



Catalyzing Precision Medicine with Integrated Rx/Dx in Oncology

January 2014



Forward Looking Statements

This document contains forward-looking statements, as that term is defined in Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, about Ignyta, Inc. (the “Company”). Statements that are not purely historical are forward-looking statements. These include statements regarding, among other things: our novel technologies and methods; our ability to leverage our technology platform in the development of RXDX-101, RXDX-102 and other potential product candidates; our ability to design and conduct development activities and preclinical and clinical studies and trials for our potential product candidates; the potential results of any preclinical or clinical studies or trials we may conduct; and our ability to obtain regulatory approvals in order to market any of our product candidates.

Forward looking statements involve known and unknown risks that relate to future events or the Company’s future financial performance, some of which may be beyond the Company’s control, and the actual results could differ materially from those discussed in this document. Accordingly, the Company cautions investors not to place undue reliance on the forward-looking statements contained in, or made in connection with, this document.

Such risks include, among others, the Company’s ability to initiate and complete clinical trials, the potential advantages of the Company’s product candidates and the Company’s capital needs. The identification and development of the Company’s product candidates and the projected commencement and completion of the Company’s clinical trials may be affected by difficulties or delays. In addition, the Company’s results may be affected by its ability to manage its financial resources, difficulties or delays in developing manufacturing processes for its product candidates, preclinical and toxicology testing and regulatory developments. Delays in clinical programs, whether caused by competitive developments, adverse events, patient enrollment rates, regulatory issues or other factors, could adversely affect the Company’s financial position and prospects. Prior clinical trial program designs and results are not necessarily predictive of future clinical trial designs or results. If the Company’s product candidates do not meet safety or efficacy endpoints in clinical evaluations, they will not receive regulatory approval and the Company will not be able to market them. The Company may not be able to enter into any strategic licensing or partnership agreements or secure product candidates from third parties when needed or desired. Operating expense and cash flow projections involve a high degree of uncertainty, including variances in future spending rates due to changes in corporate priorities, the timing and outcomes of clinical trials, competitive developments and the impact on expenditures and available capital from licensing and strategic collaboration opportunities. If the Company is unable to raise additional capital when required or on acceptable terms, it may have to significantly delay, scale back or discontinue one or more of its drug development or discovery research programs. The Company is at an early stage of development and may not ever have any products that generate significant, or any, revenue. The Company has a history of losses during its short operating history and may never be profitable.

The forward-looking statements contained in this document represent the Company’s estimates and assumptions only as of the date of this document and the Company undertakes no duty or obligation to update or revise publicly any forward-looking statements contained in this document as a result of new information, future events or changes in the Company’s expectations.

Investing in the Company involves a high degree of risk, including, among others, those described above. Investors must rely upon their own examination of the Company, including the merits and risks involved. Investors should consult all of the information, including the risk factor disclosures, set forth in the reports and other documents the Company files with the Securities and Exchange Commission, available at www.sec.gov, including without limitation the Company’s Current Report on Form 8-K/A dated December 9, 2013.

Third-party information included herein has been obtained from sources believed to be reliable, but the accuracy or completeness of such information is not guaranteed by, and should not be construed as a representation by, the Company.



Company Highlights

Precision medicine oncology company with integrated approach to Rx/Dx

- ◆ Rx programs pursuing *first-in-class* and *best-in-class* opportunities in cancer, with comprehensive biomarker strategies
 - RXDX-101: First-in-class oral Pan-Trk (i.e., TrkA, TrkB, TrkC), ROS1 and ALK inhibitor in Phase 1/2 development with multiple clinical readouts in 2014 – 2015
 - RXDX-102: Oral Pan-Trk inhibitor in preclinical development
 - Spark: Pipeline of novel, internally discovered Rx/Dx programs in discovery
- ◆ Robust target and Dx biomarker discovery platform and capabilities
 - Genomic and epigenomic analyses to discover and validate new cancer targets
 - Ability to screen and confirm molecular alterations of interest via Ignyta central lab
- ◆ Experienced management and R&D team with demonstrated “drug hunter” success in oncology
- ◆ Strong financial position with sufficient cash to fund development programs through key data points



Corporate and Financial Highlights

- ◆ San Diego based biotechnology company, incorporated in 2011
- ◆ Acquired Actogene Oncology in May 2013 to enter oncology precision medicine market
- ◆ Licensed exclusive worldwide rights to RXDX-101 and RXDX-102 from Nerviano Medical Sciences in October 2013
- ◆ Completed reverse merger in October 2013 to list on OTCQB: RXDX
- ◆ Completed two private placements for gross proceeds of \$54 million, net proceeds of ~\$51 million in November 2013
- ◆ Received \$10M capital term loan from SVB in December 2013
- ◆ S-1 submitted to SEC in December 2013
- ◆ Company has 13.9 million shares issued and outstanding



Management Team

Jonathan Lim, M.D., Chairman, CEO, and Co-Founder, Former Chair, CEO of Eclipse; Former President, CEO, Director at Halozyme; McKinsey; NIH Postdoc Fellow at Harvard; surgical resident at NYH-Cornell

Patrick O'Connor, Ph.D., CSO and SVP, Head of Research, Former VP, Head of Global Oncology Research at Pfizer; successfully discovered Xalkori (Crizotinib, Lung CA) and Inlyta (Axitinib, Kidney CA); currently on medical leave

James Freddo, M.D., Chief Medical Officer, Former CMO at Anadys; former VP, Clinical Site Head and Therapeutic Area Leader for Oncology Clinical Development at Pfizer

Zachary Hornby, CFO and VP, Corporate Development, Former Senior Director of Business Development at Fate Therapeutics; Director BD at Halozyme; L.E.K. Consulting; Harvard Business School

David Anderson, Ph.D., VP of Biology, Former CSO and Co-Founder of Proprius Pharmaceuticals; CSO at Celgene/Signal Research Division; J&J

Jean-Michel Vernier, Ph.D., VP of Medicinal Chemistry, Former VP of Discovery Chemistry at Ardea Biosciences (clinical candidates in oncology, gout, HIV); Valeant; Merck Research Laboratories

