

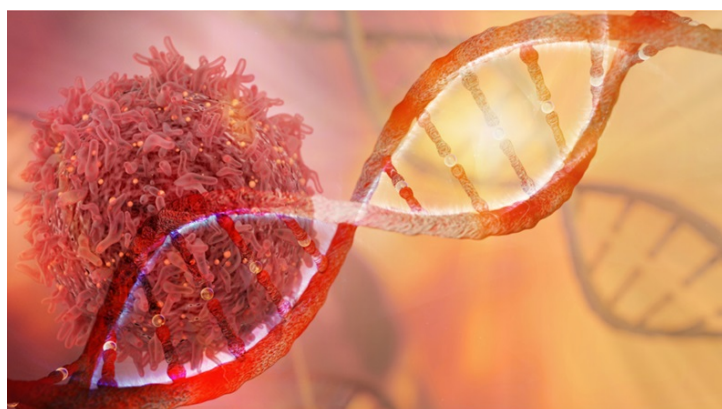
Boundless Bio Launches With \$46m And Novel Oncology Focus On Extrachromosomal DNA

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Executive Summary

Former Ignyta executive Zachary Hornby wasn't wowed by immuno-oncology pitches when looking for his next cancer drug development company, but was intrigued by ecDNA research at UCSD, which also could generate a tumor agnostic approach.



BOUNDLESS BIO IS FOCUSED ON EXTRACHROMOSOMAL DNA AS A CAUSE OF RAPID TUMOR GROWTH.

Source: Shutterstock

Former Ignyta Inc. chief operating officer Zachary Hornby helped the developer of Roche's now-approved tumor-agnostic therapy Rozlytrek (entrectinib) transition its assets to the Swiss big pharma after it was acquired for \$1.7bn, then set out to find a new cancer drug development opportunity. Hornby passed on multiple immuno-oncology technologies before settling on the extrachromosomal DNA (ecDNA) work now under way at Boundless Bio, which has raised \$46.4m in venture capital.

San Diego-based Boundless emerged from stealth mode on 19 September to announce its series A round, led by ARCH Venture Partners and City Hill Ventures. The company is focused on ecDNA research pioneered by co-founder Paul Mischel at the University of California, San Diego (UCSD) and other scientists who uncovered the link between ecDNA and rapid cancer progression in patients whose tumors have high copy number amplifications of oncogenes.

Mischel is a UCSD School of Medicine professor and a member of the Ludwig Institute for Cancer Research. Other Boundless scientific co-founders include Vineet Bafna, a UCSD professor of computer science and engineering; Howard Chang, a cancer genomics and genetics professor at Stanford University; Ben Cravatt, a chemical biology specialist at The Scripps Research Institute in San Diego; UCSD bioengineering professor Prashant Mali; and Roel Verhaak, professor and computational biology specialist at The Jackson Laboratory's Farmington, CT campus.

Former Ignyta CEO Jonathan Lim, currently a managing partner at City Hill and venture partner at ARCH, also is a Boundless co-founder and chairman of the start-up's board. Like Hornby, Lim also has spent time since Roche bought Ignyta investigating new cancer drug development opportunities. (Also see "Roche Ramps Up Cancer Portfolio With \$1.7bn Ignyta Buy" - Scrip, 22 Dec, 2017.) He co-founded and – via his VC firm City Hill – co-funded Erasca Inc., which launched in December with \$42m in series A venture capital.

Boundless's series A investors also included Vertex Ventures (a Temasek fund), GT Healthcare Capital Partners, Boxer Capital of the Tavistock group, Alexandria Venture Investments and other undisclosed backers.

Seeking Novelty In A Sea Of Me-Toos

"I went through this journey where after Ignyta I kind of stuck around for six months and oversaw the integration into Roche," Hornby told *Scrip*, "but then I spent the second half of last year looking at company formation opportunities as well as different opportunities that were pitched to me by VCs. And a lot of them were new IO plays, but it was actually hard for me to distinguish one from the other."

He noted that all of the immuno-oncology pitches seemed "incredibly risky in terms of differentiation and ability to prove that the approach would work in the clinic, so it was really refreshing for me to see this [ecDNA] science, which was completely different." The novel science also helped Boundless recruit investors and employees, he added.

