Biology needs in-situ genomics – the spatial context drives disease

Toward molecular diagnostics, drug discovery and improved clinical trials

PRESENTED BY:
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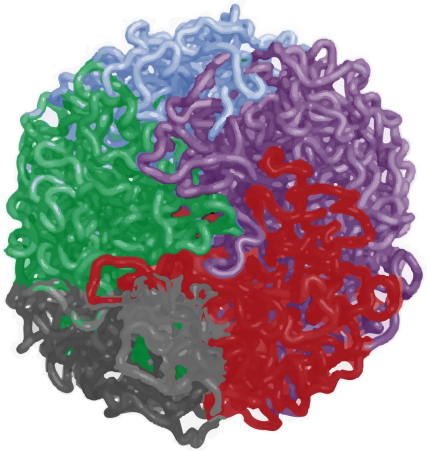
PRESENTED TO:

ARIMA GENOMICS

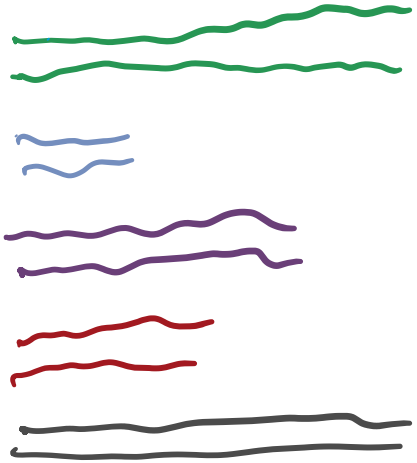
Genome is NOT flat – it is folded spatially in its native in-situ context

Arima unlocks the power of in-situ DNA by enabling read, phenotype (linking to RNA) & edit access

Reality: The native spatially folded in-situ DNA



What you actually get: Flat-genomes with no spatial context



In-situ spatial context is vital and non-substitutable genomic insight

Changes to spatial context of in-situ DNA predicts disease & is druggable (targeted / precision therapy)

Translocation Dx for undiagnosed tumors

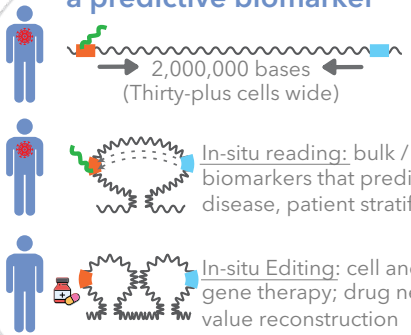
NYU Langone Health

X RNA Fusion Panel
X DNA-Panel
X CNV profiling
X DNA methylation

None of these tests could diagnose tumor in this 3-yr child

Arima's test identified PD-L1 translocation, driving Glioblastoma. Now Treatable!

In-situ DNA Folding is a predictive biomarker



Data from Arima customer; Nature Genetics 2020

Molecular Pathology labs and Biopharma **need the spatial context**

We lead translational research use-cases of in-situ spatial DNA analyses

We are a high-margin and high-repeat reagent business, serving end-to-end chemistry and informatics

Stats as of 06/2021

- **33** translational customer publications; 99 overall
- **300** active customers, including a blanket $1M PO
- **18** biopharma as active / repeat customers
- **87%** revenue CAGR (2021 forecast: $3.5M)
- **85%** consumable and 72% blended margin

Stats as of 06/2021

Series A investors

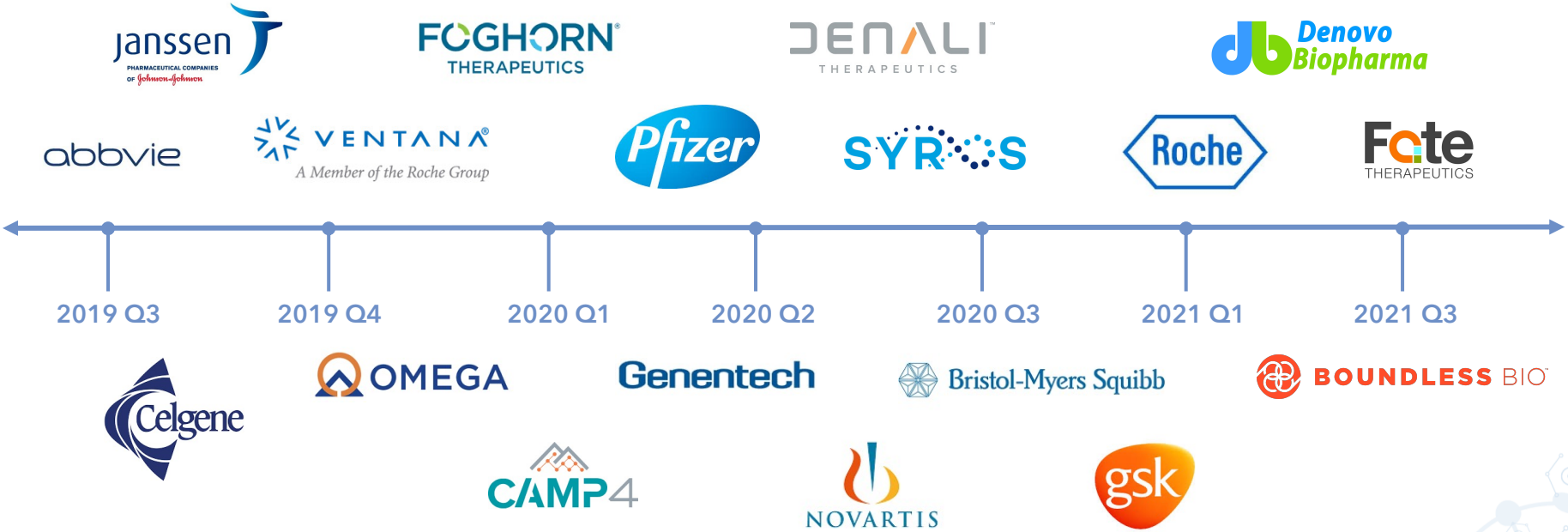
Agilent Technologies · Berkeley Catalyst Fund · 凯风创投 COWIN VENTURE · VECTR

