

Oncology Pulse

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Flight to Safety or Breakthrough? Resurgence of ADCs and Radiopharmaceuticals

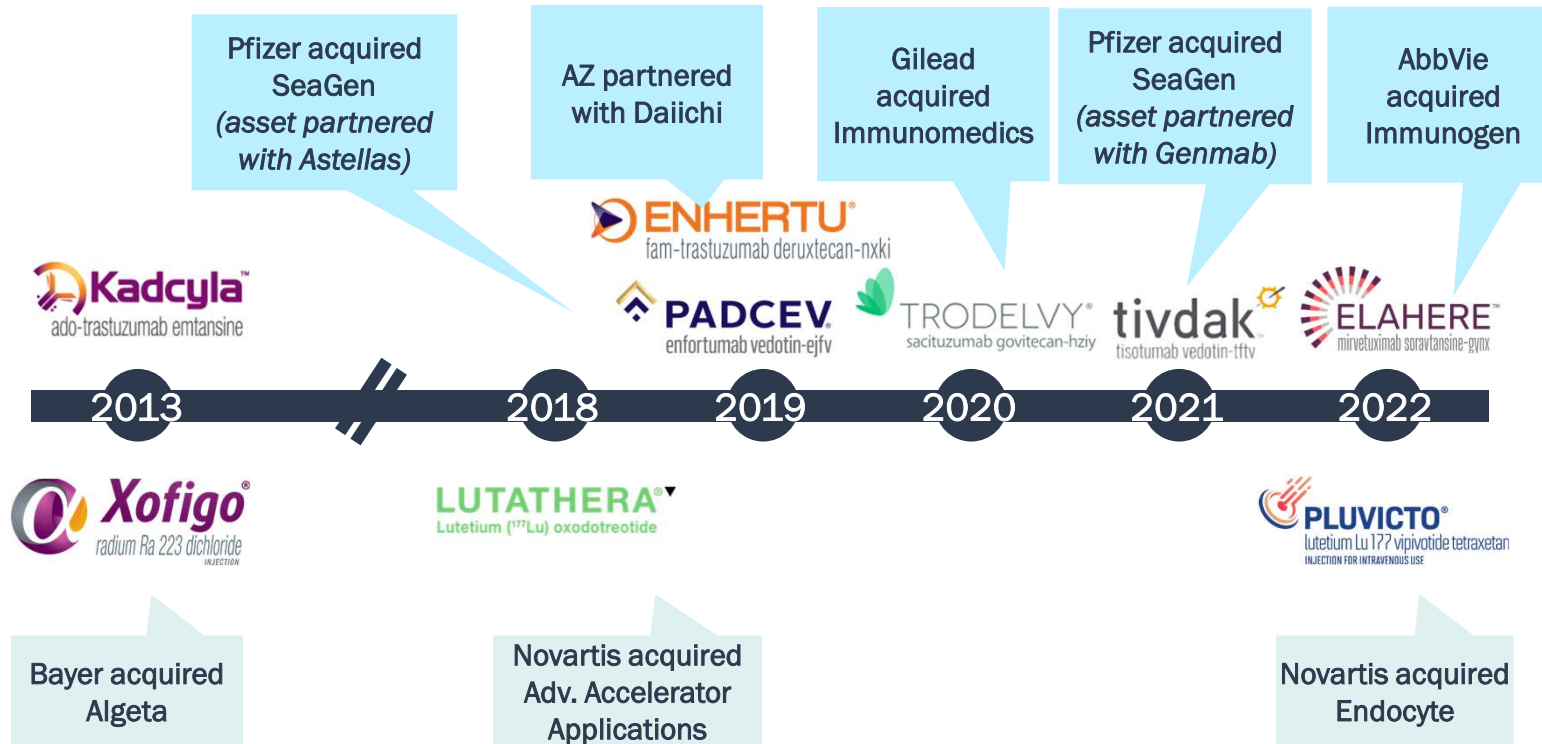
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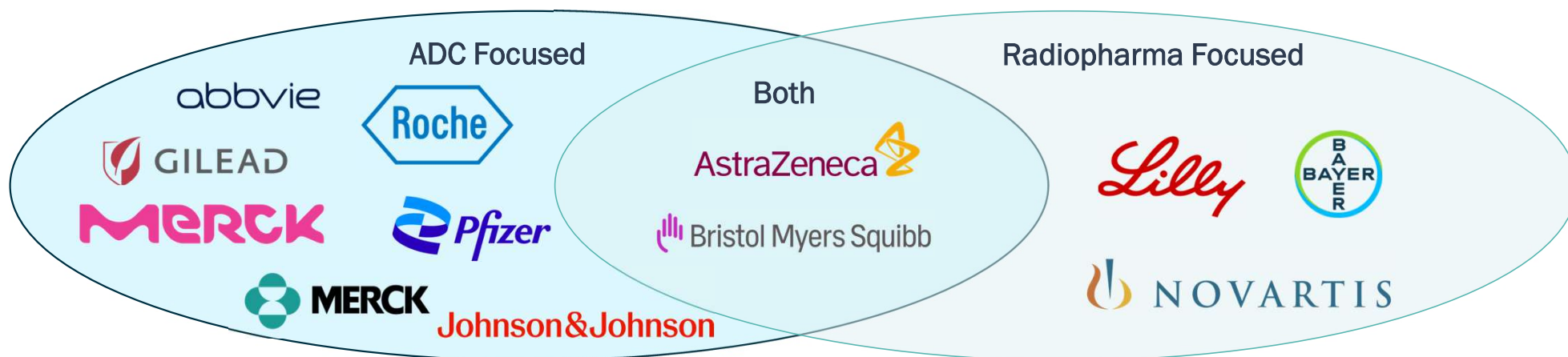
ADCs and radiopharmaceuticals have re-emerged as treatment modalities of high interest; most approved products have been tied up by big pharma