Dave Matthews, Ph.D., VP of Crystallography, Scientific founder of Agouron Pharmaceuticals; Distinguished Research Fellow, Head of Struc. Bio., Comp. Chem., and Bioinformatics at Pfizer-La Jolla

Paul Pearson, Ph.D., VP of PK, Drug Metabolism & Safety, Former Global Head and VP Pharmacokinetics and Drug Metabolism at Amgen; Exec. Director of Preclin. Drug Metab. at Merck Research Labs

David Luo, Senior Director of Clinical Operations, Former Senior Director of Elevation (acquired by Sunovion); PM at PPD

Robert Shoemaker, Ph.D., Senior Director of Biology and Informatics, Former Scientist at Illumina; Extensive bioinformatics, scientific computer programming, next generation molecular technologies experience



Ignity's Veteran Team Has a Successful Track Record in Drug Development

Inlyta[®]
(axitinib) tablets

CAPSULES
XALKORI[®]
CRIZOTINIB

 **LIPITOR**[®]
atorvastatin calcium
tablets

 **SUTENT**[®]
sunitinib maleate

 **Nplate**[®]
romiplostim

 **Vectibix**[™]
(panitumumab)

XGEVA[®]
(denosumab)

 **ISENTRESS**[®]
raltegravir tablets

 **CAMPTOSAR**[®]
irinotecan HCl injection

 **Candidas**[®] I.V.
caspofungin acetate

 **Revlimid**[®]
(lenalidomide) capsules

VIRACEPT[®]
nelfinavir mesylate


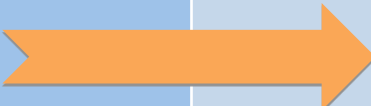



PROCRIT[®]
EPOETIN ALFA

 **Hylanex**[®]
recombinant (hyaluronidase human injection)

Collectively represent nearly \$10 billion in 2012 sales



Ignity Rx/Dx Pipeline

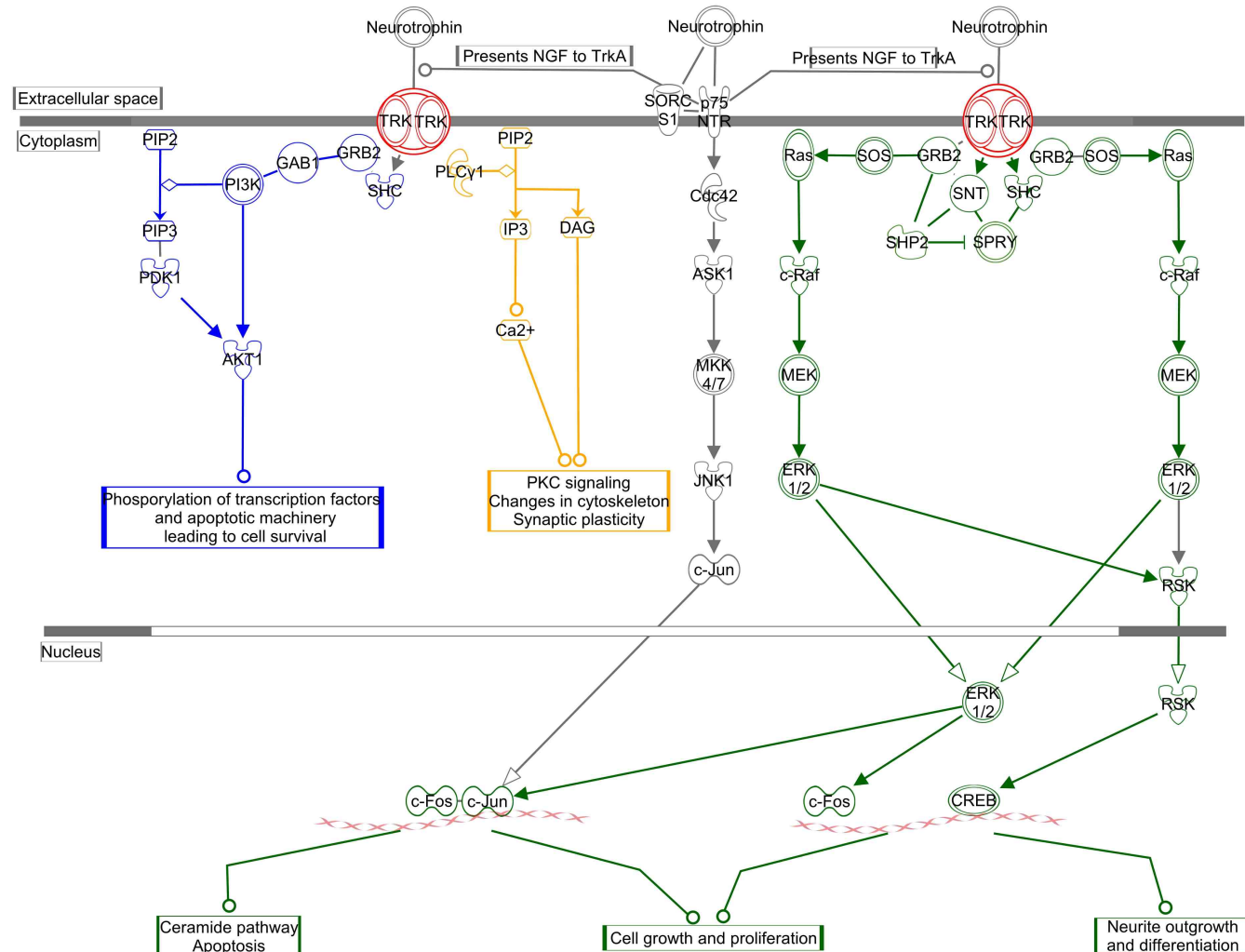
Compound	Target	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
RXDX-101*	1 st -in-Class TrkA/B/C, ROS1, ALK inhibitor					
RXDX-102*	1 st -in-Class TrkA/B/C inhibitor					
Spark-1 Rx/Dx Program						
Spark-2 Rx/Dx Program						
Spark-3 Rx/Dx Program						



TrkA Activation Drives Cell Growth and Survival

NTRK Pathway

- ◆ TrkA (red) activates PI3K/ AKT (blue), PKC (orange), and ERK1/2 (green) pathways, which promote cell growth and survival
- ◆ TrkA gene rearrangements result in ligand independent dimerization and constitutive activation¹
- ◆ TrkA overexpression, in the presence of neurotrophin NGF, is associated with metastasis and cell survival^{2,3}



© 2000-2013 Ingenuity Systems, Inc. All rights reserved.

