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Allarity Therapeutics, Inc. (ALLR: NASDAQ)

A Precision Undertaking

Based on our DCF model which uses a 15% discount rate, Allarity Therapeutics is valued at approximately $5.00 per share. Our model applies a 35% probability of ultimate approval and commercialization for dovitinib and stenoparib in OC and Ixempra® in mBC. The model includes contributions from the United States, EU and rest of world.

Current Price (9/12/2022)	$1.16
Valuation	**$5.00**

INITIATION

Allarity Therapeutics uses its proprietary DRP® companion diagnostics to identify cancer patients that will respond favorably to selected drugs. It is developing lead candidates stenoparib and dovitinib for metastatic ovarian cancer (mOC) and Ixempra® for metastatic breast cancer (mBC).

The three primary candidates are all in ongoing or planned Phase II studies for their respective indications. Stenoparib & dovitinib, in combination, are slated to begin a Phase Ib/II trial in 4Q:22 in mOC. Allarity is also conducting an ongoing Phase II study for Ixempra as monotherapy in mBC, which is pursuing approval in the EU. Additionally, an ongoing Phase II study for stenoparib as monotherapy is underway in mOC.

The DRP platform generates drug-specific companion diagnostics & uses a precision medicine approach to identify patients that will respond to a particular drug based on a tumor's gene expression signature. The process generates a DRP score for each patient which separates the most likely responders and non-responders. The approach produces a material improvement in overall response rates compared with those predicted to be resistant to the drug.

SUMMARY DATA

52-Week High	**18.20**
52-Week Low	**1.01**
One-Year Return (%)	**N/A**
Beta	**N/A**
Average Daily Volume (sh)	**291,680**
Shares Outstanding (mil)	**18.3**
Market Capitalization ($mil)	**21.2**
Short Interest Ratio (days)	**0.5**
Institutional Ownership (%)	**2.3**
Insider Ownership (%)	**18.6**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2022 Estimate	**N/A**
P/E using 2023 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of USD)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021	$0.0 A	$0.0 A	$0.0 A	$0.0 A	$0.0 A
2022	$0.0 A	$0.0 A	$0.0 E	$0.0 E	$0.0 E
2023					$0.0 E
2024					$0.0 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2021	-$0.67 A	-$1.08 A	$0.28 A	-$2.84 A	-$4.19 A
2022	-$0.37 A	-$0.52 A	-$0.26 E	-$0.19 E	-$1.06 E
2023					-$1.42 E
2024					-$0.56 E

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INITIATING COVERAGE

We are initiating coverage of Allarity Therapeutics, Inc., (NASDAQ: ALLR) with a valuation of $5.00 per share. Allarity has developed its Drug Response Predictor (DRP®) platform, which enables the creation of a drug-specific companion diagnostic to identify cancer patients that will most likely respond to an oncology drug based on a patient's tumor cell transcriptome. The company has three primary candidates in the clinic for cancers of the ovaries, breast and kidney with patient populations partitioned by each drug-specific DRP companion diagnostic.

Allarity combines genomic technology with drug performance data in its DRP platform to identify patients that robustly respond to cancer medications. The platform can be applied to almost any type of cancer drug. With two primary programs in metastatic ovarian cancer (mOC) and metastatic breast cancer (mBC), Allarity has a diverse portfolio in various stages of development. The lead program in mOC offers a combination approach that adds stenoparib and dovitinib guided by the DRP technology to identify patients that will respond best to the therapy. The other active programs are the European-centered Phase II evaluating IXEMPRA® in mBC and the Phase II studying stenoparib as monotherapy in mOC.

Allarity is distinguished from other oncology therapeutic companies by its DRP platform. DRP is a type of personalized medicine that considers a patient's unique tumor gene expression profile to match therapeutic products to those who will best respond to a particular cancer therapy. The approach requires a multi-step process that identifies genetic expression profiles that are either sensitive or resistant to the drug. The DRP algorithm then identifies the messenger RNA (mRNA) and microRNA correlated with drug response then generates the DRP companion diagnostic that scores patients most likely to respond. Before a drug-specific DRP predictive signature can be used as a companion diagnostic to select and treat cancer patients, it must be clinically validated using patient tumor biopsies. The process ensures that the biomarker can identify responder patients and improve their therapeutic benefit as compared to patients not selected by the DRP companion diagnostic.

After regulatory approval, oncologists can then provide Allarity with a tumor biopsy sample from patients for DRP therapeutic response predictions for one or more drugs. Results of the transcriptomic analysis of a specific patient's tumor are compared to the DRP companion diagnostic signature to generate a DRP matching score and identify patients who are high scorers and candidates for the drug. The DRP diagnostic directs the use of the drug only towards those patients who will likely favorably respond and excludes those that are likely to have a weak or no response to the drug allowing the latter to pursue other appropriate courses of therapy.

Each of Allarity's three primary candidates fall into unique categories of mechanism of action (MoA). The associated programs target an indication with material unmet need and rely on the DRP companion diagnostic to identify appropriate patients. Stenoparib is a poly-ADP ribose polymerase inhibitor (PARPi) which also demonstrates inhibitory action against tankyrases being investigated in mOC. This indication sees almost 20,000 new cases each in the United States and in Europe.[1] Dovitinib is a second generation pan tyrosine kinase inhibitor (TKI) that offers both anti-tumor effects and anti-angiogenic activity. The drug is also being investigated in mOC in combination with stenoparib. Ovarian cancer is burdened by 79,000 cases per year in the United States and over 115,000 in the EU. Ixempra is a European exercise as Allarity has only secured European rights. The drug is a microtubule inhibitor approved in the US for mBC and is being advanced by Allarity for approval in the EU. There are about 230,000[2] cases of mBC in the EU.

Each of Allarity's lead candidates is a follow-on product for others in its class. PARP inhibitors such as olaparib, rucaparib and niraparib produced over $3 billion in revenues last year. In the TKI class, tivozanib, regorafenib, lenvatinib, sunitinib, sorafenib and pazopanib generated over $4 billion in revenues in 2021.[3] These are large markets in oncology where subsequent products can fill in the gaps left by others. Stenoparib, for example, has activity towards PARP and differentiates itself from others in the class with its tankyrase inhibition, low myelotoxicity and blood brain barrier penetration. Combined with DRP selection, Allarity's drug portfolio provides a differentiated product in several multi-billion dollar classes hungry for new candidates.

The drug development industry faces many hurdles in the modern era including declining returns, increasing costs, fewer blockbuster indications and long timelines to generate data needed to obtain regulatory approval. According

[1] 4.3/100,000 and EU population of 447 million.
[2] Author's work - SDX
[3] Source: Evaluate Pharma, Ltd.

to a 2016 report, the principal reasons that drugs fail is due to lack of efficacy (57%) or safety (17%).[4] For clinical trials that can cost up to and in excess of a billion dollars to run, tools that help improve efficiency are extremely valuable. The drug development setting provides fertile ground for new technology and precision medicine which can improve efficacy by targeting those patients that will benefit the most and by analyzing data sets to isolate early safety signals. Allarity's DRP platform is one of the tools that can support this progress.

The benefit of precision medicine is its ability to direct the right therapy to the right patient. This has the ancillary effect of saving time and money as the tool allows for rapid identification of populations that will respond best to a therapy and does not squander resources on unresponsive patients. The approach guides construction of smaller trials that include only those patients with a complementary genomic, transcriptomic, epigenomic or proteomic profile. Applying DRP to drug repurposing is an attractive and efficient route. A repurposed drug in a new indication is able to build off of previous human safety and toxicology work and in most cases allow for a direct start to an advanced stage clinical trial. Drug repurposing or rescue can be a more efficient approach that is effective when candidates have an abundant patient history of safety and biometric data.

With DRP, Allarity Therapeutics has refined its approach to precision medicine and is employing it to advance and de-risk its pipeline. DRP enables physicians and patients to make better cancer treatment decisions.

Key reasons to own Allarity Therapeutics shares. Allarity

- **Offers proprietary DRP platform to identify responders/non-responders**
  - **Increases efficiency of drug development**
  - **DRP companion diagnostics can extend patent coverage for off-patent drugs**
  - **Enables more efficient and rapid trials**
  - **Reduces failure risk**
- **Offers best in class PARPi features with lead candidate stenoparib**
  - **Tankyrase inhibitor activity for potential dual tumor killing MoA**
  - **Blood brain barrier penetration**
  - **Absence of myelotoxicity**
- **Uses combination therapy to address cancer's multiple survival pathways**
- **Provides salvage opportunity for failed drugs with validated safety and efficacy**
- **Pursues attractive indications with material unmet need**
  - **Metastatic ovarian cancer (mOC)**
  - **Metastatic breast cancer (mBC)**

Allarity has licensed several candidates that have demonstrated safety and efficacy and will employ its DRP screening to improve the response rates of its candidates in patients with several metastatic cancers. DRP provides a competitive advantage by identifying patients that are most likely to respond to a drug. In this report we provide a description of Allarity's competitive environment, including the strengths and weaknesses of precision medicine and the argument for using combination therapies more aggressively. This is followed by an in-depth description of the DRP platform and the process from biopsy to drug response prediction. Further sections summarize Allarity's primary indications in ovarian and breast cancer and the regulatory process that it will follow in the pursuit of approval. Special considerations on the regulatory side with respect to drug-device combinations and the impact of Project Optimus on clinical trial design are addressed.

Further research investigates Allarity's primary candidates stenoparib, dovitinib and Ixempra, where we examine the individual drug's mechanism of action and completed clinical work. Intellectual property and patents are addressed as are the risks faced by biotech companies. The research report summarizes the main peers and competitors in the precision medicine oncology space and introduces the main executives managing the company. Our closing sections provide a summary of key milestones over the last year and a valuation of the company. The valuation provides the assumptions behind our discounted cash flow (DCF) model and produces a target price for Allarity Therapeutics. Based on this work we generate a valuation of $5.00 per share.

[4] Hwang, TJ, *et al.* Failure of investigational drugs in late-stage clinical development and publication of trial results. JAMA Internal Med, 176 (12) (2016), pp. 1826-1833

Precision Medicine

Pharmaceutical treatments have traditionally been developed for the average patient, leaving individuals who diverge from this hypothetical median with poor outcomes. In most cases, trials are conducted to identify a treatment effect which is extrapolated to other patients who may be older, sicker and have other characteristics that differ from those of the median trial participant. This traditional approach may only provide a benefit to a minority of patients even though all that take the drug are exposed to the costs and risks of the therapies. According to an article by the distinguished scientific director Michele Cleary, drug therapies are surprisingly ineffective with 38% of patients on antidepressants, 40% on asthma drugs, 43% on diabetes, 70% on Alzheimer's drugs and 75% taking cancer drugs failing to respond to therapy approved for their indication.[5]

With improvements in technology and lower costs of gene sequencing, the ability to genomically define a patient is now a relatively efficient process. A physician can rapidly obtain genetic test results to find a match for the most appropriate therapy. The genetic profile can indicate how the patient will respond to treatment. Precision medicine can help improve diagnostic accuracy, identify patients that require specific tests and support prevention by encouraging healthier habits.

Many patients do not respond to the first drug they are prescribed. The lack of efficacy can be linked to a number of causes from genes that produce drug-metabolizing enzymes to drug transporters or drug targets and the non-homogenous character of the disease. One example of patient-specific variation is attributable to genes that code for drug metabolizing enzymes that break down a compound more quickly in some individuals compared to others. Knowing whether or not a patient can assimilate the drug properly can help avoid adverse reactions and improve patient health.

To address some of these shortcomings in medicine, a new approach uses profiling to improve the efficiency and therapeutic benefit of medicines for particular groups of patients. It is called precision medicine and it is guided by a companion diagnostic which is used to select appropriate and optimal therapies based on a patient's genetic profile, or molecular or cellular analysis. Frequently, proteomic, transcriptomic, metabolomic and other –omics are used to classify a patient into a responding or non-responding group. Systems biology is another approach that is employed to apply precision medicine. Systems biology combines computational and mathematical analysis to analyze a patient's disease and then identify targeted treatments to address the disease process. Artificial intelligence (AI) can also be used with precision medicine to analyze and draw inferences from large volumes of data.

Next generation sequencing (NGS)[6] is closely associated with precision medicine as it can identify specific genes that allow the targeting of specific markers. While the specific marker approach has supported some therapies' success, it ignores the multifactorial nature of disease and cancer. Larger tests that measure hundreds of biomarkers may help further refine precision medicine once they are accepted.

An example of precision medicine is screening for the breast cancer (BRCA) gene, which can be identified through a blood draw and lab-based DNA analysis. The test is able to identify whether or not a patient has the BRCA1, BRCA2 or neither gene, which is associated with a 60%, 40% or 10% chance of developing breast cancer by age 70. Identification of the gene can help susceptible women take preventative measures and also guides for the use of PARP inhibitors when treatment is necessary. There are more than 15,000 tests for over 2,800 genes in a wide variety of areas both including and beyond cancer.