Initial FDA Approval of ADCs and Radiopharmaceuticals in Solid Tumors



Most major oncology companies have invested in ADCs, with AZ and BMS the only ones with major investments in both ADCs and radiopharma

Focus Areas for Top Pharma Companies (Solid Tumors)



Notable Transactions

ADCs

- Pfizer acquired SeaGen
- Merck and AbbVie executed major transactions to get access to on-market/late stage programs

Both





- BMS invested in derisked target ADCs (FOLR1, EGFRxHER3) and acquired RayzeBio
- AZ continues expansion of Enhertu with Daiichi, acquiring Fusion with PhII PSMA alpha emitter

Radiopharma

- Novartis doubles down on radiopharma with announced Mariana Oncology acquisition

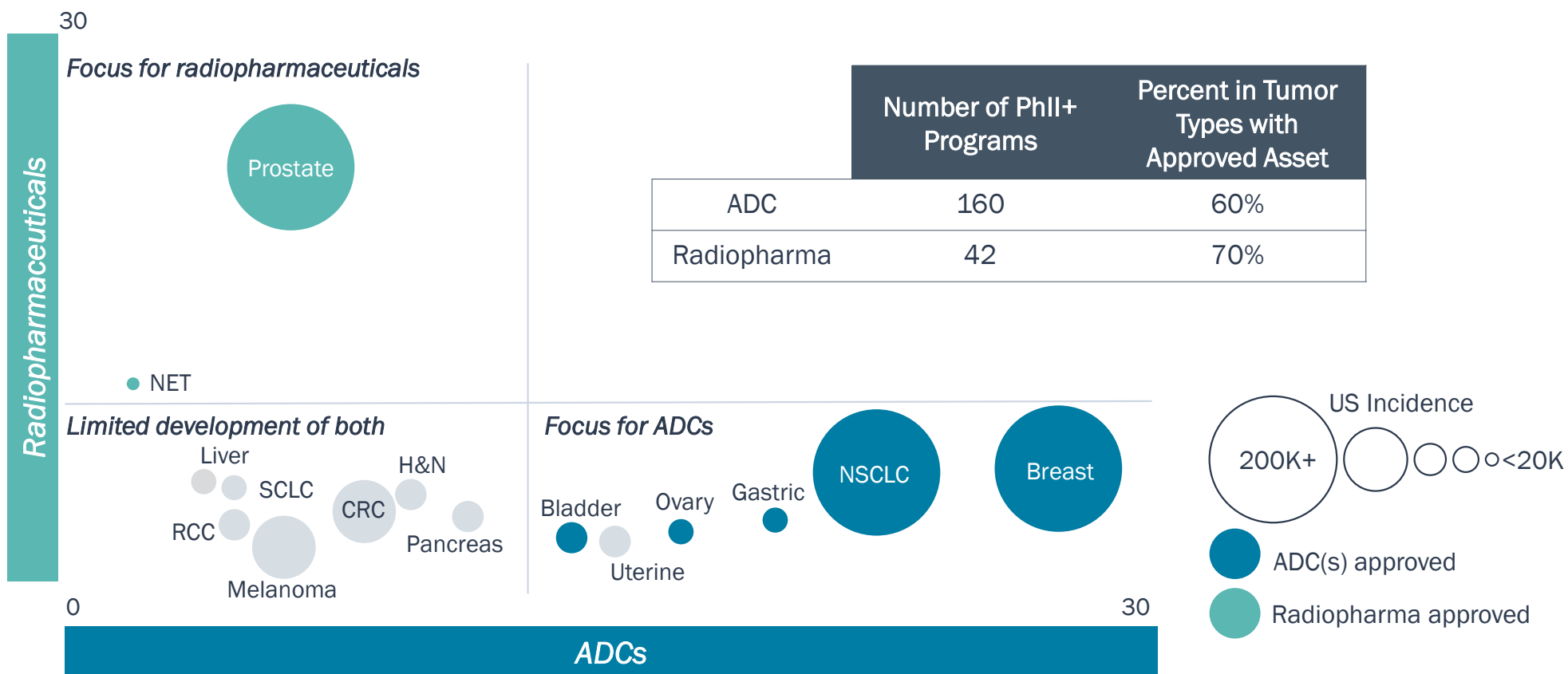
Both modalities have demonstrated efficacy improvement but come with novel toxicity, administration, and manufacturing considerations