1. Greco A, et al. Rearrangements of NTRK1 gene in papillary thyroid carcinoma. PMID: 19883730
2. Ma J, et al. Expression of nerve growth factor and tyrosine kinase receptor A and correlation with perineural invasion in pancreatic cancer. PMID: 19120874
3. Arrighi N, et al. Nerve growth factor signaling in prostate health and disease. PMID: 20166899



RXDX-101

Ignity Leveraging Team's Prior Crizotinib Experience with Next Generation Kinase Inhibitor

- ◆ RXDX-101 is in-licensed candidate from Nerviano
 - Nerviano had invested \$25MM in the program
 - Nerviano is a former Pfizer/Pharmacia R&D site with kinase expertise
 - 40 years of experience in oncology R&D
- ◆ Potent inhibitor of 5 oncogenic driver targets:

Target	TrkA	TrkB	TrkC	ROS1	ALK
IC50 (nM)	1	2	5	7	12

- ◆ Crosses the blood brain barrier, enabling targeting of CNS lesions
- ◆ In Phase 1/2 study (Ph 1 dose escalation ongoing)
- ◆ Composition of matter patent issued in the US and allowed in Europe



RXDX-101 & RXDX-102 Exclusive Worldwide License

Completed in October 2013

Deal terms compare favorably with other high profile oncology clinical-stage asset in-licenses

- ◆ \$7M upfront (paid in November 2013)
- ◆ \$55M in development and regulatory milestones for WW approval of 1st product
- ◆ \$50M in aggregate potential milestones for WW approval of additional products and/or indications
- ◆ No sales milestones
- ◆ \$112M in total upfront and potential milestones
- ◆ Single digit to low double digit royalties



RXDX-101's High Potency and Selectivity for Important Kinase Targets Creates Multiple Opportunities

Molecular Targets	Development Strategy	Rationale
TrkA/B/C	<ul style="list-style-type: none">♦ Treatment of Trk-dependent tumors<ul style="list-style-type: none">– TrkA fusion proteins drive multiple tumors (e.g., colorectal)– TrkB/C point mutations and overexpression implicated in different tumor types (NSCLC, neuroblastoma)	<ul style="list-style-type: none">♦ 1st-in-Class Pan-Trk inhibitor♦ TrkA fusions cause cell proliferation/survival♦ TrkA mutations enriched in EGFR/ALK(-) NSCLC
ROS1	<ul style="list-style-type: none">♦ Treatment of ROS1-dependent tumors<ul style="list-style-type: none">– ROS1 fusions present in NSCLC, ovarian cancer, glioblastoma, cholangiocarcinoma	<ul style="list-style-type: none">♦ >10-fold more potent on ROS1 dependent models than crizotinib♦ Opportunity for 1st-in-Class
ALK	<ul style="list-style-type: none">♦ Treatment of ALK+ cancers resistant to other ALK inhibitors♦ Treatment of ALK+ cancers with brain lesions	<ul style="list-style-type: none">♦ Active on ALK mutants that cause acquired resistance to crizotinib♦ Crosses blood brain barrier♦ Opportunity for Best-in-Class



Molecular Alterations Targeted by RXDX-101 Are Present in a Large Number of Tumors

◆ 25,000 - 35,000 tumors newly detected in the US each year have an alteration to TrkA, TrkB, TrkC, ROS1 or ALK

◆ Includes:

– NSCLC

– Colorectal

– Prostate

– Melanoma

– Papillary Thyroid

– Breast

– Pancreatic

– AML

– Neuroblastoma

– Glioblastoma



These tumors represent significant segments of the “Big 4” (NSCLC, CRC, PC, BC), as well as cancers with extremely high unmet need (pancreatic, glioblastoma)



RXDX-101 Has Both First-in-Class and Best-in-Class Opportunities

- ◆ There are no Trk-targeting agents in Phase 2 or later
- ◆ There are no agents approved for targeting ROS1
- ◆ Xalkori (crizotinib) is the only approved ALK inhibitor
 - Xalkori approved only for NSCLC
 - Xalkori does not cross the BBB:
Yet, *~50% of ALK+ NSCLC population has brain metastases*
 - NSCLC patients on Xalkori develop *de novo* ALK mutations that cause Xalkori resistance: median duration of effect is ~10 months



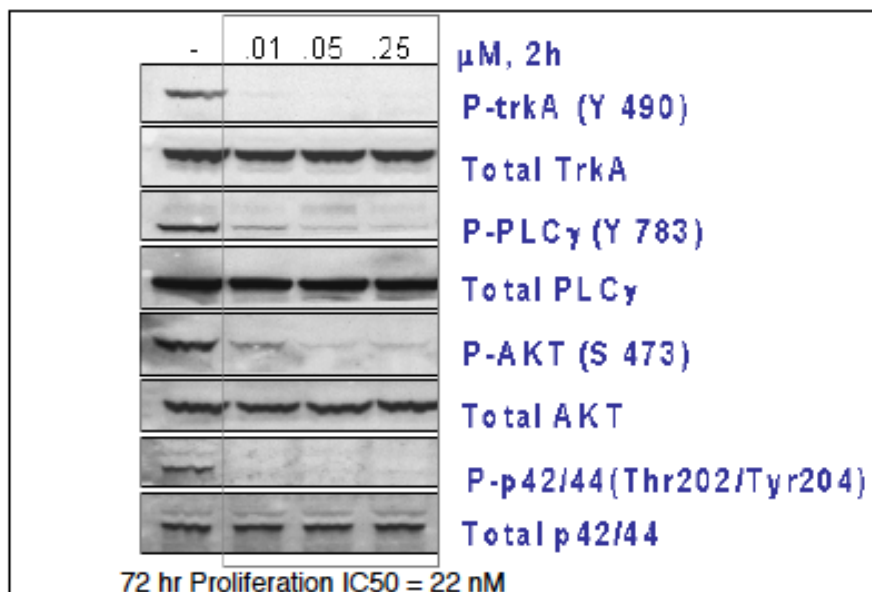
- ◆ **Xalkori had estimated sales >\$280M in 2013**
- ◆ **Candidate tumor market for RXDX-101 is a multiple larger than what Xalkori has penetrated to date**