A subcategory of precision medicine is precision oncology where researchers identify the molecular fingerprints of cancers and use this information to more precisely apply therapies. Precision oncology changes the way cancer is approached and departs from classifying the disease by the type of tissue or site in the body where the disease emerged. Cancer can now be examined in a way to identify targetable alterations.

Precision medicine targets responders and bypasses those who will not benefit from the drug. This not only reduces the cost to the system and patient, but also avoids wasting time using approaches that do not work and circumvents the side effects that come along with drug treatments. Precision medicine can also match patients with a certain mutation or protein with a drug that binds to that protein that has a higher likelihood of having a beneficial effect.

[5] Institute of Medicine (US). Genome-Based Therapeutics: Targeted Drug Discovery and Development: Workshop Summary. Washington, DC: National Academies Press; 2012. 2, The Current Landscape. https://www.ncbi.nlm.nih.gov/books/NBK116445/. Accessed June 30, 2019.
[6] Next-generation sequencing (NGS) is a massively parallel sequencing technology that offers ultra-high throughput, scalability, and speed. The technology is used to determine the order of nucleotides in entire genomes or targeted regions of DNA or RNA.

According to the previously referenced article[7] by Ms. Cleary, the use of chemotherapy in breast cancer could be reduced by 34% producing an improvement in outcomes if genetic tests were used prior to treatment. Some of the most salient benefits of precision medicine include:

- Insight into patient's family health history
- Improved understanding of disease risk, helping guide screening activities
- Tailored disease treatment

Despite the benefits of mainstream precision medicine, shortcomings exist. Precision medicine is very targeted, frequently using just a single biomarker or genetic mutation while its opponent, cancer, is multifactorial, with several co-incident components and variances driving it. This is one reason why cancer is so likely to adapt. When one tumor type is eliminated, others expand to fill the space. Gathering sufficiently large populations to power a randomized controlled trial for each cancer subtype is also difficult. Another weakness of precision medicine that it relies on a mutational test; however, not all patients have actionable mutations and there may not be a recommended treatment for them. Furthermore, physicians may lack the proper training to interpret genetic sequencing results, removing precision medicine from consideration.[8]

Drug development is expensive, time consuming and offers a low success rate when compared to innovation in other industries. With the explosion of available data in recent years, it may now be possible to analyze the complex relationships among the information sets to isolate subpopulations that can benefit from a previously failed drug using precision medicine. This approach has the advantage of building upon substantial work that has already been completed. This includes preclinical, investigational new drug (IND)-enabling efforts and clinical trials that have demonstrated the pharmacodynamic and pharmacokinetic features of the drug and successfully characterized its safety profile.

Combination Therapy

Combination therapy is a treatment modality that combines two or more agents to address a disease. One of the earliest efforts to pursue the approach was made in 1965 when Emil Frei, James F. Holland and Emil J. Freireich proposed the first ever combination chemotherapy in blood cancer. They used a composite of four agents called the POMP regimen[9] that demonstrated efficacy in acute lymphoblastic leukemia which is still used today.

The burden of cost for developing new cancer drugs shifts attention toward combination therapies, which may be able to achieve improved responses when compared to monotherapy and may employ combinations of already approved therapies. For example, checkpoint inhibitors used in monotherapy only work in a minority of patients. However, when combined with other agents, response can improve. Examples of trials yielding improved results using immunotherapy in combination with other agents include the Keynote-189 trial and the Impower 130 clinical trial as well as others[10] that both materially improved overall survival for patients in the combination arm of therapy.

In recent years combination chemotherapy has been used to more effectively treat cancer, and this approach was modified and refined to add treatments with different modes of action that would more effectively treat a heterogeneous cancer and provide synergies to the treatment. Approved combination therapies have already redefined the standard-of-care treatment in most types of cancer and most lines of therapy for a given cancer.

Some of the more popular oncology combination therapies add chemotherapy to immunotherapy in an effort to stimulate the body's response to cancer. When cancer cells are damaged by chemotherapy drugs, the immune system can more easily recognize these cells as abnormal so that the immunotherapy drugs can bring attention to them. Other approaches add an anti-angiogenesis agent with a checkpoint inhibitor or a CDK4/6 inhibitor with a PI3K inhibitor in several types of cancer including breast cancer.[11]

Monotherapy is more susceptible to drug resistance as the surviving cancer will pursue alternate survival pathways. This approach may also allow components of the cancer that do not respond to the monotherapy to grow, prolifer-

[7] Cleary, M. A Review of Precision Medicine, Companion Diagnostics, and the Challenges Surrounding Targeted Therapy. Value and Outcomes Spotlight, July/August 2019.
[8] Morash, M. *et al.* The Role of Next-Generation Sequencing in Precision Medicine: A Review of Outcomes in Oncology. J Pers Med September 2018.
[9] The drug regimen includes **P**urinethol (Mercaptopurine), **O**ncovin (Vincristine), **M**ethotrexate and **P**rednisone.
[10] Zhu, S., Zhang, T., Zheng, L. et al. Combination strategies to maximize the benefits of cancer immunotherapy. J Hematol Oncol 14, 156 (2021). https://doi.org/10.1186/s13045-021-01164-5.
[11] Vinciguerra, GL, *et al.* CDK4/6 Inhibitors in Combination Therapies: Better in Company Than Alone: A Mini Review. Front. Oncol., 27 May 2022 Sec. Molecular and Cellular Oncology

ate and develop resistance. Drug resistance is another hurdle that can be anticipated and addressed using combination therapy. Cancer is multi-factorial, heterogenous and rapidly evolving, which can allow proliferation of the component of cancer that is not sensitive to a certain drug regimen. While the susceptible part of the cancer is reduced or eliminated, the other parts will expand and grow, sidestepping the effects of the treatment. It is an example of survival of the fittest, where a type of cancer develops an acquired resistance through pre-existing genetic features or new mutations that allow it to adapt.

Drug repurposing or repositioning is another method that contributes to combination therapy as it takes a medicine that is already well understood in terms of its safety and pharmacokinetics and aligns it towards a cancer indication. Some examples of this include aspirin, which was found to inhibit proliferation and promote apoptosis of cancer cells and the use of sildenafil (Viagra) along with vincristine that provided a synergistic effect in treating prostate cancer.

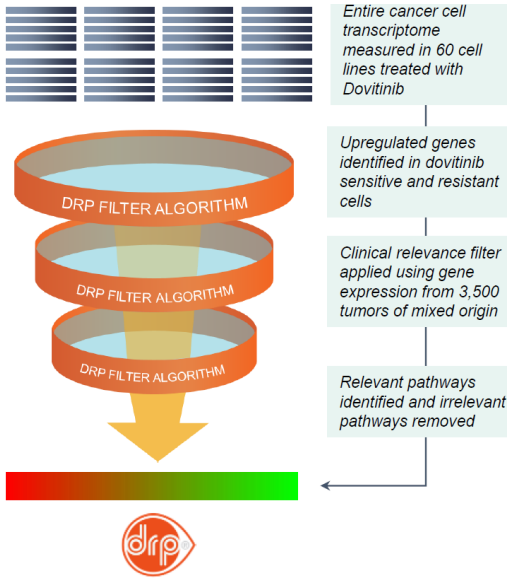
There can be downsides to using combination therapy, most notably with drug side effects. Drug interactions and the pharmacokinetics of co-administered agents that affect efficacy are other factors to consider. However, toxicity can be lower in combo therapy as lower dosages of each drug may be used and different pathways are targeted. In some cases, combination therapy may be able to reduce the toxic effects of the companion drug on normal cells which may occur if one of the drugs is antagonistic to effect of the other drug. In other cases, the effect of one agent may reduce the ability of another to leverage its mode of action. Chemotherapy, for example, can be immunosuppressive which can reduce the ability of immunotherapies to stimulate the body's cancer fighting ability.

With advancements in cancer cell genomics, epigenomics, transcriptomics, and proteomics, new combinations can be identified leveraging new molecular targets and the development of selective targeted anticancer therapies. This sets the stage for Allarity's approach that employs the DRP platform to generate drug-specific companion diagnostics, enabling oncologists to match patients with the right drug.

Drug Response Predictor (DRP®) Platform

DRP is considered precision medicine which is an approach to developing therapeutics for a specific group of patients using genetic or molecular profiling. The approach takes into account an individual's variability in genes, environment and lifestyle helping providers identify treatment and prevention approaches that are individually tailored towards that person.

Exhibit I – DRP Generation Process[12]



In the early days of drug development, the process for finding a compound relied heavily on serendipity. Many types of compounds were tested in 96 well plates against random targets to identify activity and when there was a signal, the candidate would be passed on for further testing and perhaps evaluation in animal models. Further success would lead to human clinical trials and in rare cases progression to regulatory approval. However, many failures occurred at each stage, and confined by the strict structure of clinical trials, there was insufficient adaptation al-

[12] Allarity Investor Presentation August 2022

lowed to modify trial design as studies progressed. In many cases a promising signal in a small group would fail to persist when applied to a large group. While there are very good reasons not to change things in the middle, sticking with a non-adaptive protocol contributed to low success and expensive clinical trials. When we look at historical success rates, we find that about ~15% of Phase II and ~50% of Phase III assets are ultimately approved. The lack of more consistency calls for alternative methods to improve success rates and identify patients that will respond to a particular drug.

Recognizing the shortcomings of mainstream drug development approaches, Dr. Steen Knudsen sought to develop a refined and robust approach to identifying patients that would respond well to a specific cancer drug. This led to the creation of the Drug Response Predictor (DRP®) approach which is a substantial advance in personalized cancer care.

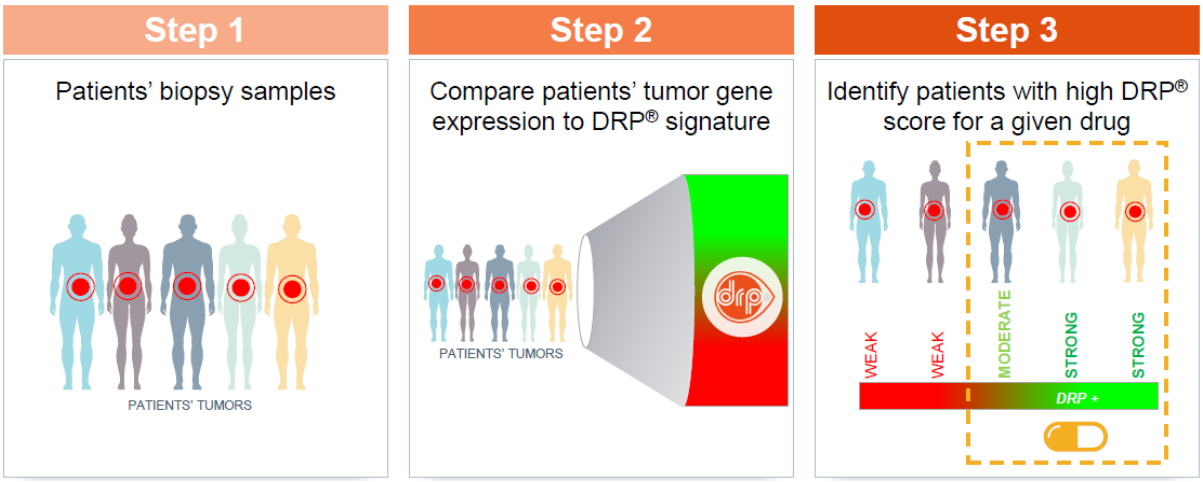
Allarity's DRP recognizes the shortcomings of other precision medicine approaches. It looks beyond a single mutation and evaluates all genes transcribed in a tumor to identify relevant biomarkers that are relevant to predict whether a tumor will respond or resist a certain drug.

DRP provides a systematic approach to identify patients sensitive to a particular therapy. The primary steps in the process include:

- Evaluation of an established panel of cancer cell lines that have been treated with the candidate:
  - The effort correlates the genetic expression profile of cell lines that are sensitive or resistant
  - The NCI-60 panel is used to identify and characterize the effectiveness of novel compounds
  - The impact of over 25,000 expressed genes is examined
- Identification of the specific mRNA & microRNA that are correlated with either response or resistance to that drug using DRP's bioinformatics algorithm
- Generation of a DRP companion diagnostic specific to the drug which identifies a subpopulation of cancer patients most likely to respond
- Validation of the DRP companion diagnostic using retrospective analysis.

In most cases, 50 to 100 biomarkers are sufficient to differentiate a tumor so that DRP can identify a drug as a matching candidate. The next step in the process is to validate the findings using retrospective data and to test the predictive capacity of the DRP. A cutoff score for patients is determined which optimizes the balance of favorable and unfavorable factors.

Exhibit II – DRP Patient Selection[13]



When the DRP companion diagnostic is ultimately used to identify responding patients, a biopsy of the tumor is taken and sent to Allarity for transcriptomic analysis. The results are then compared to the DRP signature and patients who possess a qualifying score with a strong likelihood of response are administered the drug at the discretion of their oncologist. DRP has shown utility in a wide range of cancer drugs including chemotherapeutics, as well as inhibitors in the histone deacetylase (HDAC), PARP, hormone receptor and kinase classes.