ARIMA GENOMICS

Series B Deck

We lead translational research use-cases of in-situ spatial DNA analyses

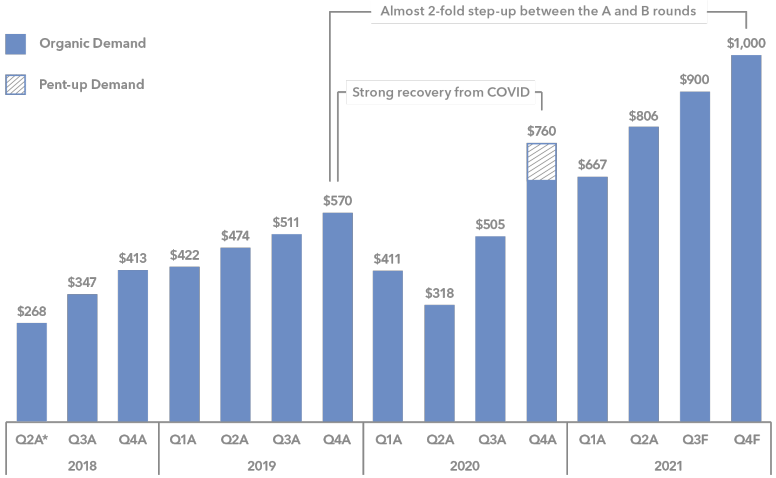
Biopharma is rapidly adopting Arima with 14 of them having reordered; Next: Patient stratification, trials



We lead translational research use-cases of in-situ spatial DNA analyses

Strong revenue momentum, repeatability and COVID recovery – showing our products are must-haves

Revenue (thousands, USD)