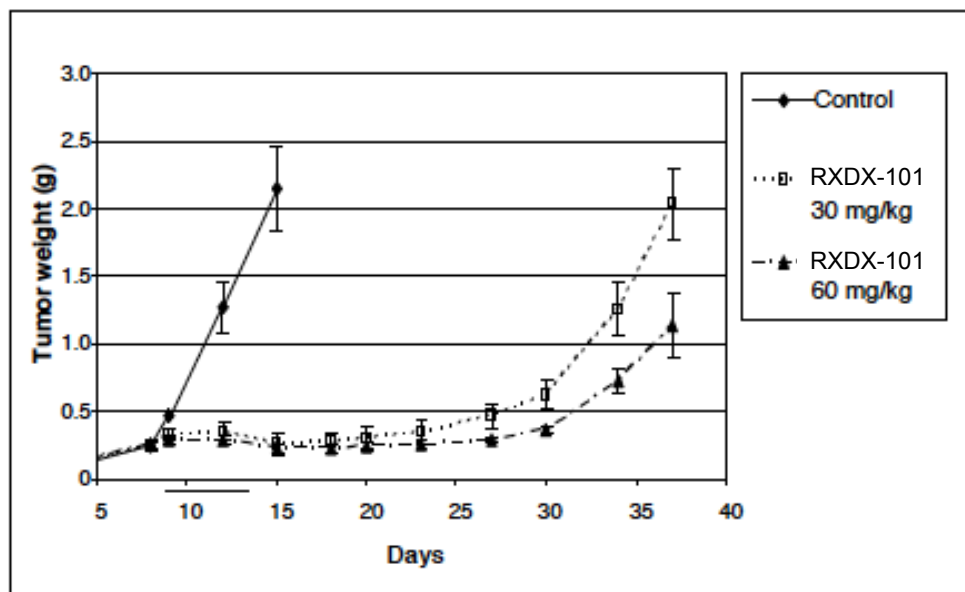
RXDX-101 Demonstrated Strong *In Vitro* and *In Vivo* Activity against Colorectal Cancer

- ◆ KM-12 is a human CRC line driven by a constitutively active TrkA fusion protein
- ◆ RXDX-101 exerts potent inhibition of TrkA phosphorylation and downstream signaling
- ◆ RXDX-101 induces *in vivo* tumor regression and durable tumor stabilization

In vitro MoA in KM12 cells



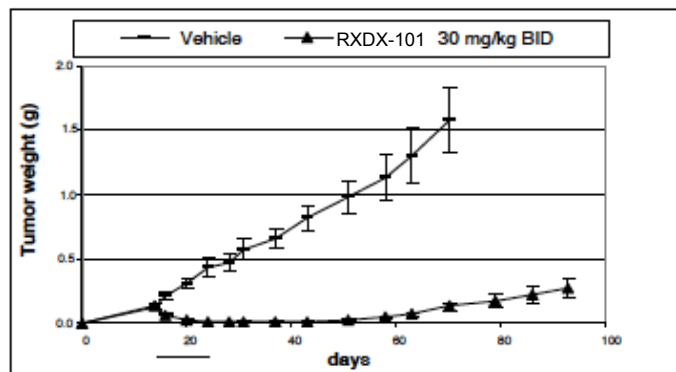
In vivo activity against KM12 tumor xenografts



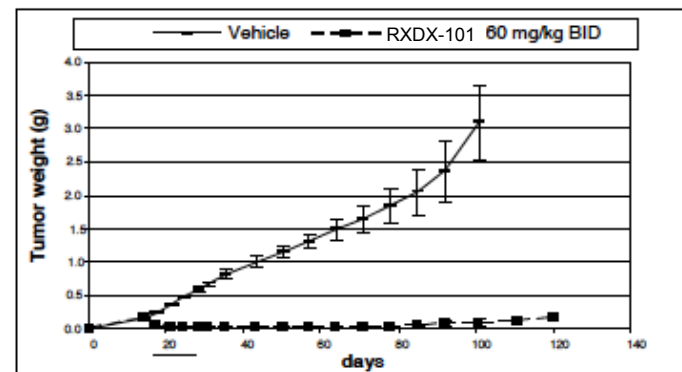


RXDX-101 Demonstrated Strong Activity against Lung Cancer and Lymphoma

In vivo activity in ALK-driven NCI-H2228 non small cell lung cancer (NSCLC) mouse xenografts treated orally BID for 10 days

