

To aid in the identification of patients for
treatment with KEYTRUDA[®] (pembrolizumab)

PD-L1
ONE



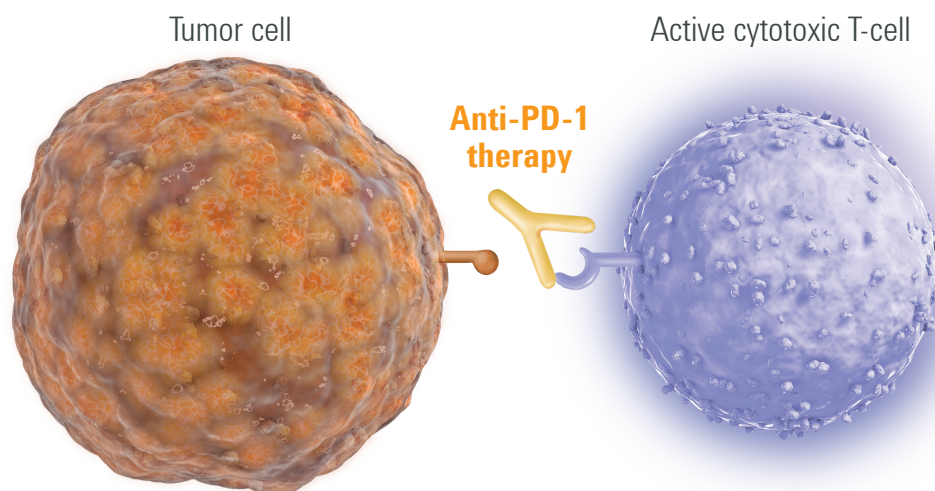
PD-L1 IHC 22C3 pharmDx is the **ONE** assay
clinical trial-proven with KEYTRUDA^{1,2}



ONE innovative class of therapy

Anti-PD-1 therapies are part of an innovative class of immuno-oncology agents expanding treatment options in multiple cancer types

- The clinical value of anti-PD-1 therapies is being shown in an increasing number of tumor types³
 - In 2016, KEYTRUDA® (pembrolizumab) became **the first** anti-PD-1 monotherapy FDA-approved to treat metastatic NSCLC **at first line** in patients with high PD-L1 expression (TPS $\geq$ 50%)⁴
 - KEYTRUDA has gained additional indications across a wide range of cancer types²
- IHC testing for PD-L1 expression continues to unlock the potential of immuno-oncology across a growing number of cancer types



As the therapeutic value of anti-PD-1 therapy is demonstrated across a growing list of cancer types, oncologists are increasingly selecting patients for treatment with KEYTRUDA

ONE test oncologists need

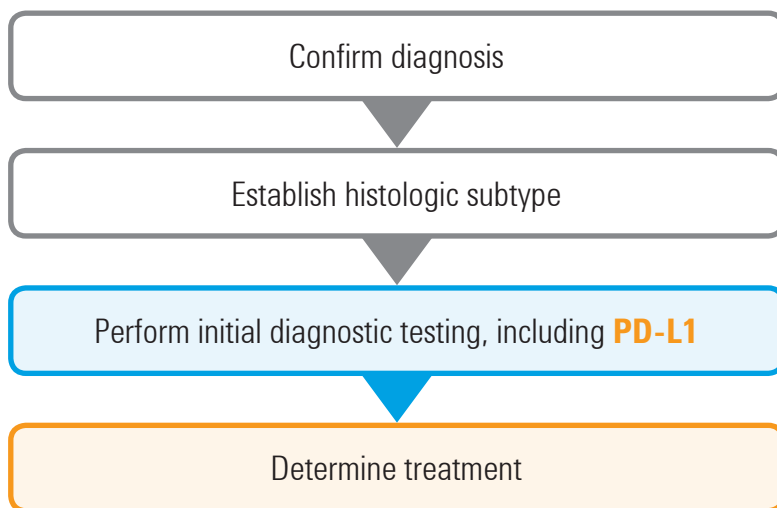
PD-L1 is a proven biomarker for response to anti-PD-1 therapy

- As anti-PD-1 therapies gain approval in more and more tumor types and earlier lines of therapy, swift evaluation of PD-L1 status can help identify patients most likely to benefit from anti-PD-1 therapy in certain tumor types
- Oncologists need prompt, accurate assessments of PD-L1 expression to identify patients most likely to benefit from treatment with KEYTRUDA in certain cancers and help inform patient management



The pivotal KEYNOTE-001 trial established PD-L1 as a biomarker for response to KEYTRUDA for patients with metastatic NSCLC⁵