[13] Allarity Investor Presentation August 2022

Indications

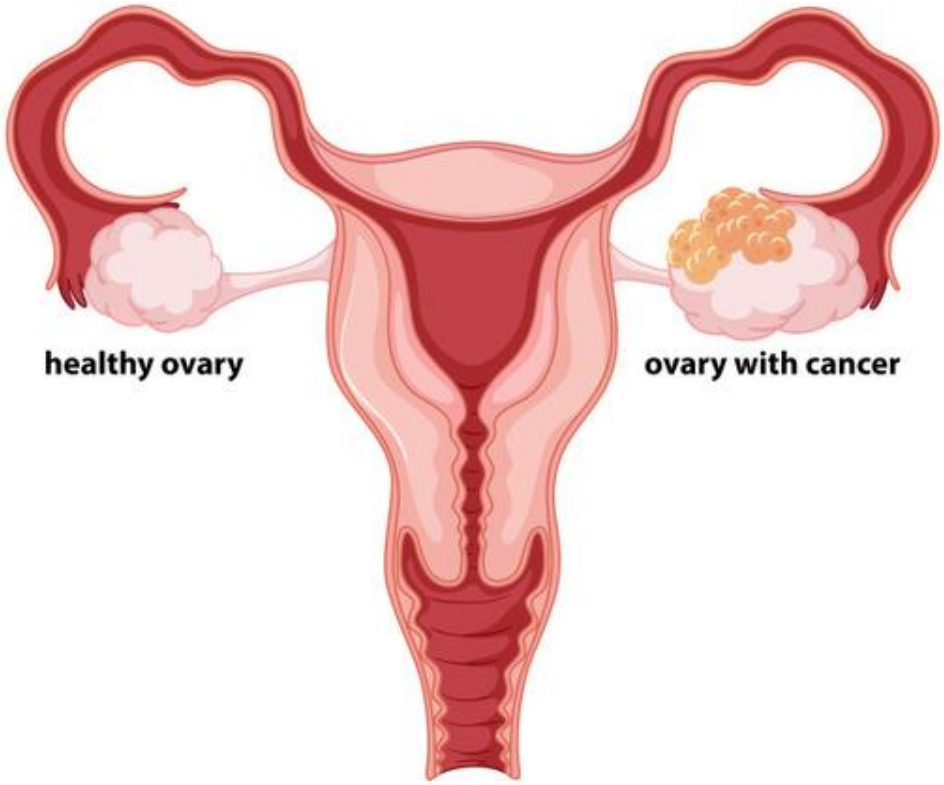
Allarity is pursuing two prevalent tumors in oncology: metastatic ovarian cancer (mOC) and metastatic breast cancer (mBC). It is also considering other indications including metastatic renal cell carcinoma (mRCC). Despite extensive efforts, existing therapies are in many cases ineffective for these lethal neoplasms and there have been only minor advances in patient survival rates. This leaves an unmet need which Allarity hopes to fill with its DRP-guided personalized medicine approach.

Ovarian Cancer

Ovarian cancer (OC) is the third most common gyneocological cancer following cervical and uterine cancer.[14] However, it has the worst prognosis and the highest mortality rate[15] which is three times greater than in breast cancer. The mortality rates due to ovarian cancer are expected to rise significantly by 2040.[16] Lifetime risk of ovarian cancer is 1.3% in the general population and it comprises of 1.3% of all new cancers. Yet, it is the fifth leading cause of cancer-related death in women.[17]

US demographic data shows that ovarian cancer most commonly affects non-Hispanic white women (12.0 per 100,000), followed by Hispanic (10.3 per 100,000), non-Hispanic black (9.4 per 100,000), and Asian/Pacific Islander women (9.2 per 100,000).[18] However, the highest mortality is reported in African populations, possibly due to the differences in access to medical care.[19]

Exhibit III – Ovarian Cancer[20]



[14] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
[15] Coburn S, Bray F, Sherman M, Trabert B. International patterns and trends in ovarian cancer incidence, overall and by histologic subtype. Int J Cancer. 2017;140(11):2451–2460. doi:10.1002/ijc.30676
[16] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424
[17] National Institutes of Health. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Statistical summaries: cancer stat fact sheets (ovary) and cancer statistics review (CSR), 1975-2013. http:// seer.cancer.gov/statistics/summaries.html. Accessed April 27, 2016
[18] Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin. 2018;68(4):284–296.
[19] Chornokur G, Amankwah EK, Schildkraut JM, Phelan CM. Global ovarian cancer health disparities. Gynecol Oncol. 2013;129(1):258–264. doi:10.1016/j.ygyno.2012.12.016
[20] Source: Shutterstock, Image 1138236809

Ovarian cancer affects women of all ages but is most commonly observed in the post-menopausal subgroup between the ages of 55 to 64. This insidious cancer is asymptomatic in its early stages and more than 75% of patients are diagnosed during the advanced stages of the disease. The most common risk factors include old age and family history of ovarian or breast cancer, whereas long term use of hormonal contraceptives decreases the risk by 50%.

90% of the tumors in post-menopausal women are epithelial in cellular origin. Germ cell tumors affect younger women, in their early 20s and comprise only 5% of all ovarian cancer types. Sex cord-stromal tumors which secrete sex steroids can occur at any age and these tumors comprise the rest.[21]

Symptoms
The early signs of ovarian cancer include bloating, pelvic or abdominal pain, trouble eating or feeling full and problems with urgency and frequency of urination. Many of these symptoms can be signs of other conditions besides cancer, which may lead to a delay in diagnosis. Less frequent symptoms include fatigue, upset stomach, back pain, pain during sex, changes in a woman's period and abdominal swelling.

Diagnosis
Following the identification of symptoms associated with ovarian cancer, a patient can visit their physician to conduct tests to diagnose the disease. Common tests and procedures include a pelvic exam, imaging tests (CT scan, transvaginal ultrasound), blood tests (CA-125 protein), biopsy analysis and genetic testing. Based on the results, the physician will stage the cancer and develop a treatment plan.

Prognosis
The most important prognostic factor is the stage of the disease at diagnosis. Five-year survival rates for women with tumors confined to the ovaries at initial diagnosis is 92%. This rate decreases to 17-28% for advanced tumors. Overall, only 45% of women diagnosed with ovarian cancer survive for five or more years.[22] While localized OC has a relatively high five-year survival rate of above 90%, symptoms are difficult to identify at an early stage and there is no screening test for the disease. Regional OC has a 5-year survival rate of 75% while metastatic OC offers a dismal 31% rate. Stromal and germ cell tumors have a slightly better prognosis compared with broader definitions of OC.[23]

Treatment
For the earliest stage of OC, surgery is recommended to remove the cancerous ovary. If the disease has spread locally, surgery may remove both the ovaries, fallopian tubes and the uterus. Chemotherapy is also used in conjunction with surgery, either before or after to improve results. Angiogenesis inhibitors and PARP inhibitors are also used in cases of OC. Bevacizumab is an example of an angiogenesis inhibitor that is used and it works by attaching to a protein called VEGF, thereby preventing the formation of new blood vessels that will feed the cancer. Olaparib, rucaparib and niraparib are examples of PARP inhibitors that prevent the repair of cell damage and produce cancer cell death.

Breast Cancer

The majority of breast cancers arise from the cells of milk forming lobules (lobular carcinoma) and cells lining the milk ducts (85%). In its initial phases, breast cancer is localized to the tissue of origin (in situ or stage 0) and has minimal potential for spread. Unfortunately, at this stage, it is difficult to detect because it causes no symptoms. In time, it grows progressively, first invading surrounding tissues and then spreading via metastasis to other organs, most commonly to lymph nodes, lungs, bones, liver and brain. As the disease becomes widespread it moves to stage 4 and ultimately leads to death.

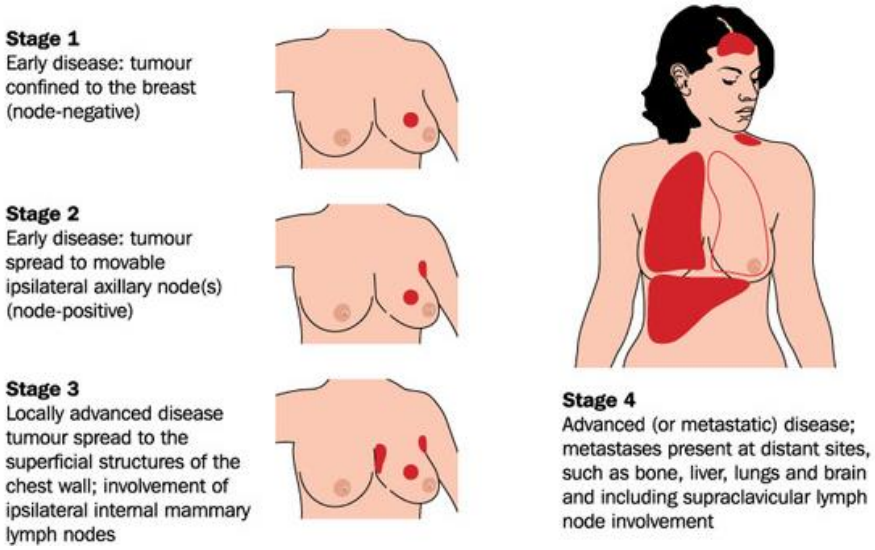
Breast cancer is the world's most prevalent cancer. World Health Organization (WHO) data shows that 2.3 million women were diagnosed with breast cancer in 2020 leading to 685,000 breast cancer-related deaths. By the end of 2020, 7.8 million women were alive and living with breast cancer that had been diagnosed with it in the previous five years.

Breast cancer can affect women of any age after puberty but is most commonly seen with advancing age. Well-known risk factors for breast cancer include increasing age, obesity, excessive use of alcohol, genetic predisposi-

[21] Doubeni CA, Doubeni AR, Myers AE. Diagnosis and Management of Ovarian Cancer. Am Fam Physician. 2016 Jun 1;93(11):937-44.
[22] National Institutes of Health. National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Statistical summaries: cancer stat fact sheets (ovary) and cancer statistics review (CSR), 1975–2013
[23] American Cancer Society Survival Rates for Ovarian Cancer.

tion and family history, radiation exposure, tobacco use, postmenopausal hormone replacement therapy and reproductive history. However, almost half of breast cancers develop in women without any of these risk factors except for their sex and age (over 40 years). Some of the modifiable risk factors to reduce incidence include prolonged breast feeding, regular exercise, weight control and avoidance of alcohol and tobacco use. However, minimizing these factors is estimated to only help reduce the risk by 30% at best.

Exhibit IV - Stages of Breast Cancer[24]



Family history for breast cancer is a well-known risk factor but the absence of family history does not protect against the disease. BRCA-2, BRCA-2, PALB-2 are examples of gene mutations with high breast cancer correlation. Selected women identified with these mutations may be recommended for prophylactic breast removal surgery to reduce their risks.

Breast cancer most commonly presents as a painless lump in the breast, yet 90% of breast masses are benign. Therefore, it is important to have a full medical work up for breast cancer in routine screenings and diagnostic tests such as mammography, ultrasound and MRI scans.

Other signs and symptoms include skin, shape and size changes such as thickening, pitting, new onset asymmetry, dimpling, retraction of the nipple, distortions and nipple discharge.[25]

Symptoms

Breast cancer symptoms include a new lump in the breast, thickening or swelling of the breast, redness or pain in the nipple area, nipple discharge and change in the size or shape of the breast among other warning signs. Similar to other types of cancers, the symptoms can indicate other diseases besides cancer or they can be benign. Breast cancer screening is an important component of early detection. For women 50 and older at average risk of breast cancer, screening is recommended every two years.

Diagnosis

Breast cancer is one of the handful of cancers that is commonly screened. Mammograms are the most common tool used for early detection. If breast cancer is suspected, further tests including a breast ultrasound, magnetic resonance imaging (MRI) and biopsy may be ordered. During the process of determining whether or not breast cancer exists, physicians and radiologists will stage the cancer to determine if it has spread or metastasized. Other factors at play which guide the ordering of diagnostic tests include the type of breast cancer, age and general health and the results of screening and earlier tests.

Prognosis

According to the American Cancer Society, survival for breast cancer is relatively high. Localized breast cancer presents a 99% five-year survival rate, which regional breast cancer falls to an 86% five-year survival rate. The most difficult stage of breast cancer, distant or metastasized, has a five-year survival rate of 29%. Fortunately, most breast cancers are caught early. On the other hand, multiple lines of treatment are frequently necessary.

[24] Source: Shutterstock.com Image 105721043. Red areas denote breast cancer metastases.
[25] https://www.who.int/news-room/fact-sheets/detail/breast-cancer

Treatment

Surgery and chemotherapy are common approaches to treating breast cancer. Radiation therapy is also commonly used. Hormonal therapy is also appropriate when a patient is estrogen receptor (ER) positive or progesterone receptor (PR) positive. Common medications for ER+ disease include tamoxifen and fulvestrant. For PR+ breast cancer, treatment with endocrine therapy is appropriate.