Comparison of Drug Modalities: ADCs and Radiopharmaceuticals

Antibody Drug Conjugates	Radiopharmaceuticals
<p><u>Enhertu in HER2+ breast and Padcev + pembro offer transformational efficacy</u>, though most boost ORR with only incremental durability benefit</p>	<p>Efficacy</p>  <p><u>OS benefit shown</u> in neuroendocrine tumors and prostate cancer</p>
<p>Unique toxicities include <u>interstitial lung disease (ILD)</u> and <u>ocular toxicities</u> in more recently approved agents</p>	<p>Safety</p>  <p><u>Precautions needed around radiation exposure</u> to minimize radiation exposure to others post treatment; also contributes to patient's overall cumulative radiation exposure and increased risk for cancer</p>
<p><u>Treatment until progression</u>: regimens designed to be given continuously, similar to many late line chemo regimens</p>	<p>Dosing/Admin</p>  <p><u>Fixed treatment</u>: Dosed every ~4-8 weeks for up to a fixed number of ~4-6 cycles depending on drug; <u>administration only at specialized centers</u></p>
<p><u>Expertise in antibody, linker and payload required</u>, but more typical pharma model for manufacturing and transport</p>	<p>Manufacturing</p>  <p><u>Significant supply chain considerations</u> – from isotope sourcing to manufacturing to transport and product half-life</p>

Radiopharmaceuticals and ADCs approvals are currently for distinct solid tumors and the majority of new programs are targeting the same tumor types

Number of ADCs and Radiopharmaceuticals in Development for Highest Incidence Solid Tumors



A number of ASCO 2024 abstracts will provide insight into the potential of new ADCs as well as Padcev's 1L UC regimen; new radiopharma data will be limited

ASCO 2024 Abstract Titles in ADCs and Radiopharmaceuticals



Under the hood of Padcev 1L UC regimen: Abstracts on QoL and outcomes by exposure to provide valuable insight into likely real-world treatment duration



HER2 continues to be a popular ADC target for investigation: Exploration of ADCs with brain-met activity, sequencing with other ADCs, and combining with other MOAs



New ADC targets aim to take center stage: Novel targets highlighted include cMET, B7H3, SEZ-6, CDH3, and TA-MUC1



Evidence in new tumor types: Focus remains in currently approved tumor types, but CRC and non-muscle invasive bladder cancer specific studies to be highlighted



Radiopharmaceutical related abstracts limited compared to ADCs or other modalities such as cell therapy: Further emphasizes the immaturity of this new radiopharma wave



Limited data related to new tumor types or novel therapies: Primarily focused on analysis of prostate cancer patient characteristics for currently approved treatments

#ASCO24



ERIN OLSEN
Managing Director



MICHELLE WHANG
Principal



ELIA FARAH, PhD
Managing Consultant

We'll be at ASCO!

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521 Fifth Avenue, 25th floor
New York, NY 10175

Office: 212-257-6030

<https://www.bluestarbioadvisors.com>