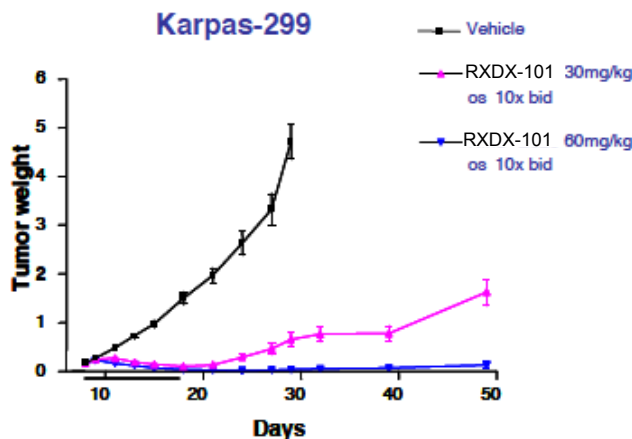


Tumor-free achieved in 2 out of 7 mice

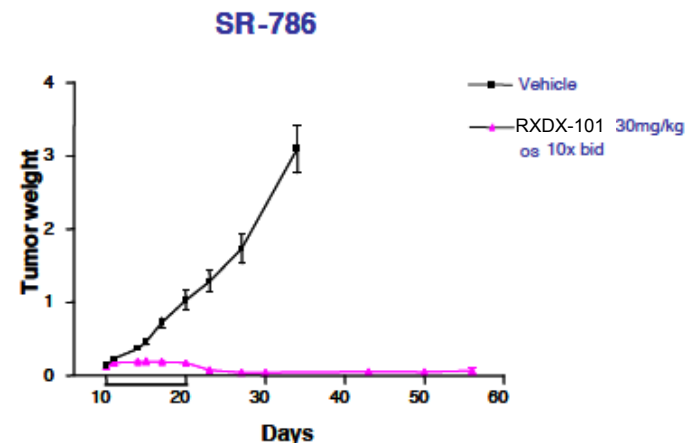


Tumor-free achieved in 5 out of 7 mice

In vivo activity in ALK-driven anaplastic large cell lymphoma (ALCL) mouse xenografts treated orally BID for 10 days



Tumor eradication in 4 out of 7 mice at day 90 (60 mg/kg)

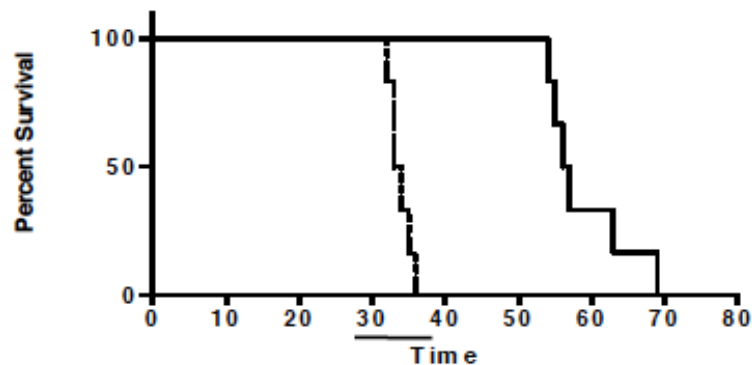


Tumor eradication in 6 out of 7 mice at day 90



RXDX-101 Demonstrated Robust Activity in NSCLC Brain Metastases Model

NCI-H2228 cells were injected intracranially, and mice were treated orally with RXDX-101 at 60 or 120 mg/kg BID for 10 days



120 mg/kg

Median survival

Control group

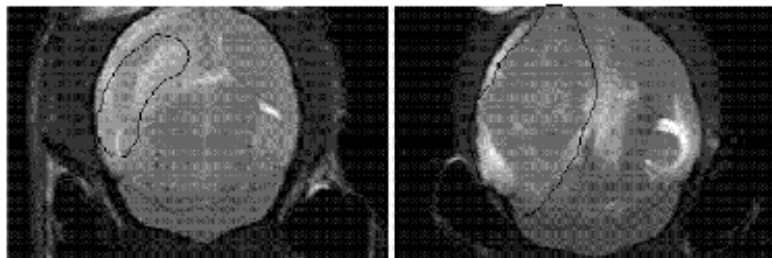
33,50 d

Treated animals

56,50 d

P

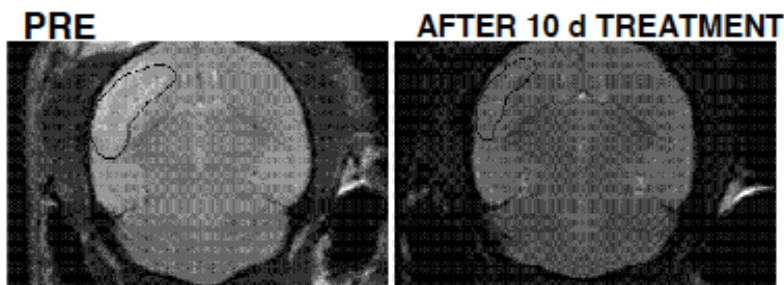
< 5x10e-4



Vehicle

Favorable BBB penetration in three species (brain/blood ratio):

- Mouse: 0.4
- Rat: 0.6 – 1.0
- Dog: 1.4 – 2.2



RXDX-101
120 mg/kg os BID,
10 days



RXDX-101 Clinical Development Strategy

Phase 1/2 Trial

Phase 1

Dose escalation:
20-30 cancer
patients with
mutations to
TrkA, ROS1 or ALK

Phase 2

Additional patients
treated at RP2D*;
N=15-20 per cohort

Accelerated registration path

Potential for “Breakthrough
Therapy Designation” in
indication with high unmet need

Traditional registration path

Can do randomized Phase 2 and
3 clinical studies in parallel in
other most promising
indication(s)

TrkA+ cohort(s)

ROS1+ cohort(s)

ALK+ cohort(s)

* “RP2D” = Recommended Phase II Dose



Ongoing Phase 1/2 Study Design and Status: Oral Single Agent In Solid Tumors

- ◆ Patient population: advanced metastatic solid tumors, positive for TrkA, ROS1, ALK
- ◆ N = 20 - 30 patients in dose escalation phase; 15 – 20 patients/cohort in RP2D expansion phase
- ◆ Objectives of dose escalation phase:
 - Primary: determine DLTs, MTD and RP2D
 - Secondary: safety, PK, antitumor activity by RECIST
- ◆ Status: Actively enrolling patients. Dose escalation will continue to MTD
- ◆ Findings:
 - AEs: No DLTs
 - PK: Cmax and AUC increase with dose, with a plasma half-life of around 20 hrs.
 - Exposure levels are approaching those efficacious in preclinical studies

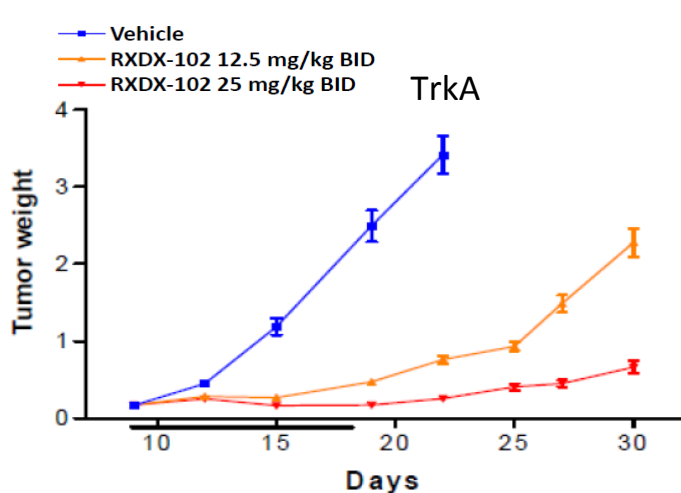
**Diagnostic methods are in place for molecular alterations of interest
(e.g., TrkA, ROS1)**