* Commercial launch in late Q1. Q2 revenue includes revenue from Q1

$4.0M
Q4-based Ann. RR

85%
Kit Margin

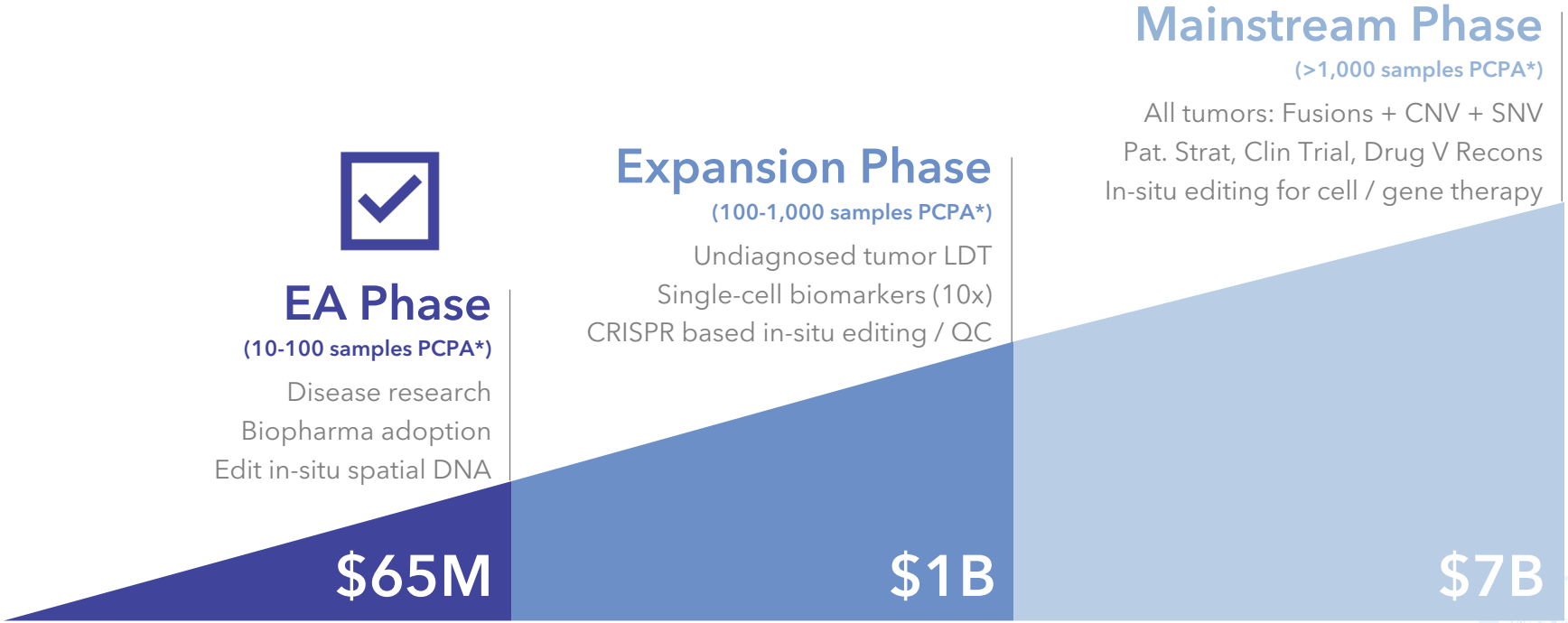
72%
Blended Margin

Repeat customers buy more and faster

Expanding into Dx (LDTs) and single-cell biomarkers, as areas of growth & impact (Series B efforts)

Already driving the NYU LDT for undiagnosed tumors (4-6M samples)

Customers already paying for plate-based single-cell folding kits; Next:10x-based folding + RNA

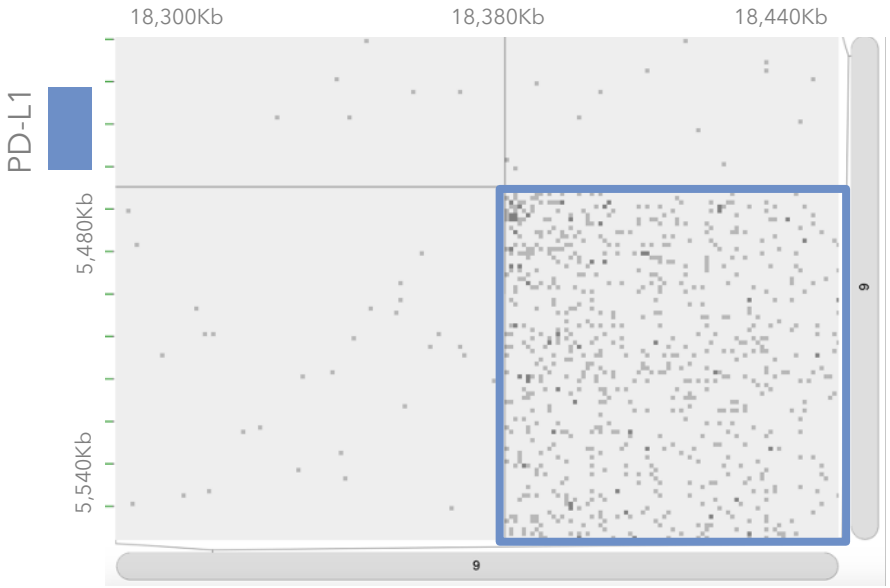


Source: DeciBio, Dr. Snuderl (NYU)
*PCPA: per customer per annum

Early Evidence (N=4) that we can explain diverse undiagnosed tumors

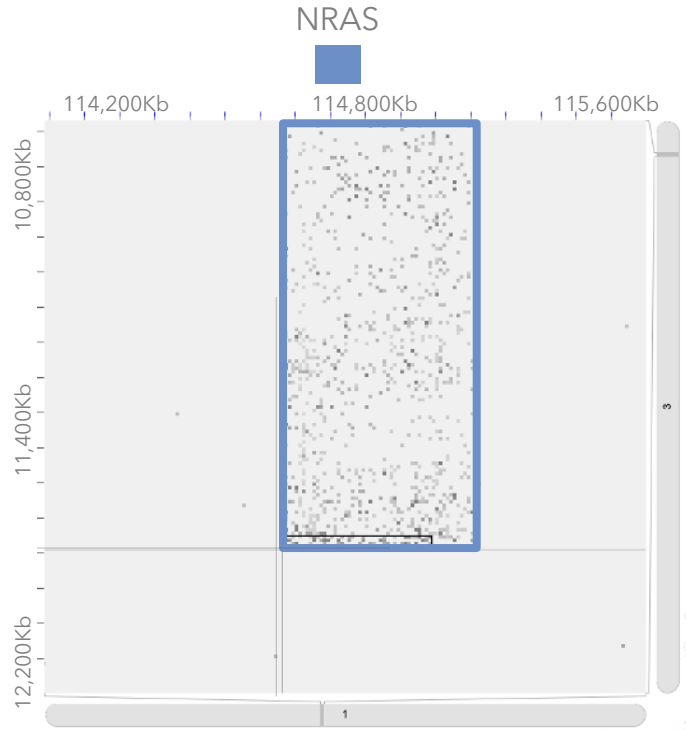
The secret of our approach is that it is NOT looking for breakpoints; Next: Increase 'N' from 4 to 50

Glioblastoma (FFPE prospective / living sample)



Breakpoint appears to be ~4kb from 3' end of PDL1

Chordoma (FFPE retrospective sample)