Boundless has 15 employees now and the company expects to grow to 20 before the end of this year. The executive team includes chief technology officer Jason Christiansen, who served as vice president of diagnostics at Ignyta, and chief business officer Scott Moorefield, the former director of oncology business development at Roche/Genentech Inc., who led the Ignyta acquisition.

"It's a great mix of a really new idea that's potentially transformative for patients; a devoted and broad set of advisory board founders; a deep-pocketed venture syndicate to fully support the exploitation of this new idea; and a great local team of folks who have a nice track record of translating new innovations into products," Hornby said.

New Company, Big Goal: Serial Entrepreneur Jonathan Lim Launches Erasca To 'Erase Cancer'

By Mandy Jackson

18 Dec 2018

Lim, CEO of Ignyta when it was sold to Roche earlier this year, has moved on to the start-up Erasca with \$42m in Series A venture cash to develop "precision oncology" drugs.

[Read the full article here >](#)

Novel Science, New Pathways To Treat Cancer

Mischel's findings about the role of ecDNA in tumor growth were published in *Science* in 2014, bringing greater attention to this area of biology. Extrachromosomal DNA resides outside of the chromosome but remains inside the nucleus of cancer cells, where the ecDNA replicates and forms multiple copies of genes – including oncogenes that drive tumor growth – very quickly. In almost half of all tumor types, ecDNA is a driver of rapidly progressing, treatment-resistant cancer.

"This is where the preponderance of high copy number gene amplifications of oncogenes occur – usual suspect oncogenes like MYC, KRAS, MET, EGFR," Hornby said. "The [cancer drug development] field has been pretty successful at drugging oncogene products, such as gene fusions like ALK and ROS and RET and TRK – my former company Ignyta was successful in doing that – but the one area the field has not been successful at drugging is gene amplifications, like MET amplifications or MYC amplifications."

"Instead of trying to drug the oncogene product, we're trying to drug the process that gives rise to that product in the first place – in other words, impede the cell's ability to use ecDNA as a mechanism to generate high copy number gene amplifications," he explained.

Boundless has three areas of focus going forward: drug discovery against newly identified targets; identification and validation of additional targets; and continued creation of tools and technologies for mapping, visualizing and tracking ecDNA to understand how it functions.

"The amount that we raised, the \$46m, should probably be several years of runway – on the order of three or more – because we're an early-stage company," Hornby said. "Certainly, our goal would be to take our lead programs through preclinical proof of concept – to really prove out this biology – and hopefully get into IND-enabling studies within this financing round."

He said Boundless also plans to partner with big pharma companies as interest in ecDNA grows and noted that the start-up hopes to become the go-to expert in the field.

Another Tumor-Agnostic Approach, Like Ignyta?

The company will leverage both its novel science and its experience at Ignyta to advance its programs, including a potential tumor- or tissue-agnostic approach – an area where the Boundless team has a lot of expertise from their days at Ignyta. Roche won approval for the Ignyta-developed Rozlytrek in August in the treatment of ROS1-positive, metastatic non-small cell lung cancer (NSCLC) and solid tumors with a neurotrophic tyrosine receptor kinase (NTRK) gene fusion regardless of tumor type.

"We think the presence of ecDNA is a characteristic that's driving the biology and therefore we would want to try to target any patients who have this present," Hornby said. "Hopefully it will prove out that it's a driving factor irrespective of the tumor

Roche/Genentech Set Lower Rozlytrek Price To Catch Up With Bayer's Vitrakvi

By Mandy Jackson

15 Aug 2019

Entrectinib clinched double approvals in the US for ROS1-positive NSCLC and for tumors with NTRK gene fusions – making it the third tumor-agnostic and second NTRK-fusion approval in the US.

[Read the full article here >](#)

environment and therefore efficacy would be observed across multiple tumor types."

He noted that Boundless has assembled in-house diagnostic expertise, because accurate patient selection will be crucial for clinical trials. "We think there is definitely a precision medicine component here, albeit we're attacking it with a different angle than your typical targeted therapies," Hornby said.