CDK4/6 inhibitors may also be prescribed for patients with hormone receptor positive HER2 negative disease, which include palbociclib, ribociclib and abemaciclib. Metastatic breast cancer can be treated by tamoxifen, toremifene and fulvestrant. mBC can also be addressed with combination therapy adding CDK4/6 inhibitors to hormone therapy. Depending on the type of breast cancer and which line of therapy is administered, the drug combinations are various and include aromatase inhibitors, kinase inhibitors, checkpoint inhibitors and other immunotherapies.

Early detection and appropriate treatment can achieve survival rates of 90% in breast cancer. Loco-regional treatment requires surgery including partial or entire removal of breast tissue and/or regional lymph nodes and radiation therapy. Specific features of each breast cancer are crucially important to determine the best approach for each patient according to their tumor type. Systemic therapy includes chemotherapy, endocrine (hormonal) therapy and targeted biologic therapy (antibodies). Depending on the timing of administration of medications, medical therapy for breast cancer can be adjuvant (after surgery) or neoadjuvant (before surgery). In addition to the stage of the disease at the time of diagnosis, the subtype of the tumor and its specific genetic subgroup are other major determinants for what kind of therapy is used and when it is administered.

Hormonal therapies are effective only in hormone (estrogen and progesterone) receptor positive tumors. These drugs (tamoxifen and aromatase inhibitors) are administered orally for 5-10 years to decrease the chance of disease recurrence. Tumor types that do not express hormone receptors, called hormone receptor negative tumors, do not benefit from these drugs and chemotherapy remains the mainstay of treatment.

A second well-studied molecule that is implicated in specific prognosis and treatment methods in breast cancer is HER-2/neu oncogene. HER-2 positive cancers are responsive to targeted biological agents such as trastuzumab. These agents are antibodies and are usually co-administered together with chemotherapeutics to boost efficacy.[26]

[26] https://www.who.int/news-room/fact-sheets/detail/breast-cancer

Regulatory Considerations

Drug-Device Combinations

Allarity is distinct in the domain of oncology therapeutics companies in that its drug candidates are integrally tied to the DRP companion diagnostic. Since regulatory agencies require approval for both the drug and the diagnostic, multiple submissions will be made for the combination product. The FDA has provided guidance for this class of submission with details found in the January 2022 guidance document entitled: Principles of Premarket Pathways for Combination Products.

A combination product is a product that is composed of two or more regulated components including drug, biologic and device that are physically, chemically or otherwise combined or missed and produced as a single entity. It can also be multiple separate products packaged together as a unit. Further definition includes any investigational product that according to its proposed labeling is for use with another individually specified investigational product where both are required to achieve the intended use. A combination product is assigned to an FDA center that will assume the lead role for shepherding the product through the regulatory process. The primary mode of action of the combination product determines which center will be the sponsor's chief point of contact during the review process. A sponsor may submit separate applications for the multiple components of a combination product unless the FDA determines that a single application is necessary.

In Allarity's case, its pipeline programs are composed of a candidate drug and its DRP companion diagnostic and are appropriate to be submitted as a new drug application (NDA) for the drug and a pre-market approval (PMA) for the DRP companion diagnostic. An NDA is a collection of documents that sponsors submit to the FDA which includes information related to patent and manufacturing, drug safety and effectiveness, clinical trials, and proposed labeling. A PMA is a required scientific and regulatory review to evaluate the safety and efficacy of a Class III medical device. The PMA is the most stringent type of application used for new devices and must include compelling scientific evidence that the device is safe for use. It sits above a 510k application in terms of complexity and effort.

In Allarity's case, the FDA is likely to also require pivotal studies that require a direct comparison of DRP companion diagnostic-identified subjects to the overall patient group that would otherwise be appropriate for the drug regimen. Dose optimization studies will also likely be required before a regulatory submission can be made to the FDA as per the agency's new emphasis on Project Optimus. To merit approval, the results would need to show a statistically significant benefit attributable to the DRP-guided treatment.

Project Optimus

The FDA is undertaking an effort to improve the dose-finding and dose optimization of candidates in oncology in an effort called Project Optimus. Drug development in prior decades sought to identify and apply the maximum tolerated dose that a patient could withstand. This approach assumed that the best approach was to deliver as much drug as possible balanced against the tolerability of side effects. The framework is changing and under the goals of Project Optimus, the FDA wants to improve the sponsor's understanding of the physical and chemical properties of the pharmaceuticals that they develop in order to better optimize a dose before moving into later stage trials. The effort will attempt to find a balance among the competing goals of efficacy, safety and tolerability.

An example of Project Optimus in action was observed in the development of Amgen's Lumakras for treating non-small cell lung cancer. Approval was granted on the condition that Amgen run a trial to compare a smaller dose of Lumakras than the one used in the pivotal trial. Another example is Kura Oncology which announced it would conduct a new dose-optimization trial for its KO-539 candidate in acute myeloid leukemia.[27,28]

If consistently implemented, the guidance provided in Project Optimus could force some programs to take a step back and run additional dose-optimization trials before moving on to later stage pivotal trials.

[27] Five Broad Implications for FDA's Project Optimus: How to Prepare for the Future of Oncology Trials. Jason Birri, Mamta, Puri-Lechner & Anna Hertzberg. June 2, 2022
[28] FDA's renewed focus on oncology dosing spooks investors, but companies say they're ready. Annalee Armstrong. June 28, 2021

Candidates

Pipeline

Allarity is advancing three primary oncology candidates in its pipeline and has one secondary asset. The lead program employs a combination approach with both stenoparib and dovitinib in the pursuit of second line or later metastatic ovarian cancer. Stenoparib is a poly-ADP ribose polymerase (PARP) and tankyrase inhibitor that compares favorably with other PARP inhibitors. Dovitinib is a pan-tyrosine kinase inhibitor (TKI) that has been the subject of numerous clinical trials conducted by Novartis in a number of indications including Phase III studies for renal cell carcinoma (RCC). The third active candidate is Ixempra, generically known as ixabepilone, a microtubule inhibitor that is approved in the US and in-licensed by Allarity to develop in the EU for the treatment of second line metastatic breast cancer. 2X-111 is the secondary pipeline candidate comprised of doxorubicin encapsulated in a GSH-linked liposome enabling blood brain barrier penetration. It is intended to treat primary brain cancer or glioblastoma and is in discussions for continuing partnered development with Smerud Medical Research International. Below is a visual depiction of Allarity's pipeline.

Exhibit V – Clinical Development Pipeline[29]

			PHASE 1/1b	PHASE 2	PHASE 3	NDA	STATUS/ PARTNER
Primary Pipeline	Dovitinib	Pan-tyrosine kinase inhibitor	Combination Rx with Stenoparib – 2nd + line Ovarian Cancer				
	Stenoparib	PARP and tankyrase inhibitor	3rd line Ovarian Cancer				
	IXEMPRA	Microtubule inhibitor	2nd line Metastatic Breast Cancer				US Approved and out-licensed to Allarity in EU
Secondary Pipeline							
	2X-111	Doxorubicin in GSH-linked liposome enabling BBB penetration	Primary Brain Cancer (Glioblastoma)				

Stenoparib

Stenoparib is a selective inhibitor of the DNA damage repair enzymes poly-ADP-ribose polymerase (PARP) and tankyrases. PARP is a family of enzymes that are involved in multiple cellular processes including transcription, replication and DNA repair. Tankyrases also belong to the PARP family of enzymes, are implicated in cancer and involved in signaling pathways related to telomere length and vesicle trafficking among other functions. Other approved PARP inhibitors lack tankyrase inhibition, allowing stenoparib to offer a different mechanism of impeding cancer cell growth. Prior PARP inhibitor success relied on tumors that are already defective in the breast cancer (BRCA) genes. However, stenoparib activity in DRP-selected patients is not dependent on BRCA mutation status, differentiating it from the rest of the field. The synergistic inhibition of multiple DNA damage repair pathways can lead to synthetic lethality and cell death, thereby eradicating the cancer cells. Based on the research generated to date, stenoparib has demonstrated a superior therapeutic and toxicity profile and exhibits less myelotoxicity compared with other PARP inhibitors. The drug may also cross the blood brain barrier, providing additional treatment opportunities in brain metastases.

In a retrospective, blinded clinical analysis of patients treated with the drug, those selected by the stenoparib-DRP companion diagnostic have a fourfold improvement in overall survival (OS) compared with patients not selected. The stenoparib DRP was able to identify a broader responsive population compared with the use of single biomarkers such as BRCA and selects patients independent of BRCA mutation status.

Allarity is pursuing the use of stenoparib for mOC in an ongoing Phase II trial being conducted at the Dana-Farber Cancer Institute and other global sites in conjunction with its stenoparib-DRP companion diagnostic. An interim data readout for this trial is anticipated in late 4Q:22. Additionally, Allarity plans to initiate a new Phase Ib/II study of stenoparib in combination with dovitinib for the treatment of 2nd line or later mOC. Further, Allarity has an ongoing partnership with OncoHeroes Biosciences for the monotherapy development of stenoparib for pediatric cancers.

[29] Allarity Investor Presentation August 2022

Allarity holds responsibility for developing stenoparib with its path forward guided by a joint development committee consisting of six members evenly split between Allarity and Eisai. Over the arc of development, Allarity will owe payments at key points related to clinical trial and regulatory milestones. If stenoparib is approved and it generates sales, royalties from the low single-digit to low double-digit range will be owed to the license holder. Eisai holds an option to buy back stenoparib for a short period following the end of the ongoing Phase II clinical trial.

Exhibit VI – Stenoparib Competitive Landscape[30]

Product	Owner	Stage	Response biomarker	Export Resistance (PgP mediated)	Absence of Myelotoxicity (Myelotox)	Multi-targeted (PARP/ Tankyrase)	PARP trapping	BBB penetration	Strong maintenance opportunity
Olaparib	AstraZeneca	Approved	BRCA	✗	✗	✗	✓	✗	✓
Niraparib	gsk / TESARO	Approved	BRCA/HRD	✗	✗	✗	✓	✗	✓
Veliparib	abbvie	Phase 3	BRCA	✗	✗	✗	✗	✗	✗
Rucaparib	CLOVIS ONCOLOGY	Approved	BRCA	✗	✗	✓	✓	✗	✓
Talazoparib	Pfizer	Approved	BRCA	✓	✗	✗	✓	✗	✓
Stenoparib	allarity	Phase 2[2]	DRP®	✓	✓	✓	✓	✓	✓

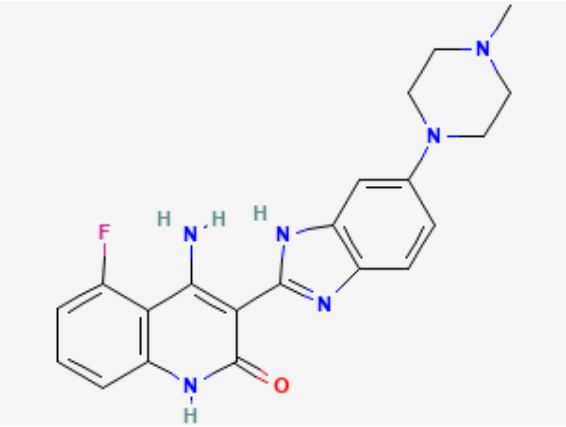
Dovitinib

Dovitinib is Allarity's co-lead candidate along with stenoparib in the pursuit of second line or later mOC. The drug was designed as a second-generation pan-TKI that can inhibit multiple tumor-driving kinases including fibroblast growth factor receptor (FGFR), vascular endothelial growth factor receptor (VEGFR), platelet-derived growth factor receptor (PDGFR), c-Kit, Flt-3, and colony stimulating factor (CSF)-1. Dovitinib was previously investigated in 56 clinical trials, including a Phase III trial where it demonstrated therapeutic equivalence to Bayer's sorafenib in third line renal cell carcinoma. Allarity is also evaluating additional clinical development opportunities for dovitinib, in the combination setting, in a number of indications including mRCC. Further, Allarity has an ongoing partnership with OncoHeroes Biosciences for the monotherapy development of dovitinib for pediatric cancers.

Mechanism of Action

Dovitinib is an orally active potent inhibitor of multiple receptor tyrosine kinases with anti-tumoral action. Specifically, it binds to and inhibits the phosphorylation of type III-V RTKs, such as vascular endothelial growth factor receptor (VEGFR) and platelet-derived growth factor receptor (PDGFR). These growth factors promote tumor cell proliferation and survival in certain cancer cells. In addition, this agent also inhibits other members of the RTK superfamily, including fibroblast growth factor receptor (FGFR) 1 and 3, FMS-like tyrosine kinase 3, stem cell factor receptor (c-KIT), and colony stimulating factor receptor 1. This may further lead to a reduction of cellular proliferation and angiogenesis and an induction of tumor cell apoptosis.[31]

Exhibit VII – Dovitinib's Molecular Structure[32]



[30] Allarity Investor Presentation August 2022
[31] https://pubchem.ncbi.nlm.nih.gov/compound/Dovitinib#section=2D-Structure
[32] National Library of Medicine, National Center for Biotechnology Information. Dovitinib.