Breakpoint appears to be ~50kb from 3' end of NRAS

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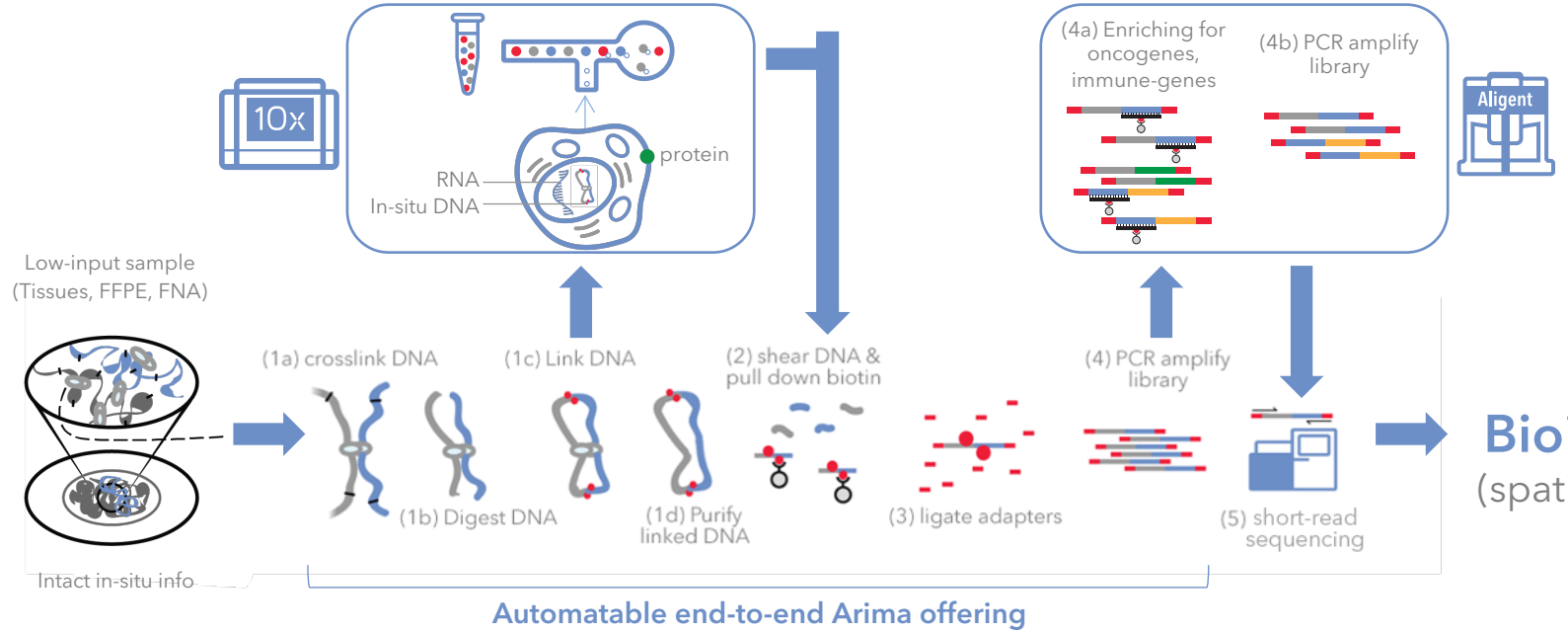
Arima reads in situ spatial context in bulk and single-cell, via NGS