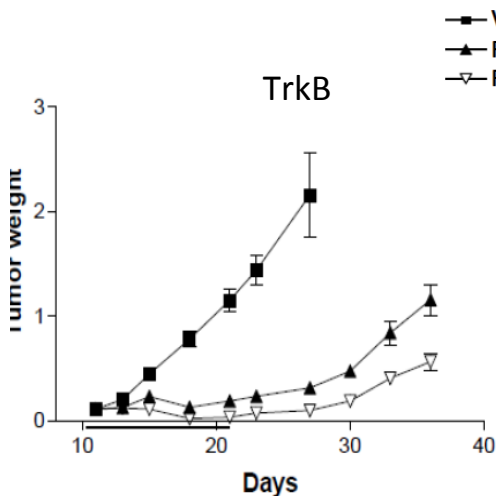
RXDX-102

1st-in-Class Pan-Trk Inhibitor

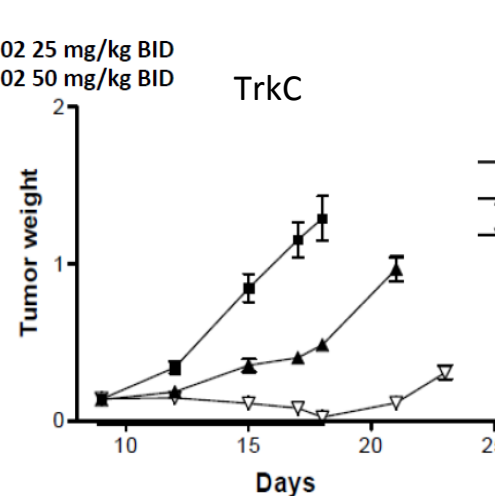
- ◆ Oral, potent, selective inhibitor of TrkA, TrkB & TrkC (each < 5 nM)
- ◆ Potent, durable anti-tumor activity in TrkA/B/C xenograft models
- ◆ Favorable therapeutic window in non-GLP tox studies
- ◆ Ready for IND-enabling tox
- ◆ Trk activating alterations found in colon carcinoma, neuroblastoma, multiple myeloma, secretory breast carcinoma and other tumors



RXDX-102 was orally administered to nude mice bearing KM12 tumors

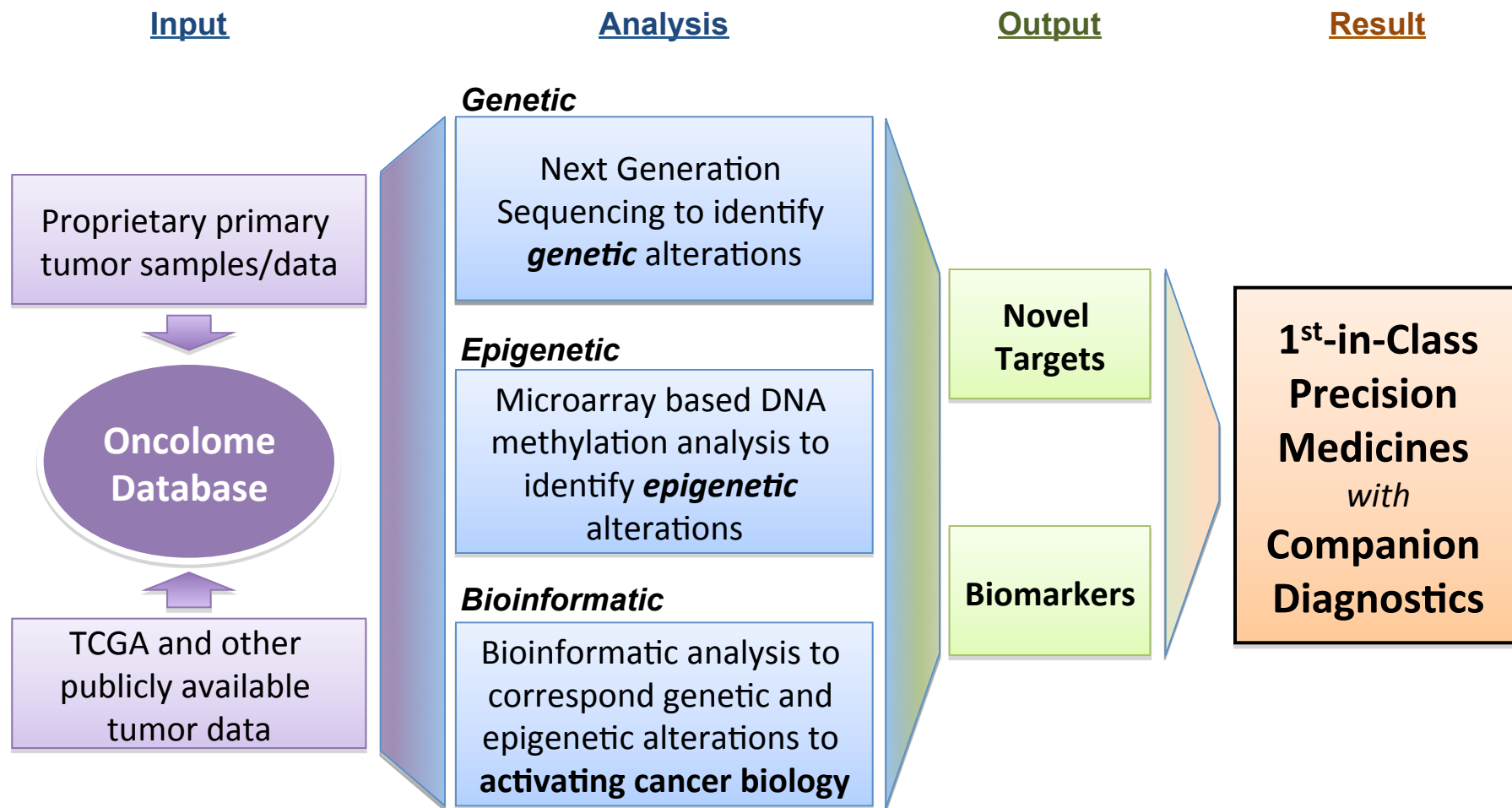


TrkB and TrkC-driven Ba/F3 cells were injected s.c. in SCID mice and animals were treated as



