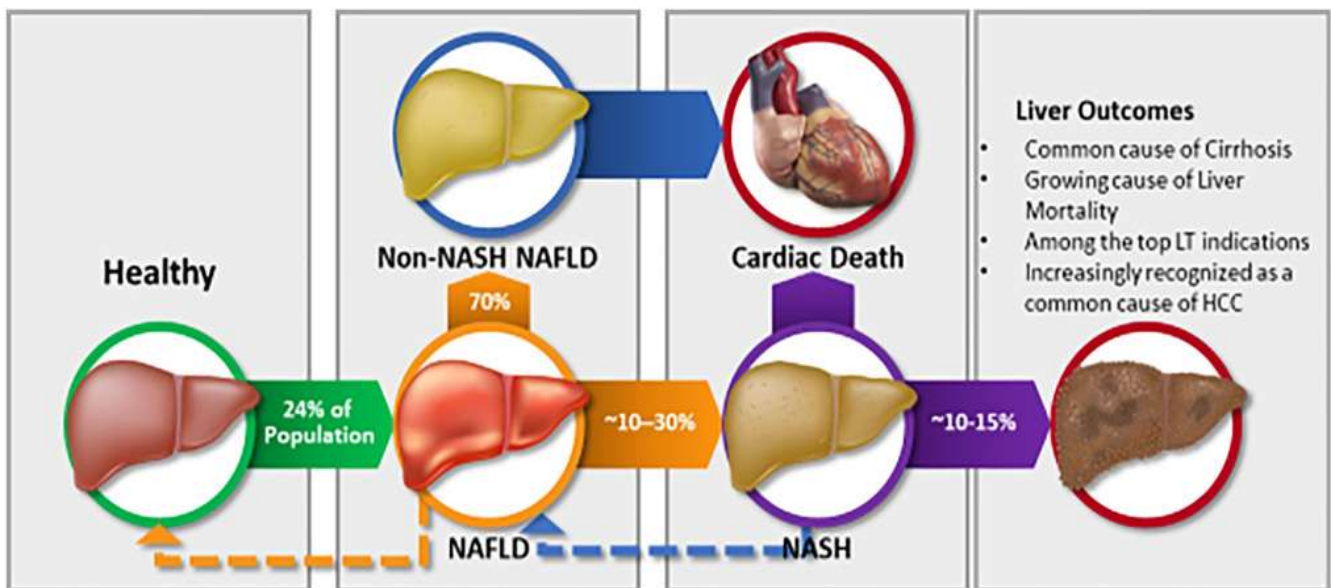

Figure 2: A simplified version of the natural history of NAFLD and NASH[2]

It is estimated that the prevalence of NAFLD in the general global population is sitting between 24% and 30%[3], meaning that between 1.8 and 2.3 billion people may be affected at present. This is expected to grow year-on-year consistent with increasing rates of obesity. In North America, NAFLD is now the leading cause of liver disease, and with no treatments readily available for this disease, it is a leading cause for liver transplant.

Liver disease is the 3rd leading cause of death in patients with NAFLD compared to the 11th in the general population. Results from a recent meta-analysis has revealed that the presence of NAFLD carries an increased overall mortality due to increased cardiovascular disease mortality and increased liver disease mortality as well as increased risk of developing type 2 diabetes. NAFLD can also affect disease progression and the treatment response in patients with hepatitis C and the prognosis of liver transplantation recipients.

NAFLD is thought to represent the hepatic manifestation of metabolic syndrome, which also includes central obesity, dyslipidaemia, hypertension, insulin resistance and glucose intolerance or diabetes. The pathogenesis of steatosis is not yet fully understood, nor what triggers the progression to NASH with or without fibrosis or cirrhosis in some individuals but not in others.

Of the 1.8 to 2.3 billion individuals estimated to have NAFLD, it is estimated that 20%, or up to 468 million, will also develop NASH. NASH is the most severe form of NAFLD where inflammation can cause liver damage and fibrosis. Fibrosis can worsen over time and lead to severe scarring of the liver, called cirrhosis. Patients who develop cirrhosis have an increased risk of liver failure and liver cancer. In instances such as these, the Company's HepaFat-AI solution can be used by clinicians as an aid for the patient's management of these conditions.

In the United States alone, it is estimated that 64 million people have some form of NAFLD, ranging from simple fatty liver to late-stage cirrhosis costing their healthcare system up to $103 billion annually. In the European countries of Germany, France, Italy, and the United Kingdom, there are approximately 52 million people with NAFLD, with an estimated healthcare system cost of approximately €35 billion annually.

If the prevalence of NAFLD continues to rise in line with the obesity epidemic, it is predicted that the healthcare burden of NAFLD over the next 10 years could increase to $1.005 trillion in the United States, and €334 billion across Germany, France, Italy, and the United Kingdom[4].

1. VanWagner LB, Ning H, Allen NB, et al. Alcohol Use and Cardiovascular Disease Risk in Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology. 2017;153(5):1260–1272.e3. doi:10.1053/j.gastro.2017.08.012
2. Younossi, Z.M. (2018), The epidemiology of nonalcoholic steatohepatitis. Clinical Liver Disease, 11: 92-94. doi:10.1002/cld.710
3. Sayiner M, Koenig A, Henry L, Younossi ZM. Epidemiology of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis in the United States and the rest of the world. Clinics in Liver Disease. 2016;20:205-214
4. Younossi, Z. M. et al. The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. Hepatology 64, 1577–1586 (2016).