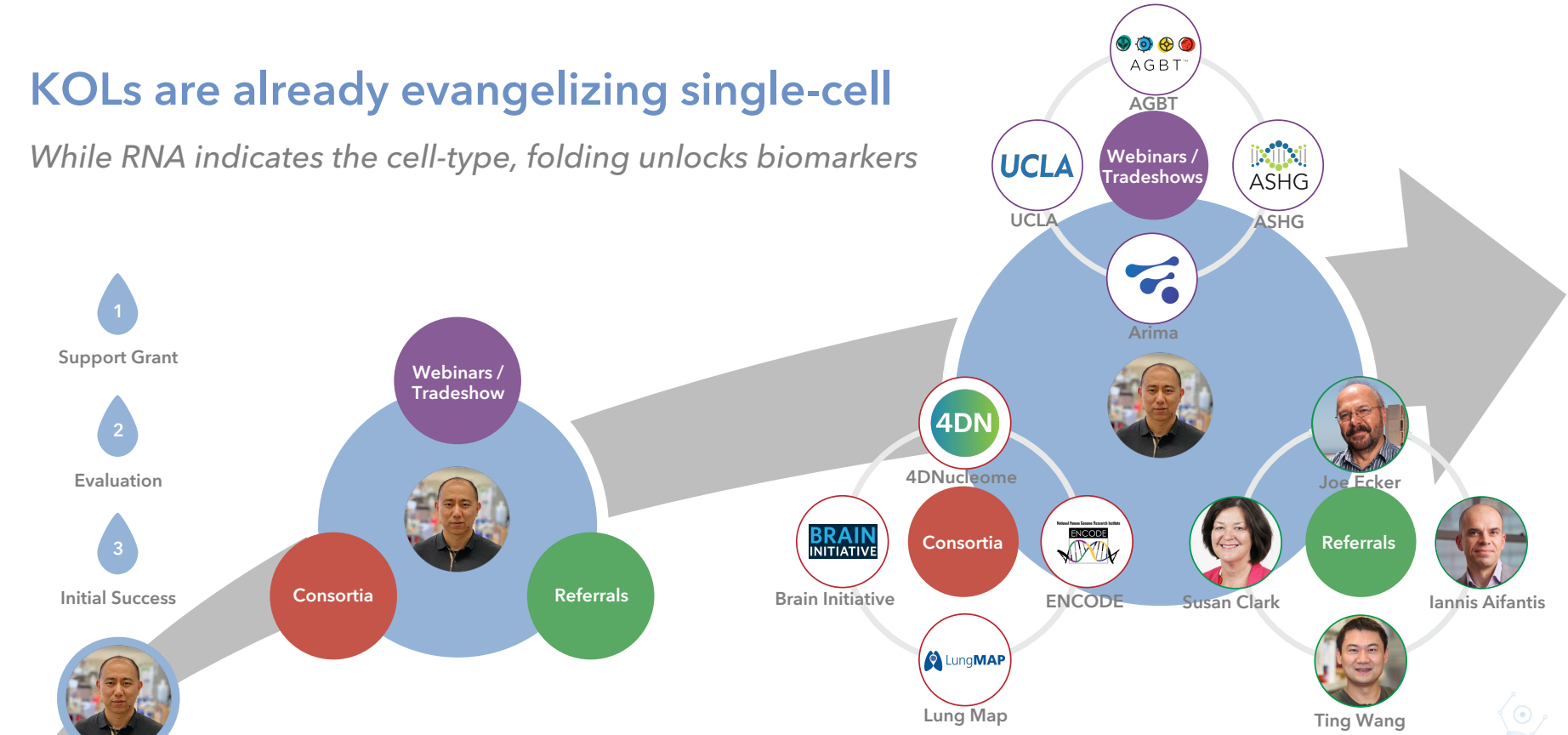
Arima links the in-situ spatial changes in DNA with RNA (or Protein) on 10X for biomarker discovery



Arima Bioinformatics
(spatial + sequence)

KOLs are already evangelizing single-cell

While RNA indicates the cell-type, folding unlocks biomarkers



Targeting $10M Series B fund to lay the path to $100M revenue

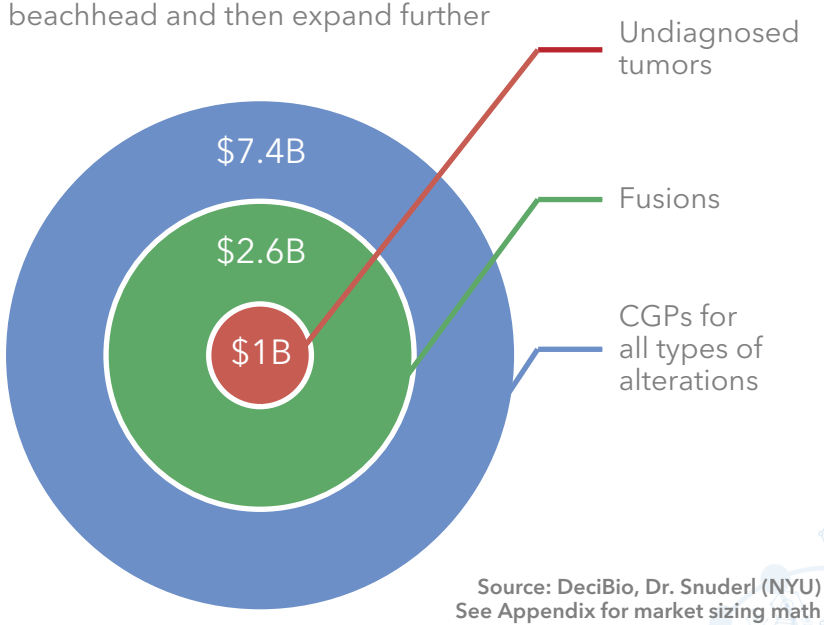
Series A investors have committed $5M; Targeting $5M from lead / syndicate (close by Nov)

2-year plan: Lay the path toward $100M revenue.

Use of the Series B Proceeds:

- ✓ Validate LDT with NYU and approach FMI /Tempus
- ✓ Launch into single-cell (in-situ DNA + RNA) on 10X
- ✓ Initial proof of concept for fusions
- ✓ Expand global commercial organization
- ✓ Scale supply chain and manufacturing
- ✓ Move to a larger space to support growing team needs

Strategy: Focus on the undiagnosed tumor beachhead and then expand further



Source: DeciBio, Dr. Snuderl (NYU)
See Appendix for market sizing math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NT (Neighborhood Translocation) storyline

Histology-agnostic diagnoses of undiagnosed solid / liquid tumors

Goal: The preferred translocation assay (fusions + neighborhood) in tissue samples for LDT and Dx