Clinical trials have been conducted for dovitinib in a number of indications including Phase III trials in renal cell carcinoma. Phase II trials for gastrointestinal stromal tumor (GIST), breast cancer, endometrial cancer and other solid tumors were conducted by Novartis. According to Allarity's filing, of the 56 dovitinib clinical trials, 23 of them were sponsored by Novartis and 33 were investigator initiated.

Dovitinib's Pivotal Trials in RCC and Efficacy
Renal cell carcinoma is highly dependent on new blood vessel formation for growth and anti-angiogenetic agents play a major role in addressing the unmet need for metastatic disease. Therapeutics targeting vascular endothelial growth factor (VEGF) and mammalian target of rapamycin (mTOR) signaling pathways comprise the standard first and second lines of treatment in metastatic RCC. However, nearly all patients who receive these treatments develop drug resistance leading to continued and further need for anti-angiogenetic therapeutics in this disorder.

Fibroblast growth factor (FGF) plays a crucial role in the initial and later stages of new blood vessel formation and FGF pathway has been blamed for the escape from VEGF-targeted drugs. Supporting this theory, increased levels of FGF2 were reported in blood of metastatic RCC patients who developed VEGF-targeted drug resistance.

Earlier studies on RCC xenograft models have shown greater tumor reduction activity with dovitinib than sunitinib and sorafenib.[33,34]

With its dual antagonistic actions for both VEGFR and FGFR, as well as anti-PDGFR effects, the oral tyrosine kinase inhibitor dovitinib has been tested for use in metastatic RCC as a third-line targeted drug. The results of this open label, randomized, Phase III trial were published in 2014. They compared the efficacy of dovitinib to the standard agent sorafenib in mRCC showing comparable (but not superior) efficacy as sorafenib in patients who showed disease progression with previous VEGF-targeted therapies and mTOR inhibitors.[35] Allarity has conducted a retrospective, blinded analysis of a Phase III mRCC study and shown that the dovitinib-DRP companion diagnostic identifies likely responder patients and provides an increase in median overall survival (OS) by six months in mRCC when compared to patients not selected by the DRP.

Side Effects
Most common reported side effects for dovitinib include diarrhea, nausea, vomiting, fatigue, reduced appetite, rash and other side effects that on the whole were slightly higher than that observed for sorafenib.[36]

IXEMPRA® (Ixabepilone)

Ixempra is a member of the epothilone class, which are 16-membered macrolides named for their molecular structure, which includes an epoxide, methyl thiazole and ketone. It a selective microtubule inhibitor which interferes with cancer cell division through mitotic arrest, thereby leading to cell death. Microtubules are structural elements of a cell's cytoskeleton that are composed of polymers of tubulin. Microtubules play an important role in cellular mitosis and an inhibitor in this class is able to block cell cycle progression leading to apoptosis. Microtubule inhibitors include agents such as taxanes, vinca alkaloids and epothilones that are used against many solid and hematologic malignancies.

In the United States, Ixempra is approved by the FDA and indicated for the treatment of metastatic or locally advanced breast cancer in combination with capecitabine for patients who have failed an anthracycline and a taxane. It is also used as monotherapy for mBC in the second line setting after failure of an anthracycline, a taxane, and capecitabine.

[33] Angevin E, Lopez-Martin J, Lin CC, et al. Phase I study of dovitinib (TKI258), an oral FGFR, VEGFR, and PDGFR inhibitor, in advanced or metastatic renal cell carcinoma. *Clin Cancer Res*. 2013;19:1257–68
[34] Sivanand S, Peña-Llopis S, Zhao H, et al. A validated tumorgraft model reveals activity of dovitinib against renal cell carcinoma. *Sci Transl Med.* 2012;4:137ra75
[35] Motzer, R. J., Porta, C., Vogelzang, N. J., et al. (2014). Dovitinib versus sorafenib for third-line targeted treatment of patients with metastatic renal cell carcinoma: an open-label, randomised phase 3 trial. *The Lancet. Oncology*, *15*(3), 286–296. https://doi.org/10.1016/S1470-2045(14)70030-0
[36] Motzer, R. J., Porta, C., Vogelzang, N. J., et al. (2014). Dovitinib versus sorafenib for third-line targeted treatment of patients with metastatic renal cell carcinoma: an open-label, randomised phase 3 trial. *The Lancet. Oncology*, *15*(3), 286–296.

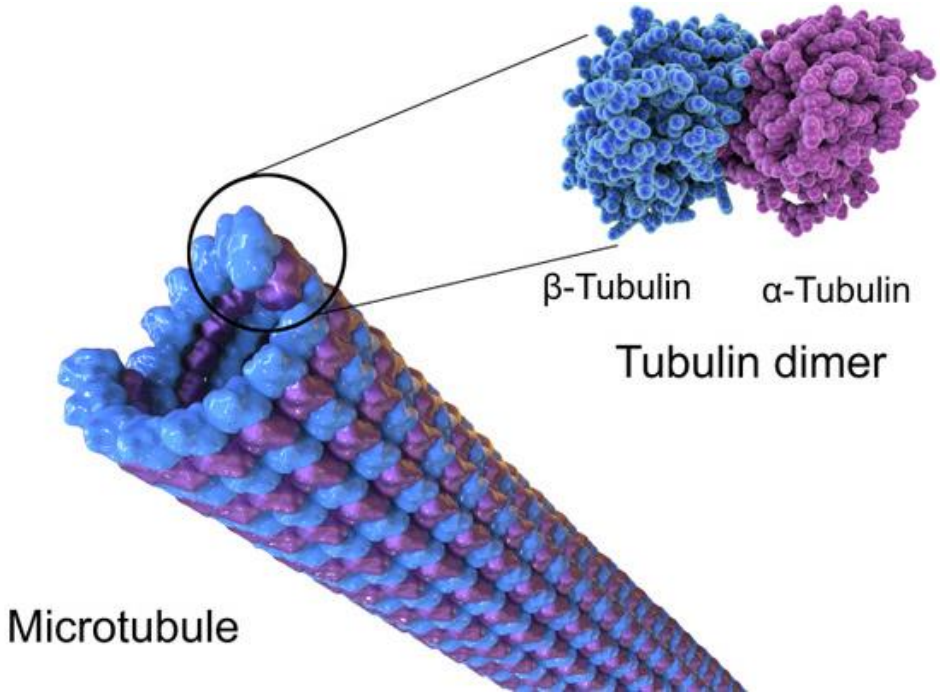
Exhibit VIII – Approved and In-development Microtubule Inhibitors[37]

Compound Class	Related Agents	Microtubule Effect
Taxane	Paclitaxel	Polymerization/stabilization
Taxane	Docetaxel	Polymerization/stabilization
Taxane	Albumin-bound paclitaxel	
Taxane	DJ-927	
Epothilone	Ixabepilone (Ixempra)	
Epothilone	KOS-1584	
Vinca alkaloid	Vinblastine	Depolymerization/destabilization
Vinca alkaloid	Vincristine	
Vinca alkaloid	Vinorelbine	
Halichondrin b	Erubilin mesylate	

Mechanism of Action

Microtubule structure is composed of noncovalent polymers of α- and β-tubulin heterodimers assembled in a filamentous tube-shaped structure (see below). Ixempra binds directly to β-tubulin subunits on microtubules, stabilizing the microtubule and inducing apoptosis. The compound suppresses the dynamic instability of αβ-II and αβ-III microtubules. The drug is able to circumvent several tumor resistance mechanisms such as efflux transporters. Ixempra destroys the tumor cell by blocking cells in the mitotic phase of the cell division cycle, leading to cell death. It offers several mechanistic differences that maintain its antitumor activity in taxane resistant or refractory tumors. These characteristics include links to Ixempra-induced apoptosis in breast cancer occurring through p53-dependent activation of Bax, a protein which stimulates apoptosis.

Exhibit IX – Microtubule Structure[38]



Ixempra's Clinical Trials

Allarity is conducting a DRP-guided Phase II trial for Ixempra in second line metastatic breast cancer with sites located in Europe. The trial was slowed by pandemic-related restrictions and shortages and is expected to provide a readout of interim results in late 1Q:23.

[37] Compiled by Zacks Analyst from Perez, E. Microtubule inhibitors: Differentiating tubulin-inhibiting agents based on mechanisms of action, clinical activity, and resistance. Molecular Cancer Therapy, 2009.
[38] Source: Shutterstock Image 706022503

Ixempra was developed through Phase III clinical trials and brought to market in the United States by Bristol-Myers Squibb. Clinical trials examined efficacy and safety in breast, colon, head and neck, ovarian, endometrial, vulvar and peritoneal cancers, melanoma and non-Hodgkin's lymphoma.

Phase I/II trials identified common toxicities for Ixempra of fatigue, nausea, hand-foot syndrome, and sensory neuropathy. Activity for the candidate was measured in advanced breast cancer, non-small cell and small-cell lung cancers, prostate cancer and gastric malignancies. Toxicities in the Phase II were similar to those in the Phase I and dissipated after discontinuation.

Results from the previous investigations were sufficient to support a large international Phase III study. Patients recruited were taxane-resistant and anthracycline-pretreated with resistant metastatic or locally advanced breast cancer. This program combined capecitabine with Ixempra and produced a statistically significant improvement in progression-free survival (PFS) and response rate (RR) compared to capecitabine monotherapy. A second Phase III trial for Ixempra was conducted also in combination with capecitabine which found a clinically meaningful improvement in PFS and RR and a modest improvement in overall survival (OS), the last of which was not statistically significant. The two studies enrolled over 1,200 patients and over 3,140 patients have been treated with the drug in all phases prior to Allarity advancing the program under its sponsorship.

The FDA approved Ixempra based on its Phase III results in 2007; however, when presented to the EMA, the European agency determined that there was insufficient risk-benefit and did not grant approval. This decision provides an opportunity for Ixempra's DRP companion diagnostic to identify strong responders that may improve the risk-benefit ratio to a level that justifies EU approval.

Allarity is now conducting a DRP-guided Phase II study to investigate Ixempra as monotherapy in second line therapies for mBC. The European-based study expects to enroll 60 subjects and began in April 2021. Interim results from the study are expected in late 1Q:23.

Intellectual Property

Allarity holds a portfolio of issued patents with the key intellectual property related to the Drug Response Predictor (DRP) platform and its related predictive signatures. Over 70 anti-cancer drugs have a DRP-related patent issued or pending. The DRP is able to identify patients most likely to respond based on their tumor biopsy. The approach is protected by a patent that identifies the list of expressed genes that comprise a predictive signature used to select responding patients. The method used to generate the predictive signature is not patented and is considered to be a trade secret.

Barriers to entry for competitors who seek to generate a similar screen are the patents for the DRP predictive signatures and patient response predictor (PRP) signature. A competitor would have to develop a different, non-infringing, *de novo* prediction technique. Regulatory barriers also exist that require a high level of enforcement discretion, FDA approval and a Clinical Laboratory Improvement Amendments (CLIA) certification for each DRP companion diagnostic.

Dovitinib is licensed from Novartis Pharma, granting Allarity's worldwide rights to therapeutic and diagnostic uses related to cancer in humans. Stenoparib is licensed from Eisai providing Allarity rights to therapeutic and diagnostic uses for the drug related to cancer in humans. Allarity licenses Ixempra from R-Pharm U.S. receiving rights to develop and commercialize the drug in the E.U. The agreement includes an option for R-Pharm to re-acquire the license rights in return for a negotiated payment prior to September 1, 2023.

Allarity has retained exclusive rights stenoparib and dovitinib around the globe and holds exclusive European rights for Ixempra. While the drugs are licensed from others, the patent portfolio around DRP is exclusively owned by Allarity. All products licensed by Allarity have a patented DRP companion diagnostic which will be listed on the approval label. Allarity controls remaining composition of matter, formulation, and methods of use patent coverage on dovitinib and stenoparib which extend out to 2028 or 2032 depending on the product and the relevant patents.