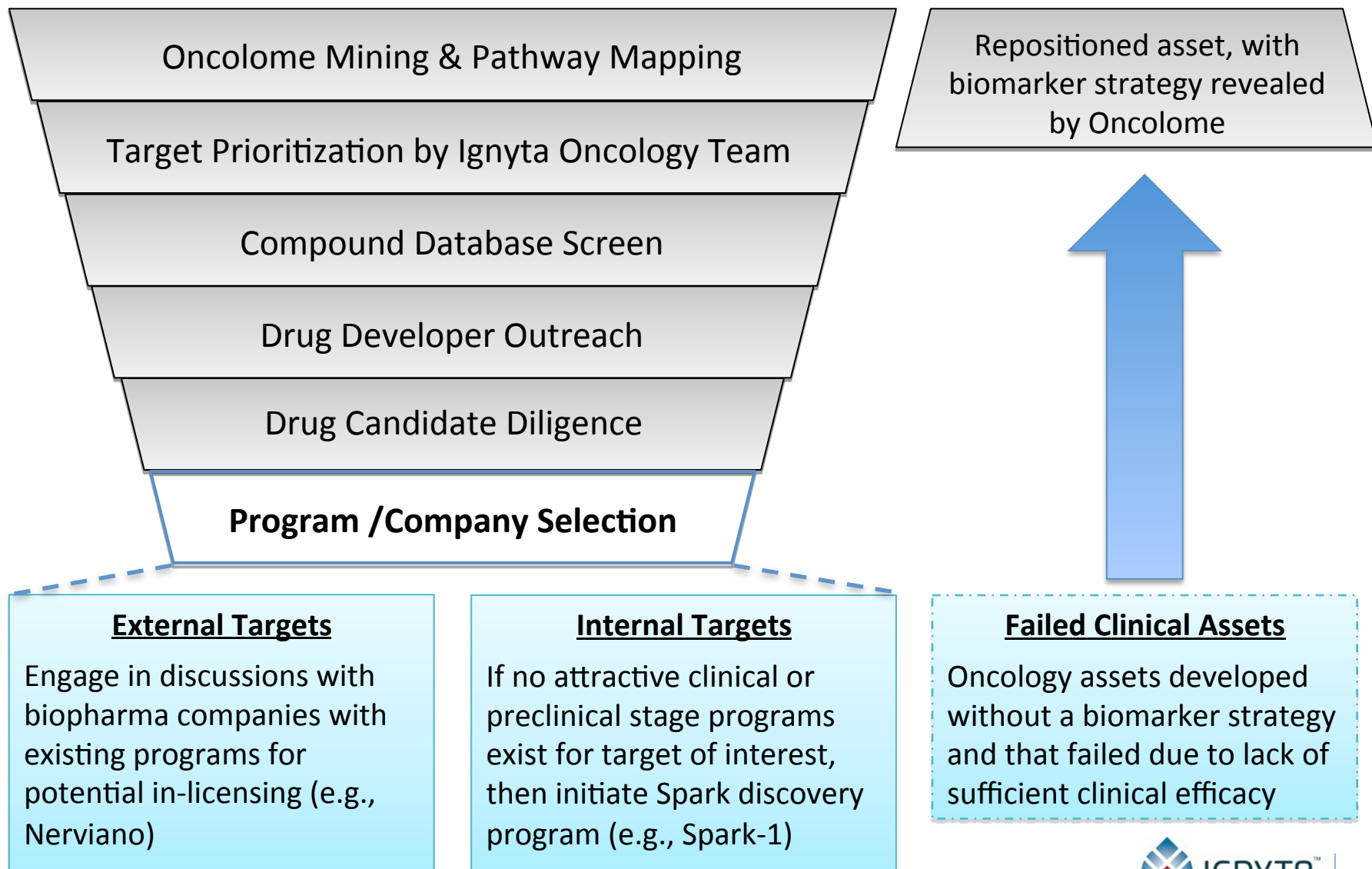


Ignyta's Genomic & Epigenomic Synergies Uniquely Enable Its Integrated Rx/Dx Strategy



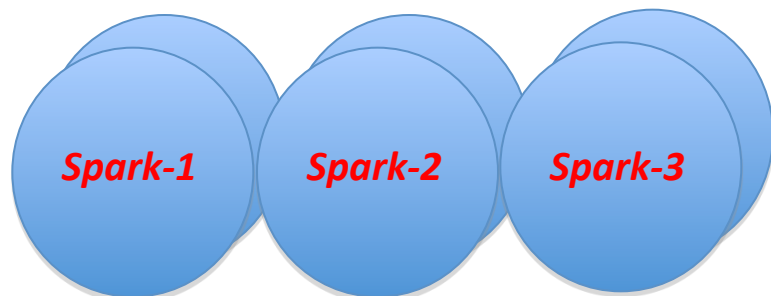


Ignity's Two-Pronged Approach to Generating Value from Novel Targets Identified by Oncolome