- 20-30% tumors are undiagnosed. Evidence suggests (n=4) they might have translocations in the oncogene's neighborhood, which controls the oncogene drives tumor. We define neighborhood translocations (NT), where the breakpoint is in the neighborhood of an oncogene and does NOT cause oncogenic fusion. Neighborhood can be as large as 100Kb. Because RNA fusion panels do not detect NTs and because transcriptome is unreliable in FFPE samples, these tumors are mismanaged, leading to acute conditions and death. ***Arima sees as an opportunity here.***

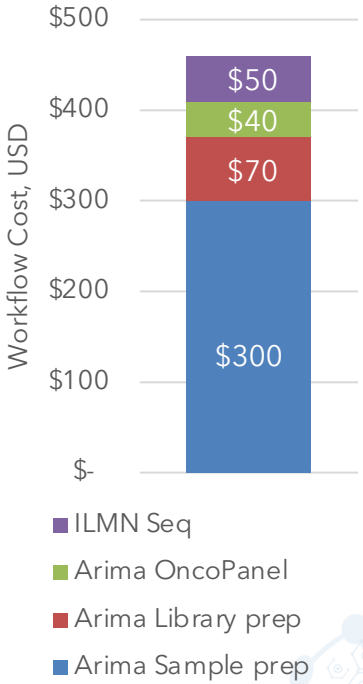
- Regardless of the histology, the Arima assay detects NTs (use-case A) in undiagnosed solid and liquid tumors. It also detects genic translocations (fusions, use-case B) agnostic of the fusion partner, even in >5-year FFPE samples and low-grade tumors, where RNA fusion panels are unreliable. Importantly, Arima assay is DNA based and therefore is reimbursable as a standalone (unlike RNA that needs to be coupled with DNA / Protein expression for reimbursement). Therefore, Arima assay is the sole test for NTs in undiagnosed tumors and reliable / reimbursable compared to RNA fusion panels for fusions.

- The Arima assay is 100%-sensitive (n=24) and 100%-specific (n=100+). Our secret for high performance is that we are NOT looking for the breakpoint (but dramatic changes in *in-situ* DNA). We quantified our method using fusions because only they were detectable by orthogonal methods (i.e., no prior data for NTs). ***Sensitivity and Specificity data available on request.***

Histology-agnostic diagnoses of undiagnosed solid / liquid tumors

Large market opportunity, affordable <$500 workflow cost, protected IP and an LDT headstart at NYU

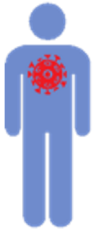
- The entire Arima workflow is <$500 (assuming $10 per Million ILMN reads). The price for Arima prep is $410 at $60 COGS, resulting in 85% margin.
- We are focused on LDT as the opportunity. Use-case A: NTs is $1B (2.4M[1] undiagnosed samples x $400 ASP); Use-case B: Fusions is $1.6B (4M[1,2] samples x $400 ASP). Eventually, we will target point-mutations and CNVs (Use-case C). Use-Cases C = $4.8B (12M[1,3] samples x $400 ASP). Total Market (A + B + C) = $7.4B; Market sizing is based on 20M annual cancer incidence worldwide. ***For market sizing math, see references.***
- Arima is initiating an LDT with NYU Langone (Matija Snuderl) for use-case A first (use-cases B and C could be next). As preliminary data, 4 tumors were analyzed – in all 4, we found NTs implicating oncogenes that is suspected to drive the tumor (see next slides).
- We have 2 PCT Arima-owned patent applications that include translocations in claims.



NTs (Use-case A) implicate diverse oncogenes / diverse tumors

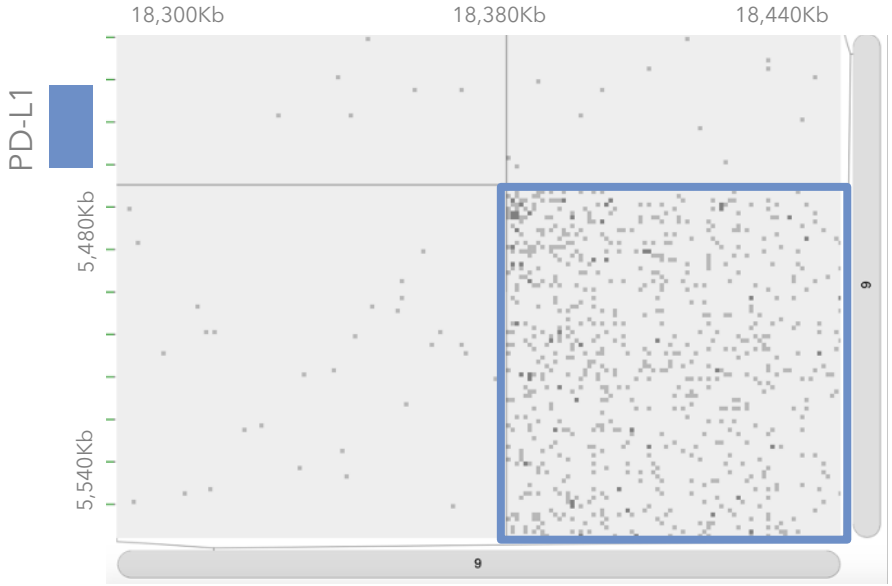
Tumor 1: Glioblastoma with an NT implicating PD-L1 oncogene (and PAX5, not shown)

NYU Langone Health



X RNA Fusion Panel
X DNA-Panel
X CNV profiling
X DNA methylation

3yr old with glioblastoma and no known driver mutations



Breakpoint appears to be ~4kb from 3′ end of PDL1

NTs explaining Undiagnosed tumors

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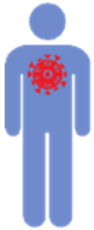
Our PD-L1 finding from FFPE sample was validated by IHC. NYU's prognosis is to give the child anti-PDL1 drug. Without Arima, this child would likely not have a clinical course of action.