Exhibit X – Selection of Allarity DRP Patents[39]

Title	Patent #	Expiry	Region	Filed
Methods for predicting drug responsiveness	1057045782	9/25/35	US	9/25/15
Methods for predicting drug responsiveness in cancer patients	20200340067A1		US	7/13/20
Methods, kits and devices for identifying biomarkers of treatment response and use thereof to predict treatment efficacy	8445198B2	9/20/28	US	5/9/08
Methods for predicting drug responsiveness in cancer patients	20180087113A1		US	9/27/16
Methods for predicting drug responsiveness in cancer patients	20160199399A1		US	1/8/16
Methods and devices for predicting treatment efficacy of fulvestrant in cancer patients	20160138111A1	3/30/34	US	2/5/14
Methods and devices for identifying biomarkers of treatment response and use thereof to predict treatment efficacy	2631236C	12/1/26	CA	12/1/06
Methods for predicting drug responsiveness in cancer patients	3342879B1	12/29/37	EU	12/29/17
Methods and devices for prognosis of cancer relapse	2714927B1	6/1/32	EU	8/10/16
Methods for predicting drug responsiveness in cancer patients	2019219759A1		EU	5/15/19
Method for combining several dna microarray datasets	2006125440A1		EU	5/24/06
Methods for predicting ixabepilone responsiveness in cancer patients	2021152107A1		EU	1/29/21
Compositions comprising 2x-121 and methods for treating coronavirus infection	2021249996A1		EU	6/8/21
Methods and devices for predicting treatment efficacy	2011246976B2	4/29/31	AU	4/29/11
Methods and devices for prognosis of cancer relapse	2012265177A1	6/1/32	AU	6/1/12
Methods for predicting drug responsiveness in cancer patients	2018202878A1		AU	4/26/18
Methods for predicting drug responsiveness in cancer patients	2020294893A1		AU	6/17/20
Methods, kits, and devices for identifying biomarkers of treatment response and use thereof to predict treatment efficacy	2008138578A3		PCT	5/9/08
Methods and devices for predicting treatment efficacy (PRP miRNA)	9,598,734	3/14/34	US	4/29/11
Methods for predicting drug responsiveness in cancer patients (Irofulven)	9,725,769	10/7/36	US	10/7/16
Methods and devices for predicting treatment efficacy of fulvestrant in cancer patients	10,392,667	3/30/34	US	5/2/14
Methods for predicting drug responsiveness (5-FU)	10,570,457	9/25/35	US	9/25/15
Methods for predicting drug responsiveness in cancer patients (Dovitinib)	10,835,531	6/18/39	US	11/17/20
Methods for predicting drug responsiveness in cancer patients (Doxorubicin)	10,900,089	7/27/38	US	5/14/18
Methods for predicting drug responsiveness in cancer patients (LiPlaCis)	10,907,214	3/25/38	US	12/29/17
Methods and Devices for Predicting Treatment Efficacy (PRP miRNA)	2,563,936	4/29/31	EU	4/29/11
Methods for predicting drug responsiveness in cancer patients (LiPlaCis)	EP3342879	12/29/37	EU	12/29/17
Methods and devices for predicting treatment efficacy (PRP miRNA)	2011246976	4/29/31	AU	4/29/11
Identifying method, apparatus & the purposes of prediction curative effect thereof of the therapeutic response biomarker	2006 80052220.2	12/1/26	CN	12/1/06
Method and apparatus for identifying biomarkers of therapeutic response and use thereof for estimating therapeutic effect	5984324	12/1/26	JP	12/1/06

[39] Source: Analyst compiled from Allarity public filings and public information from patent websites

Risks

All investments contain an element of risk which reflects the uncertainty of a business and what it will ultimately achieve. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

The biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical powerhouses that have multiple products currently generating revenues, to small operations with a handful of employees conducting pre-clinical studies. Many of the risks faced by the large pharmaceutical companies and smaller biotechnology-focused firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products. The typical risks faced by those operating in the biotechnology space relate to liquidity, financing & trading, clinical trials, regulatory, personnel, intellectual property, marketing the therapy, and geopolitics.

Liquidity, Financing & Trading

Any company may find that securing funding may depend on its position in the economic cycle. During periods of improving confidence, capital may be easy to obtain; however, during a liquidity crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they are dependent on the financial markets to fund their work. Pre-revenue biotech firms rely primarily on equity issuance to fund their operations. The duration of drug development is considerable, and can and can last over a decade before a product is sold. Funds can be sourced through debt or grants and tax credits; however, these sources may reduce the flexibility of the company and can create difficulties if debt is unable to be repaid.

If capital is required to sustain operations and it is not readily available, a company may be forced to suspend research and development, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising therapies without a viable route forward or force a company to accept onerous terms. The pandemic has disrupted capital markets, and any economic effects may last well into the future.

Trading volumes are lower for smaller biotech firms, creating liquidity risk for the investor and large transactions may have a material impact on share price. In periods of crisis or heightened risk perception, share price may be volatile. Companies with smaller capitalizations are typically considered riskier and changes in sentiment may adversely affect their trading prices and volumes. Smaller firms may also have less visibility, compete for investor dollars in a shallow market and be excluded from market indices.

Allarity has endured operational losses since inception and expects to continue to do so into the future. Allarity may fail to monetize its development programs and may never become profitable. Allarity raised $20 million in a Private Investment in Public Equity (PIPE) last December which is expected to provide sufficient funding to support a year of operations. The funds will advance planned studies in the pipeline including the Phase II studies in ovarian and breast cancer. However, it is insufficient to advance the work for the combination trial for stenoparib and dovitinib in metastatic ovarian cancer. While Allarity holds funds on the balance sheet, there are additional research and development expenditures necessary before submission and potential regulatory approval may be granted. There is no guarantee that capital markets will support further raises after the current balance is consumed. Allarity carries $1 million in a convertible promissory note on its balance sheet that is owed to Novartis Pharma AG related to the dovitinib license.

Allarity's prior auditor, Marcum LLP, provided notice to Allarity that it was terminating the client-auditor relationship with Allarity as of August 5, 2022. The termination was related to Marcum's anxiety over Allarity being able to continue as a going concern. Given the short period between the termination of the relationship and the required filing date for the third quarter Form 10-Q, Allarity was not able to engage a new auditor prior to the deadline for submission. This led to the filing of a not timely report while the company sought a new auditor. Allarity announced on September 12th, that is has engaged Wolf & Company, P.C. (Boston, MA) as its new auditor. While second quarter financials were provided, Allarity expects it will take several weeks for the 2Q:22 Form 10-Q to be filed.

Clinical Trials

For smaller early-stage companies, investing in drug development is a lengthy process. The timeframe for conducting pre-clinical research to eventually commercializing a drug can take from 12 to 15 years or even longer given market and company-specific conditions. And with, on average, only one in one thousand compounds eventually making it to the market from the preclinical stage, the risks are substantial.

Exhibit XI – Success of Phased Trials and Regulatory Approval[40]

Phase	I - II	II - III	III - NDA/BLA	NDA/BLA - Approval	I - Approval
Probability	**52.0%**	**28.9%**	**57.8%**	**90.6%**	**7.9%**

The future of Allarity Therapeutics is dependent on the data produced from expensive clinical trials. Due to the cost, magnitude and complexity typical of Phase III trials, partners are often sought to help finance and manage them. Partners may have competing demands which can adversely affect the work they are managing on behalf of the firm. CROs and subcontractors must abide by strict execution and trial parameters that if violated can jeopardize trial execution or data validity. Patient recruitment may be difficult. Subcontractors supervise and execute research, biometric and pharmacovigilance, which are complex tasks. Clinical investigational centers need sufficient capacity and the candidate drug needs to be manufactured in compliance with current Good Manufacturing Practices (cGMP) and be available to administer. Finally, the data itself needs to achieve statistical significance to justify regulatory approval.

Allarity's proprietary DRP platform seeks to identify cancer patients most likely to favorably respond to a drug. By identifying a transcriptomic signature that predicts patient response, Allarity has developed a mechanism to increase the likelihood of therapy success in clinical trials. We believe that a platform such as DRP can improve the likelihood of a successful trial and is a critical component of successful future trials for the industry. Despite all successful retrospective work that has been done, real world outcomes may differ. Furthermore, patient populations with the desired characteristics may be difficult to identify and enroll in future clinical trials.

Regulatory

Regulatory risk centers on clinical trial requirements, marketing approval of the candidate, expedited pathways and associated oversight. Regulations extend to post-marketing surveillance and pricing dynamics. Furthermore, biotechnology firms typically have a presence globally and must navigate the regulatory approval process, clinical trial requirements and marketing regulations in the jurisdiction where they seek to commercialize. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Companies that have a long history of research success in drug development, with opinion leaders and experts advocating for the product in the field will have an advantage. Previous success with the FDA or other regulatory agencies is another attractive attribute for a sponsor.

Some accelerated pathways to approval are available such as those outlined in the Orphan Drug Act and the Breakthrough Therapy designation; however, changes in sentiment or perceived safety could change the regulatory environment to demand a more thorough process and these pathways may be extended or additional requirements may be put in place. Depending on the regulatory environment, government mandates can influence marketing dynamics as well. The US has experienced legislative disruption recently with the Patient Protection and Affordable Care Act (PPACA) of 2010, amended by the Health Care and Education Reconciliation Act that imposes nondeductible excise tax on pharmaceutical manufacturers or importers that sell branded prescription drugs to government programs. Under the PPACA, some firms are required to provide a discount on branded prescription drugs. The PPACA increases the level of Medicaid rebates payable by manufacturers of brand-name drugs and requires collection of rebates for drugs paid by Medicaid managed care organizations.

[40] Summarized from Clinical Development Success Rates 2011-2020. Compiled by Zacks Analysts.

Personnel

Biotechnology startups rely on the expertise and leadership of management to make decisions and investments on their behalf. Competition for talented and experienced management is intense and matching the optimal skill set with the right company is difficult. Change in management can be disruptive if leaders or scientists are lured away by other firms. Both the former CEO and CFO of Allarity recently resigned following the FDA's refusal to file letter issued for dovitinib. Additionally, early-stage biotech companies are often virtual and have a small team. This can put them at a disadvantage when compared to larger firms, with full-time specialized personnel. A smaller company with much of the upside tied to stock price may deter certain talent from joining the firm.

Intellectual Property

Despite the existence of patents and trade secrets, the loss of intellectual property is a risk. DRP is protected by a series of global patents for methods of predicting drug responsiveness for a number of compounds and indications. While this can limit competing in the specific settings identified in the patents, technology can be worked around and approaches can be copied if they demonstrate success, raising the risk that the platform could be imitated or replicated, especially by a larger firm with more resources. While this does not affect Allarity's current portfolio of products, it may affect the pursuit of future candidates. Despite numerous patents relating to the DRP technology, Allarity must still maintain its licenses for the drug candidates it is developing.

Market Risk

Successful marketing of approved drug candidates relies on adoption by patients and providers. An approved drug must have convincing clinical trial data and maintain a favorable reputation amongst prescribers. Marketing is expensive and requires an experienced sales force and a presence in the marketing area. Marketed products remain under surveillance and any unexpected adverse effects may lead to regulatory authorities revoking marketing authorization. Inclusion of the drug in insurance plan offerings is also important. Rapidly obtaining a preferred position on health plan and payor formularies is critical to achieving target penetration rates. If health plans and payors cannot agree on appropriate pricing for the drug and the compound fails to offer a significant benefit above standard of care, sales may be limited.

Geopolitical

Trade tensions between the US and China threaten the world economy, and have been exacerbated by the recent pandemic. There has been a cross-pollination of capital and drug development between China and the United States which may slow as a result of the trade and political dispute between the countries. This conflict may reduce the availability of capital, partnerships and future development deals between companies in the two nations. The UK withdrew from the European Union on January 31, 2020. Previously, a drug approved under the centralized procedure in the European Union would be approved in all member states. However, with the withdrawal of the UK additional efforts and expense may be required to obtain marketing approval in this top five European market. Conflict between Ukraine and Russia has led to disruptions in clinical trials in these countries. Sanctions have also been placed on Russia and many of its businesses which may lead to shortages of certain products. Refugees fleeing the war in Ukraine may also impact nearby countries and their productivity. R-Pharm provides Ixempra drug product to Allarity. While R-Pharm U.S.'s parent company is headquartered in Russia, Allarity's agreement and drug supply are with the US subsidiary and we do not expect any direct disruption due to the parent's ties.

Peers and Competitors

Allarity participates in a number of medicinal spheres including oncology and precision medicine. It is also competing against other TKIs, PARPis and microtubule inhibitors in the ovarian, breast and kidney cancer spaces. Allarity's distinguishing characteristic is its DRP platform which employs a precision medicine approach to match medicines with responding patients.

One of the most closely related companies to Allarity is Kura Oncology, a precision medicine, small molecule-focused company targeting solid tumors and blood cancers. The company's pipeline is targeting the HRAS mutant proto-oncogene among other mutations in its trials. Bioxcel Therapeutics is another similar peer using AI to evaluate candidates in the neuroscience and immuno-oncology spaces to more efficiently run clinical trials. The company has several candidates in development including BXCL701, a dipeptidyl peptidase inhibitor, for prostate and other solid tumors. Gritstone Bio, an immunotherapy-oriented oncology company targeting KRAS and microsatellite stable solid tumors including colorectal cancer is another relevant comparator. The firm uses its Gritstone EDGE AI platform to identify antigens that appear on cancer cells and are visible to T cells. Lantern Pharma is a neighbor to Allarity with a portfolio of previously investigated assets using AI-assisted methods to target specific populations. Lantern's lead active candidate is LP-300, a chemo-enhancing and chemo-protecting agent being investigated in never-smoker NSCLC. Small-molecule Syros is developing a portfolio of candidates using its gene control platform which identifies disease-causing alterations in gene expression and create medicines that control the expression of genes. The primary asset is an RARα agonist tamibarotene targeting multiple oncology indications along with secondary candidates SY-2101 and SY-5609.