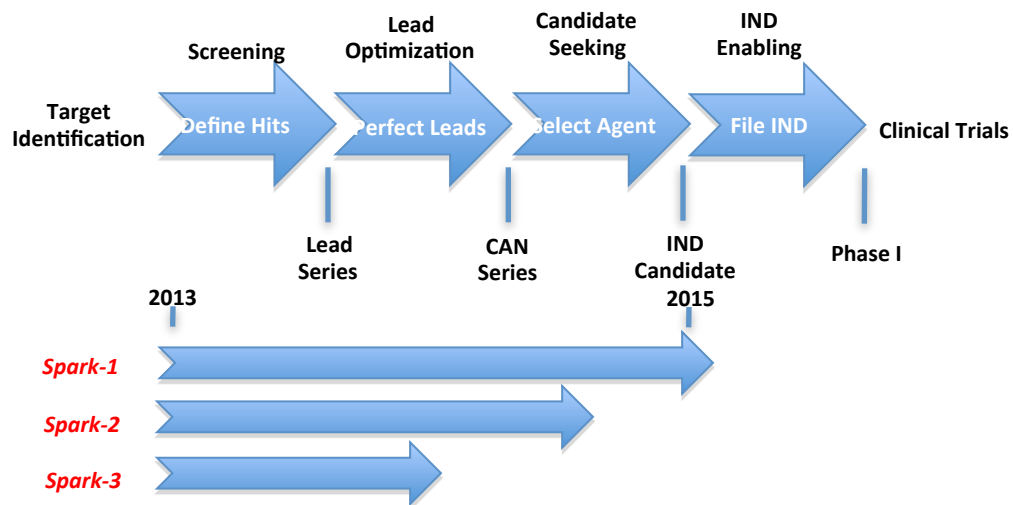


Genomic and Epigenomic Mining of Oncolome Identified Six Novel Targets (Spark-1 to Spark-6)



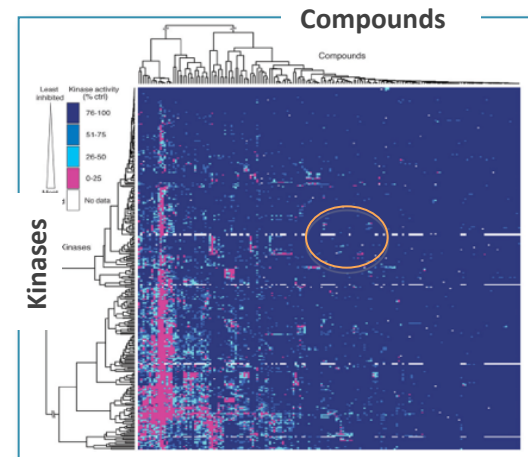
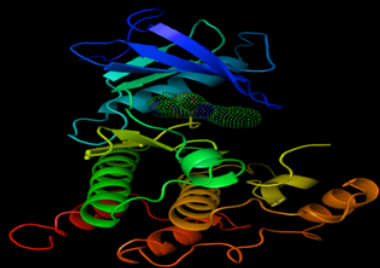
Spark Targets (1 -6)

- ♦ Genetic (mutated)
- ♦ Epigenetic
- ♦ Oncolome mining reveals presence in:
Lung, Breast, Ovary, Pancreas, Liver, Colon, Kidney



Ignity's

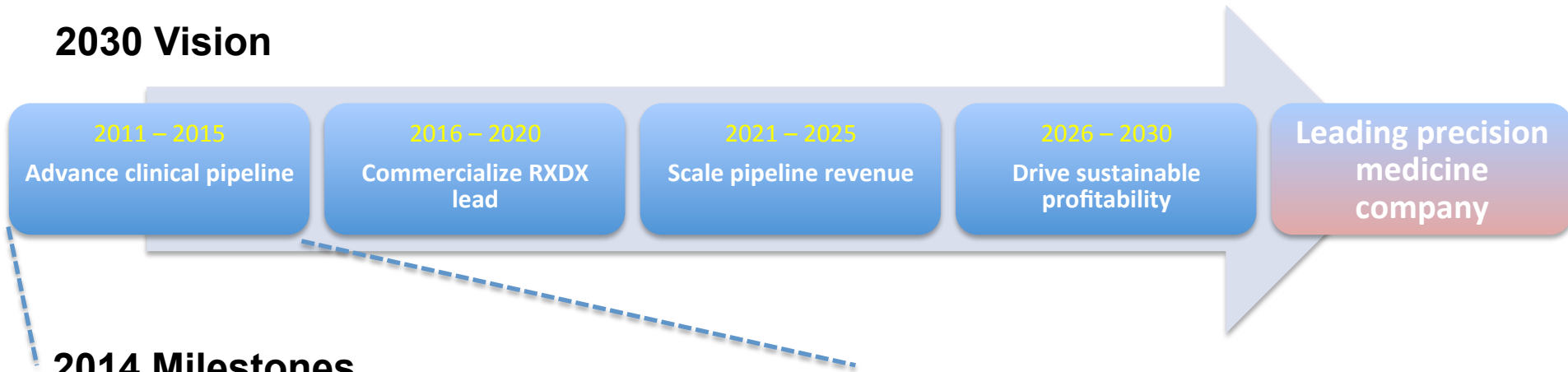
X-Ray Crystallography &
MedChem expertise enables a
Structure-Based-Drug-Design
route to 1st-in-class clinical
candidates





2014 Corporate Milestones

2030 Vision



2014 Milestones

- ◆ Initiate IND-enabling studies for RXDX-102, 1Q14
- ◆ File U.S. IND for RXDX-101, 2Q14
- ◆ Initiate and enroll Phase 2a expansion cohorts for RXDX-101, 2H14
- ◆ Report patient response data from current RXDX-101 Phase 1/2 clinical study, 4Q14
- ◆ Generate potential lead candidate(s) from Spark discovery programs by year-end
- ◆ Seek Nasdaq uplisting, 2014



Company Highlights

- ◆ Targeted oncology company with integrated approach to Rx/Dx development
- ◆ Experienced management team, excellent track record in oncology
- ◆ Pipeline targeting *first-in-class* and *best-in-class* opportunities in cancer
- ◆ Lead oncology asset: Phase 1/2 highly potent, selective kinase inhibitor
- ◆ Multiple potential clinical readouts in 2014 – 2015
- ◆ Cutting edge genomic/epigenomic platform technology provides deep molecular insights that derisk and enable targeted development of new drugs
- ◆ Comprehensive biomarker strategies for patient screening and confirmation
- ◆ Composition of matter IP for clinical and preclinical drug candidates
- ◆ Strong financial position