NTs (Use-case A) implicate diverse oncogenes / diverse tumors

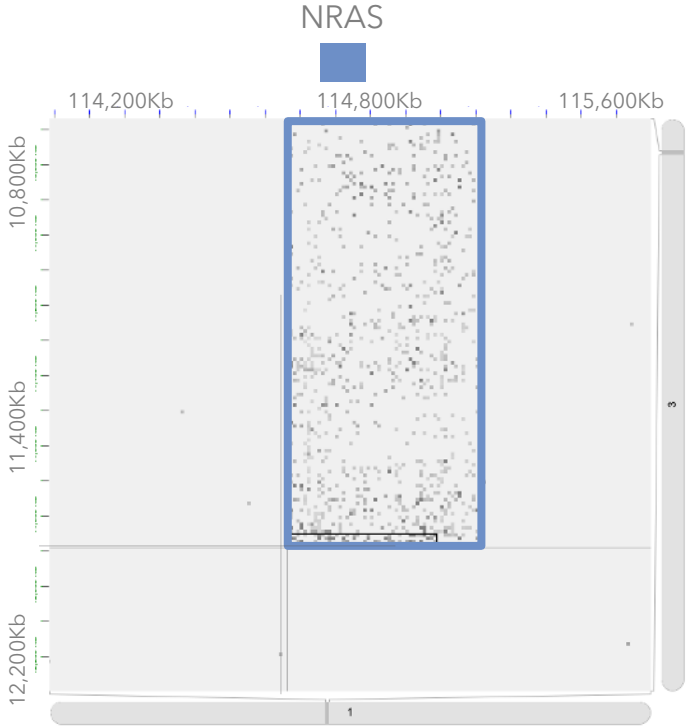
Tumor 2: Chordoma with an NT implicating NRAS oncogene (and EPHA3, not shown)

NYU Langone Health



X DNA-Panel
X CNV profiling
X DNA methylation

RNA Fusion Panel was not done because Chordoma's are not known to be driven by fusion



Breakpoint appears to be ~50kb from 3' end of NRAS

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NTs explaining Undiagnosed tumors

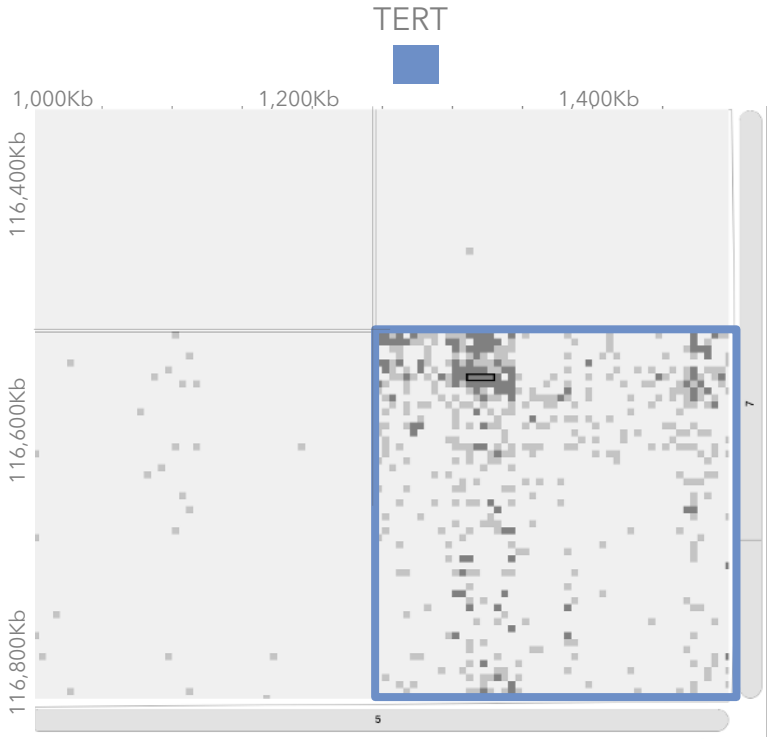
NTs (Use-case A) implicate diverse oncogenes / diverse tumors

Tumor 3: Chordoma with an NT implicating TERT oncogene

NYU Langone Health

X DNA-Panel
X CNV profiling
X DNA methylation

RNA Fusion Panel was not done because Chordoma's are not known to be driven by fusion



Breakpoint appears to be ~5kb from 3' end of TERT

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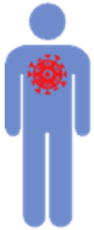
NTs (Use-case A) implicate diverse oncogenes / diverse tumors