Other peers and competitors include the large pharmaceuticals and biotechnology companies Abbvie, Novartis, Merck and Roche with dominant and broad oncology portfolios. Others offer assets in the TKI space such as Kronos Bio, Turning Point and Bayer. Clovis Oncology and Abbvie have PARPi offerings while only Eisai markets an approved microtubule inhibitor, Halaven to compete against Ixempra.

Exhibit XII – Public Companies[41]

Ticker	Company	Price	MktCap (MM)	EV (MM)	Therapeutic Area
ABBV	Pharmacyclics	$142.24	$251,494	$302,535	Bruton's tyrosine kinase inhibitor (ibrutinib) for cancer
BAYRY	Bayer	$13.72	$53,915	$85,700	Regorafenib (TKI) for mCRC
CLVS	Clovis Oncology	$1.50	$217	$744	Rucaparib (PARPi) in ovarian, prostate & other
KTRA	Kintara Tx	$0.16	$11	$14	Developing VAL083 for GBM
ETX.L	e-Therapeutics	£19.23	£98.90	£73.00	Analyze complex networks of molecular interactions in cells.
TAK	Takeda	$13.72	$42,542	$70,692	Iclusig (kinase inhibitor) for Ph+ CML or ALL
LTRN	Lantern Pharma	$5.31	$58	($5)	Rescuing failed drugs using AI to identify responsive populations
ABBV	AbbVie	$142.24	$251,494	$302,535	PARPi (veliparib) for BRCA BC + other oncology drugs
ESALY	Eisai	$41.90	$12,015	$10,453	Halaven, Lenvima
AZN	AstraZeneca	$61.75	$191,353	$212,818	Broad portfolio of products including Enhertu
AMGN	Amgen	$237.62	$127,110	$155,632	Wide range of modalities, cancers & molecules in oncology
TPTX	Turning Point Tx	Acquired by	BMY		Pipeline of TKIs: repotrectinib (NSCLC)/BMY buying
BMY	Bristol-Myers Squibb	$72.36	$154,507	$178,386	IO,CAR-T,CBI,TYK2i (deucravacitinib),
GILD	Gilead Sciences	$68.01	$85,242	$105,762	Trodelvy for BC, CAR T, kinase inhibit + dev portfolio
BTAI	BioXcel Tx.	$14.50	$406	$234	Repurpose existing drugs using AI
GRTS	Gritstone Bio	$3.86	$281	$127	Targeted immunotherapies for cancer & infectious disease
SYRS	Syros Pharma	$0.73	$46	($6)	Genomically defined cancers using small molecules
KURA	Kura Oncology	$15.00	$1,003	$553	Precision & targeted oncology using small molecules
GSK	GlaxoSmithKline	$32.45	$65,993	$81,243	IO, cell therapy, epigenetics, synthetic lethality; large dev portfolio
LLY	Eli Lilly	$315.22	$299,514	$311,469	Verzenio for BC + portfolio of other oncology medicines
NVS	Novartis	$83.60	$184,973	$187,447	Oncology assets + Kisqali, Piqray for BC
MRK	Merck & Co.	$88.16	$223,334	$241,890	Keytruda + broad portfolio of other oncology
PFE	Pfizer	$47.76	$268,046	$269,036	Ibrance + others in development for BC & oncology portfolio
RHHBY	Roche	$42.19	$288,124	$291,455	Broad oncology portfolio for liquid & solid tumors
ALLR	Allarity Tx	$1.16	$11.28	$4.67	DRP for RCC (dovitinib), ovarian (stenoparib) & mBC (Ixempra)

[41] Price as of September 12, 2022

Management Profiles

James G. Cullem, J.D., Chief Executive Officer

Mr. Cullem has held his role since June 2022. He is an experienced biotechnology executive and previously served as Allarity's Chief Business Officer and Senior Vice President, Corporate Development from August 2014 to June 2022. From 2017 to 2020, Mr. Cullem was the co-founder and a board member of 2X-Oncology, Inc. (later Oncology Venture US, Inc.), its first U.S. subsidiary. From July 2014 to September 2018, he was also the Vice President of Corporate Development of the Medical Prognosis Institute, a predecessor diagnostics affiliate of the company. He brings more than 20 years of diverse experience in life sciences organizational management, business development & licensing, intellectual property & technology transfer/commercialization, partnership creation/management, and strategic planning as a member of executive teams. During his tenure, Mr. Cullem has been responsible for the identification and acquisition of most of our lead clinical oncology assets, including dovitinib (from Novartis) and stenoparib (from Eisai). He leads the company's business development discussions as well as clinical program out-licensing and partnership negotiations, both in the U.S. and worldwide. Mr. Cullem has experience in designing and negotiating a broad span of life science deals, has founded and led several early-stage biotech companies, and is a catalyst for businesses taking the next step in the fields of precision medicine and predictive/companion diagnostics, novel drug targets, proteomics and genomics, and clinical-stage cancer therapeutic development. He holds a B.S. degree in Biochemistry from The University of California at Davis, a Juris Doctorate (JD) degree from The University of New Hampshire Franklin Pierce School of Law, specializing in patent & I.P. law, and is a registered patent attorney before the United States Patent & Trademark Office.

Steen Knudsen, Ph.D., Chief Scientific Officer

Dr. Knudsen has held his role as Chief Science Officer since 2006. He is a co-founder of Allarity's predecessor and the inventor of DRP®, the Drug Response Prediction Platform, which is Allarity's core technology and companion diagnostics platform. Dr. Knudsen was a Professor of Systems Biology with extensive expertise in mathematics, bioinformatics, biotechnology, and systems biology. He co-founded the company's predecessor in 2004 and served as its CEO from 2004 to 2006. Dr. Knudsen also previously served as a member on Oncology Venture's Board of Directors from 2016 to 2020. Additionally, Dr. Knudsen serves as the Chief Executive Officer of MPI, Inc., Allarity's operating subsidiary in the U.S. Dr. Knudsen holds an M.Sc. degree in Engineering from the Technical University of Denmark and a Ph.D. degree in Microbiology from the University of Copenhagen. He received Postdoctoral training in computational biology from Harvard Medical School.

Marie Foegh, M.D., Chief Medical Officer

Dr. Foegh has been Chief Medical Officer since January 2018. She previously served as Chief Medical Officer of the Allarity subsidiary, 2XOncology, Inc. (later Oncology Venture US, Inc.) from 2016 to 2018. Dr. Foegh brings thirty years of experience in the pharmaceutical and biotechnology industries to the senior management team and has a strong track record leading successful clinical development of therapeutics, including regulatory and medical affairs. She is Adjunct Clinical Professor at Georgetown University, Department of Medicine and Adjunct Professor at New York Medical College, Department of Pharmacology. Dr. Foegh was the Chief Medical Officer and co-founder of Ell Imaging, LLC, an ultrasound device company, from 2014 to 2016. She serves as the Chair of the Board of Directors at the device company, Injecto A/S, since 2014. She leads clinical development of Allarity's current precision medicine oncology pipeline, including lead assets stenoparib, dovitinib, and Ixempra. Dr. Foegh previously led the successful development and regulatory approval of more than 10 novel drug products in the U.S. and U.K., within oncology, endocrinology and cardiology. Dr. Foegh has fluency in regulatory interactions with the FDA and EMEA, including INDs, NDAs, IDEs (for predictive biomarkers and/or companion diagnostics), and product issues. She also manages interactions with the oncology key opinion leaders including Allarity's Scientific Advisory Board. Dr. Foegh holds both a Medical Doctorate (M.D.) degree and a Doctorate of Science (Dr.Sc.) degree from Copenhagen University, Denmark, and is a member of the American College of Physicians (ACP), American Medical Association (AMA), the American Society of Clinical Oncology, and the American College of Obstetricians and Gynecologists (ACOG).

Operational Milestones

Recent Milestones

Allarity weathered many events over the last few years, submitting its first PMA, raising additional capital and converting from a stock listed on the Stockholm exchange to one listed on the US NASDAQ stock market. The company ran into a rough patch following the receipt of the Refusal to File letter from the FDA for its dovitinib monotherapy program and now has promulgated a new combination strategy that reflects the direction most oncology therapies are heading. Allarity's lead program will advance stenoparib and dovitinib in combination against mOC. The Ixempra monotherapy program in breast cancer and stenoparib monotherapy program in mOC will continue unchanged. Below we list key milestones.

- Submission of PMA application to FDA for dovitinib DRP diagnostic – April 2021
- Acceptance and review for PMA application by FDA for dovitinib DRP – July 2021
- Manufacture dovitinib for clinical development by Lonza – September 2021
- Corporate listing on NASDAQ – December 2021
- NDA submission of dovitinib in 3rd line RCC – December 2021
- Agreement with OncoHeroes for pediatric development of dovitinib and stenoparib – January 2022
- Issuance of Refusal to File Letter by FDA for dovitinib – February 2022
- Type C meeting for dovitinib NDA & PMA submission – April 2022
- James G. Cullem named CEO – June 2022
- Strategy shifted toward combination therapies – August 2022
- Delay in filing third quarter Form 10-Q – August 2022

On December 21st, 2021, Allarity completed the closing of its recapitalization share exchange and was listed on the NASDAQ under the ticker symbol ALLR. Approximately 8.1 million shares were listed. In concert with the listing, Allarity closed a $20 million private investment in public equity (PIPE) that issued 20,000 shares of preferred stock at $1,000 per share. The PIPE instrument also included a common stock purchase warrant for 2.0 million shares. The investor taking the 20% ownership interest in the company is 3i, LP, a €23 billion assets under management private equity and infrastructure investment company. Shortly after the recapitalization, Allarity submitted its NDA for dovitinib for third line treatment of renal cell carcinoma (RCC) to the FDA. The submission was the companion to the July 2021 pre-market authorization (PMA) submission that was made on behalf of the DRP diagnostic.

Despite an optimistic pre-NDA meeting with the FDA, in mid-February, Allarity received a Refusal to File (RtF) letter from the FDA.[42] According to the company, the reasons for the RtF were insufficient clinical trial data which did not allow for a conclusion of efficacy based on the non-inferiority data set. The RtF was applicable to both the PMA and the NDA. After seeking additional guidance from the agency, the company's response to the letter noted that an additional clinical trial and resubmission of the PMA and NDA would be required to overcome the FDA's objections.

Due to the additional burden of another trial, Allarity's board elected to pursue a combination strategy using DRP for stenoparib and dovitinib. The pair of PARPi and TKI assets would pursue an indication in metastatic ovarian cancer with first studies expected to begin in the next few quarters.

Allarity shared positive news regarding the relationship with Oncoheroes Biosciences, a biotech focused on the discovery and development of better drugs for children and adolescents with cancer. The arrangement will include use of both dovitinib and stenoparib in childhood cancers and will employ the DRP companion diagnostic. Oncoheroes will have global, exclusive rights to the two candidates for pediatric cancer indications. Allarity will provide access to the DRP diagnostic for use in clinical trials. The arrangement will include an upfront payment, regulatory milestones and royalties as detailed in company filings.

The company also added to its scientific advisory board (SAB) with the appointment of Roberto Pili, M.D. Dr. Pili is an oncologist and associate dean for cancer research and integrative oncology and professor at the Jacobs School

[42] A refusal to file letter notifies a drug company that FDA will not review a marketing application because of significant deficiencies that cannot promptly be resolved, making the application substantially incomplete.

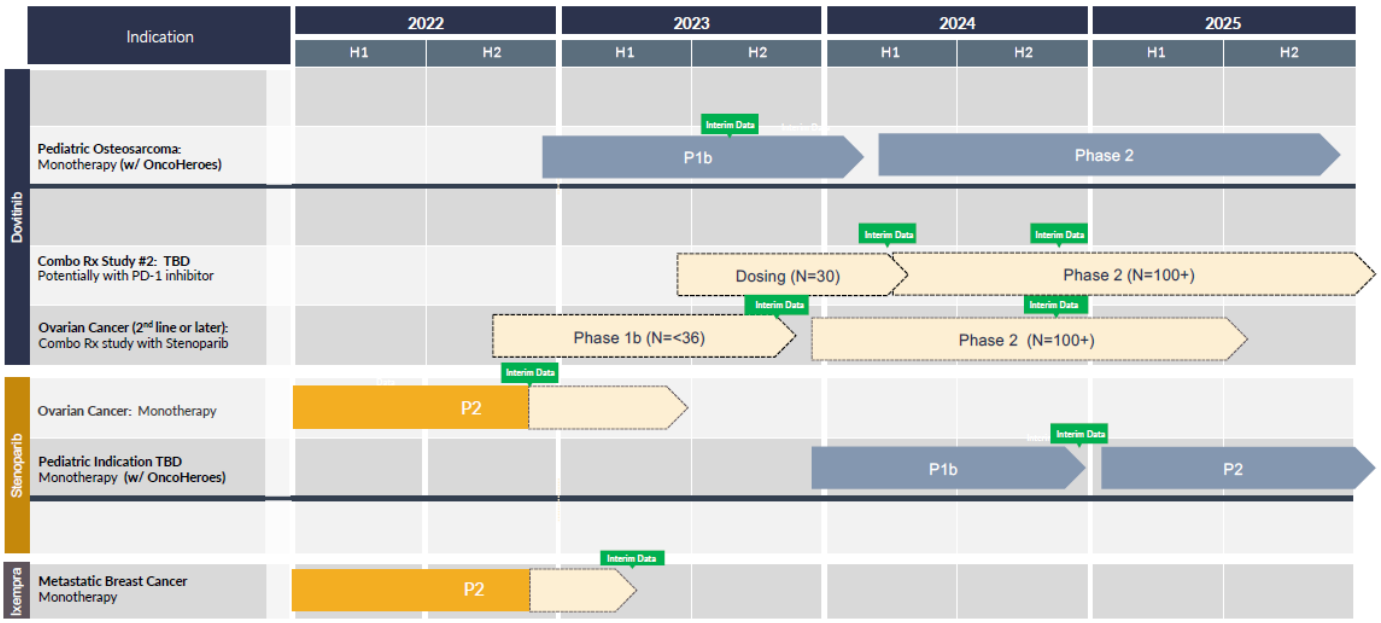
of Medicine and Biomedical Sciences, University at Buffalo, New York. He will join the other four members of the SAB detailed in the June 15th press release.

Following the appointment of James G. Cullem as CEO, additions to the board of directors were made including Mr. Cullem, company co-founder and SVP of IR Thomas Jensen and clinical researcher and oncology drug developer, David A. Roth M.D. Dr. Roth is expected to bring deep experience and expertise in the development and commercialization of oncology therapeutics and regulatory strategy to Allarity. Dr. Duncan Moore, Ph.D. will continue to serve as the Board's Chairman and as Chair of the Audit Committee. Ms. Gail Maderis will continue to serve as Chair of the Board's Compensation Committee while Mr. Søren Gade Jensen will continue to serve as Chair of the Board's Nominating & Governance Committee.

Upcoming Milestones

- Begin Phase Ib combination trial in mOC, stenoparib & dovitinib – 4Q:22
- Interim data for ovarian cancer monotherapy trial, stenoparib – 4Q:22
- Interim data Phase II mBC trial, Ixempra – 2Q:23
- Potential combination study, dovitinib with PD-1 inhibitor – 2023
- Phase Ib combination trial in mOC readout – 2H:23

Exhibit XIII – Milestones for Allarity Programs[43]



[43] Allarity Investor Presentation August 2022

Valuation

Allarity Therapeutics is an oncology research and development company that uses precision medicine to identify patient populations that will respond to selected therapeutics. The company has three primary assets in its pipeline with the lead program a combination approach for metastatic ovarian cancer (mOC). The mOC program comprises the majority of the company's value with another component of value coming from the metastatic breast cancer (mBC) program with Ixempra.

mOC is one of the more difficult cancers with low survival due to the low early detection rate. Many patients who fail standard of care move on to later lines therapy creating demand that Allarity expects to satisfy with its combination approach. First line mOC therapy is commonly carboplatin and paclitaxel following surgery. Anti-angiogenesis treatments are also offered. In patients who progress and who express the BRCA mutation, additional therapies are needed, providing an opening for the stenoparib/dovitinib combination.

We anticipate that the stenoparib and dovitinib programs will advance in tandem in pursuit of an indication in mOC. A Phase II trial is expected to run in 2024 and 2025 followed by a Phase III trial in 2026 and 2027. In 2028 a new drug application is expected for both with approval granted in time for a 2029 launch of stenoparib and dovitinib in the United States. We see areas outside the U.S. begin to be commercialized in 2030. Our model forecasts that stenoparib, with its superior characteristics relative to other PARPi will command a net price of $150,000 in 2029 for a course of treatment and will see annual inflation of 3%. Net pricing for dovitinib is expected to be approximately $100,000 in 2029 with annual price increases of 3%. On average, the international price for a course of treatment using stenoparib and dovitinib will be at 40% of the U.S. price.

There are approximately 79,000 cases of ovarian cancer in the U.S. and 212,000 in the rest of the developed world in 2022. We anticipate a 1% annual increase in this population per year. Metastatic OC comprises about 80% of this group. Initial penetration into each of the addressable markets of mOC is expected to be 3% in the initial year rising to 20% by year five.

Allarity owes milestone and royalty payments to patent holders of the underlying assets. Royalties range from 5% to 15% for both stenoparib and dovitinib and we assume a 15% rate overall to capture both the milestones and royalty amounts over the course of our forecast. This value is subtracted from the royalty of 30% we expect Allarity to receive from a third party who will be selected to ultimately commercialize the product. This yields a net 15% royalty to Allarity.

Allarity has licensed Ixempra for treating metastatic breast cancer in Europe. We estimate approximately 355,000 cases of breast cancer per year in the target geography of which 59% are assumed to be metastatic. We further expect that about half of this population will be appropriate for DRP screening. This leaves an addressable market of 104,000 in 2022 that we forecast to grow with population growth trends of 0.6%. Ixempra is now the subject of a Phase II study which we expect will be followed by a pivotal trial in 2024 generating an NDA by 2027 and approval and first sales in 2028.

While cancer of the breast is one of the most prevalent cancers, there are also many therapies to address it, suggesting a competitive environment for Ixempra. For Europe, we forecast an initial 1% penetration into the addressable market rising to a terminal penetration rate of 3% by year four. Milestones are a maximum of $12.5 million and royalties range from a high single digit to a low double-digit rate. We assume that Allarity will find a partner to commercialize the product and will receive a 30% royalty, which will be netted against the 9% royalty owed to R-Pharm, producing a net royalty of 21%.

Our model expects Allarity to sell commercialization rights to a partner with a sales force already in place. Gross royalties paid to Allarity are expected to be 30% of sales. This amount is reduced by the estimated amount of the milestones and royalties owed to the license holders of each of the products in development. We use a single royalty rate to reflect the value of both the milestones and the royalty for simplicity.

Probability of success (PoS) is an important component of our valuation model and a number of factors drive the variable. Some of the elements that we consider include whether or not a candidate is first in class, results of previous studies and their phase, side effect profile, the benefit of the DRP companion diagnostic and other components. Based on our assessment of dovitinib, which has completed a Phase III study in RCC and is soon to be in a Phase II study for mOC, we apply a 45% PoS to its success. Stenoparib, which has only completed Phase I work but belongs to a class where others have been approved, is assigned a 20% PoS. Ixempra has been approved in

the U.S., but was initially rejected in the E.U. We see the DRP diagnostic as providing a sufficient benefit to raise the PoS to 60%. Weighting each of these by the NPV of the associated programs generates an overall PoS of 35.5%.

We use a DCF model to value Allarity's cash flows employing a 15% discount rate and a weighted 35.5% probability of ultimate commercialization for the portfolio of assets. Cash taxes are estimated at 26%, which consists of 21% federal and 5% state and local which will be recognized when net operating losses are exhausted. We assume outstanding options and warrants below our target price will be exercised, and add resulting cash to the balance sheet. Allarity holds 17,018 shares of Series A Convertible stock as of June 30, 2022 which are convertible to common equity at a variable price. We estimate that this equates to approximately 9.3 million shares and add this to shares outstanding. Capital raises will be required in the near future to support anticipated clinical trials. We estimate that nine million shares will be issued this year at $1 per share to raise $9 million in funds and that 30 million shares will be issued in 2023 at $1 per share to raise $30 million which will support the ongoing costs of running Phase II and Phase III trials for stenoparib, dovitinib and Ixempra. This approach also fully addresses the impact of dilution expected at current share price levels.

The result of our forecasts and estimates generates a valuation and present value of Allarity Therapeutics of $5.00 per share.

Conclusion

Allarity Therapeutics is building on the foundation of precision medicine using its proprietary Drug Response Predictor platform with monotherapy and combination approaches. It offers three primary assets pursuing mOC and mBC in Phase II trials. The company has global aspirations with programs targeting the U.S., Europe and rest of world.

Allarity's portfolio consists of stenoparib, dovitinib and Ixempra. Stenoparib is a novel inhibitor of the DNA damage repair enzyme PARP with additional activity against tankyrases. Dovitinib is a second generation pan-TKI with the ability to inhibit numerous classes of tumor-driving tyrosine kinases. Ixempra, which the company is developing exclusively in Europe, is a U.S.-approved microtubule inhibitor which can interfere with cancer cell division. Stenoparib and dovitinib are in combination therapy for metastatic ovarian cancer while Ixempra is pursuing monotherapy approval in metastatic breast cancer. Stenoparib is also being investigated in a monotherapy setting for mOC.

mOC is one of the more difficult cancers given that it is usually detected in its later stages and there are few effective treatments for it. Most patients move on to second and later lines of treatment creating an unmet need that new combination therapies may address. mBC is a very common cancer, and while there are numerous treatments for the disease, there remains an unmet need for patients that advance through standard of care.

Allarity's differentiating characteristic is its use of the proprietary and patented DRP platform to identify patients that will respond to oncology therapies based on their gene expression profile. It addresses one of the primary shortcomings of existing therapies which assume all patients will respond similarly. In taking a holistic approach to the genetic profile of patients, DRP recognizes the influence of multiple genomic factors to determine a patient's affinity for a specific therapy. Allarity is integrating DRP with combination therapy in its lead program, recognizing the heterogeneous nature of tumors which proliferate using multiple mechanisms. Successfully attacking these diverse tumors requires a multi-pronged effort that can be accomplished with the stenoparib and dovitinib combination.

Allarity raised approximately $34 million late last year through a variety of financial transactions and a move to the NASDAQ. These funds will fund operations in 2022; however, additional capital will be needed to continue the advance of the company's pipeline into 2023. With a portfolio of Phase II assets, our model assumes a 35.5% chance of commercial success, with the probability of success enhanced by the benefits of the DRP platform, the follow-on nature of the assets and the numerous supportive trials that have already been conducted. Drug development is expensive, requires years of clinical development and suffers from a low success rate. By leveraging the benefits of DRP, Allarity may be able to improve trial outcomes, reverse some of the pressures on the industry and bring new treatments to market.

Key reasons to own Allarity Therapeutics shares. Allarity

- **Offers proprietary DRP platform to identify responders/non-responders**
  - **Increases efficiency of drug development**
  - **DRP companion diagnostics can extend patent coverage for off-patent drugs**
  - **Enables more efficient and rapid trials**
  - **Reduces failure risk**
- **Offers best in class PARPi features with lead candidate stenoparib**
  - **Tankyrase inhibitor activity for potential dual tumor killing MoA**
  - **Blood brain barrier penetration**
  - **Absence of myelotoxicity**
- **Uses combination therapy to address cancer's multiple survival pathways**
- **Provides salvage opportunity for failed drugs with validated safety and efficacy**
- **Pursues attractive indications with material unmet need**
  - **Metastatic ovarian cancer (mOC)**
  - **Metastatic breast cancer (mBC)**

Based on our analysis of Allarity's portfolio of stenoparib, dovitinib and Ixempra, we see a pathway forward for development and commercialization in the US, EU and rest of world following the raise of sufficient capital. We initiate on Allarity Therapeutics with a valuation of $5.00 per share.

PROJECTED FINANCIALS

Allarity Therapeutics, Inc. - Income Statement

Allarity Therapeutics, Inc.	2021 A	Q1 A	Q2 A	Q3 E	Q4 E	2022 E	2023 E	2024 E
Total Revenues ($US)	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Research & Development	$14,196	$1,289	$1,402	$1,100	$950	$4,741	$15,000	$18,000
General & Administrative	$12,360	$3,013	$2,927	$2,320	$2,205	$10,465	$13,200	$14,000
Other Operating Costs	$0	$14,007	$0	$0	$0	$14,007	$0	$0
Income from operations	($26,556)	($18,309)	($4,329)	($3,420)	($3,155)	($29,213)	($28,200)	($32,000)
Net Interest Expense	$499	$39	$28	$27	$21	$115	$200	$200
Other Income	($540)	($14,041)	$296	$0	$0	($13,745)	$0	$0
Pre-Tax Income	($26,515)	($4,307)	($4,653)	($3,447)	($3,176)	($15,583)	($28,400)	($32,200)
Provision for Income Tax	($133)	$1,227	($4)	$0	$0	$1,223	$0	$0
Tax Rate	*0.5%*	*-28.5%*	*0.1%*	*0.0%*	*0.0%*	*-7.8%*	*0.0%*	*0.0%*
Net Income	**($26,648)**	**($3,080)**	**($4,657)**	**($3,447)**	**($3,176)**	**($14,360)**	**($28,400)**	**($32,200)**
Reported EPS	**($4.19)**	**($0.37)**	**($0.52)**	**($0.26)**	**($0.19)**	**($1.06)**	**($1.42)**	**($0.56)**
Basic Shares Outstanding	6,359	8,288	9,017	13,250	17,000	13,500	20,000	57,000

Source: Company Filing // Zacks Investment Research, Inc. Estimates

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HISTORICAL STOCK PRICE

Allarity Therapeutics, Inc. – Share Price Chart[44]



[44] Source: Zacks Research System

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