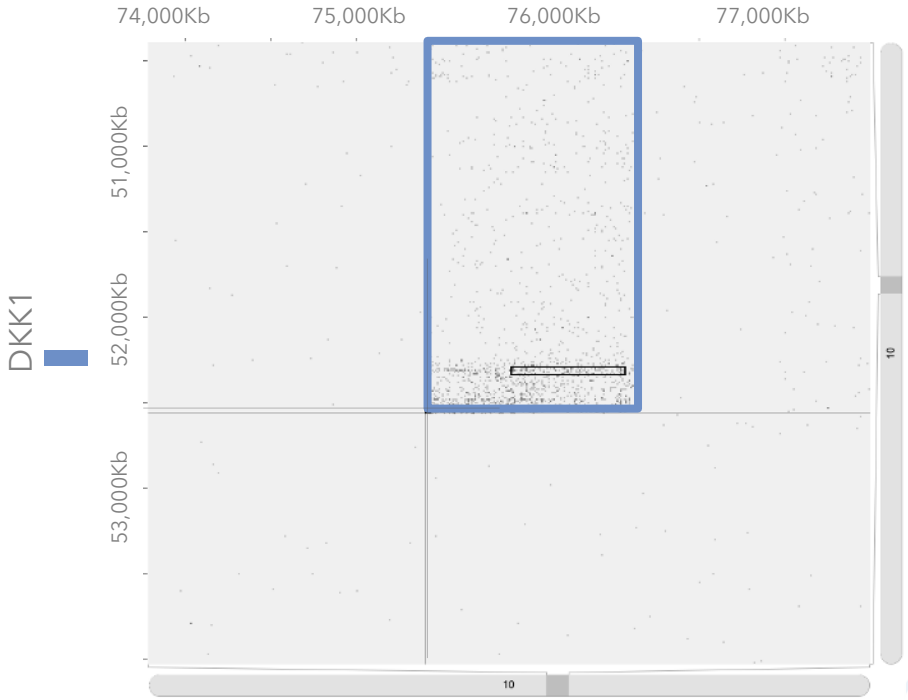
Tumor 4: Chordoma with an NT implicating DKK1 oncogene

NYU Langone Health



X DNA-Panel
X CNV profiling
X DNA methylation

RNA Fusion Panel was not done because Chordoma's are not known to be driven by fusion



Breakpoint appears to be ~245kb from 3' end of DKK1

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NTs explaining Undiagnosed tumors

Sole and non-substitutable for NTs and reliable than RNA for fusions

NTs / Undiagnosed tumors is a large $1B opportunity that addresses diverse oncogenes and tumors

- Arima is proposing to serve three clinical use-cases: A: NTs for undiagnosed tumors; B: fusions; C: SNVs/CNVs. The three segments together have a market size of $7B+. The target customer is molecular pathology labs (LDT model).
- Arima's strategy is to create a wedge into molecular pathology labs using use-case A (NTs for undiagnosed tumors). The market size for NTs is somewhere between $0.3B to $1.6B (worst-case to best-case, reference 1). We took a mid-point of $1B. The proof-of-concept data on 4 samples suggest that NTs are implicated in tumors not known to be driven by fusions (e.g., Chordoma), indicating that we are trending toward the best-case, although we need more samples tested to be definitive. Indeed, we are receiving a library of new samples to be tested (beyond the initial 4).
- Arima's proof-of-concept for NTs is based on 4 samples (1 Glioblastoma and 3 Chordomas). The Glioblastoma analyses occurred in late-July – where Arima's PD-L1 finding has created a clinical course of action. The Chordoma analyses occurred in mid-August and our findings (NRAS, TERT, DKK1) of diverse oncogenes explaining diverse tumors has encouraged Dr. Snuderl. The Chordomas are retrospective samples while the Glioblastoma is prospective.
- Analyses of these 4 samples suggests that NTs implicate diverse oncogenes and drive diverse tumors (regardless of the histology). Because of this diversity and because existing methods such as RNA fusion panels cannot detect NTs, Arima is the sole solution provider and NOT substitutable. We are processing 50 additional samples from Dr. Snuderl in Sept.

References

1. Matija Snuderl, NYU Langone.

   Relevant Information: *The best estimate (based on his experience) is that point mutations and CNVs drive 60% of tumors, fusions account for 20%, and the remaining 20% are undiagnosed. As per current knowledge, these undiagnosed tumors represent diverse tumor types, and it is unclear whether NTs could explain all of them. Worst case, NTs explain 4% (assuming NTs behave like fusions and so it would explain 20% of the 20% undiagnosed); Best case, NTs explain all the 20% undiagnosed. For market sizing, we assumed mid-point of 12% (2.4M samples, $1B size). As we increase the sample size, the market sizing gets more accurate.*

2. Zehir et al. Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients. Nat Med 2017 Jun;23(6):703-713. doi: 10.1038/nm.4333. Epub 2017 May 8.

   Relevant Information (Use-Case B): *15% of all metastatic cancers' present fusions.*

3. Max Jorgensen, DeciBio.

   Relevant Information (Use-Case C): *60% of cancer samples / tests target point-mutations and CNVs.*


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