Incorporate PD-L1 Testing Early



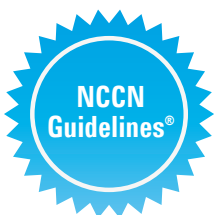
PD-L1 testing can provide oncologists
fundamental information to plan for the best patient care

From many options, there is **ONE** clear

As the number of available PD-1/PD-L1 inhibitors and associated diagnostics increases, choosing the right PD-L1 solution can seem challenging

- Worldwide, there are now five approved PD-1/PD-L1 inhibitors with over 20 indications between them^{6,7}
- With each new therapy developed for use with diagnostic tests, the number of clones, indication-specific tests, staining characteristics, and interpretation parameters increases
- As complexity increases, pathologists are challenged with choosing and standardizing on a single PD-L1 solution for their lab

NCCN Clinical Practice Guidelines In Oncology (NCCN Guidelines®) advise⁸:



- Various antibody clones have been developed for IHC analysis of PD-L1 expression, and **while several show relative equivalence, some do not**
- The potential for **multiple different assays for PD-L1 has raised concern** among both pathologists and oncologists

“...it will be very difficult to demonstrate with any scientific rigor that there is predictive equivalence, in terms of patient outcome, should a test other than the trial-proven approach be used for selecting patients to receive a particular treatment...

***any deviation from practice validated in the trials could be disadvantageous to patients.**”*

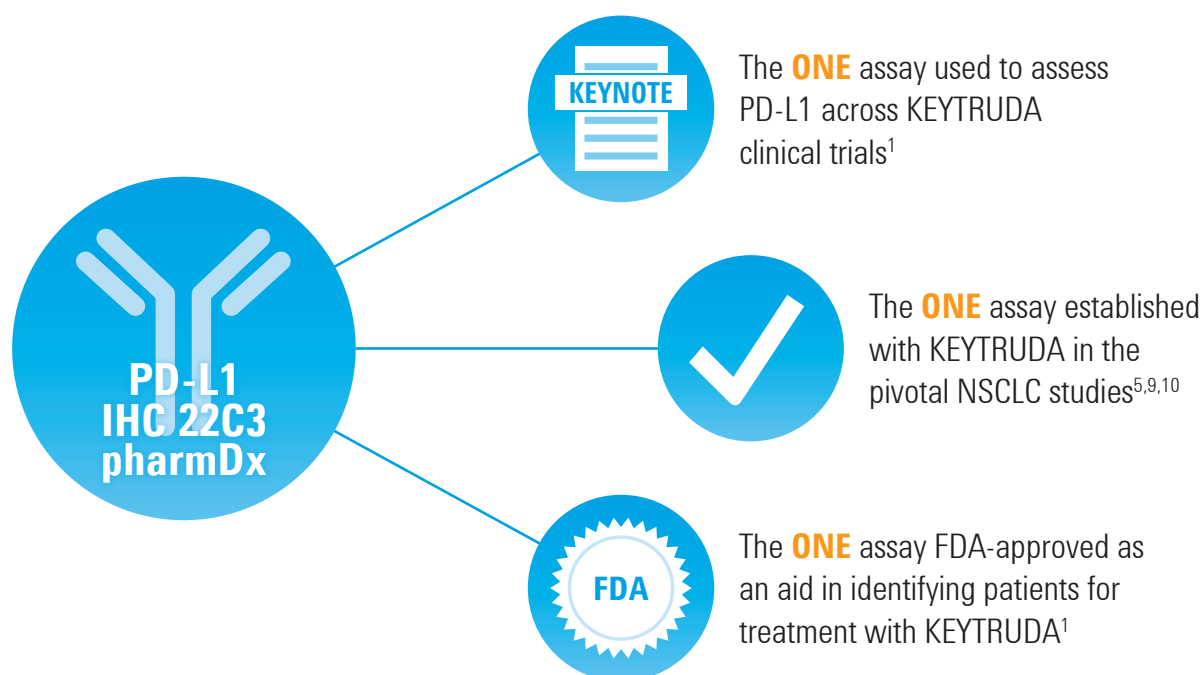
— Kerr KM and Nicolson MC, *Arch Pathol Lab Med*, 2016



choice

For PD-L1 testing, the choice is clear: use PD-L1 IHC 22C3 pharmDx, the one assay clinical trial-proven with KEYTRUDA® (pembrolizumab)

- With indications across a wide range of cancer types, oncologists are increasingly selecting patients for treatment with KEYTRUDA
- PD-L1 IHC 22C3 pharmDx is the clinically relevant option when considering patients for treatment with KEYTRUDA¹



Trust the **ONE** PD-L1 test clinical trial-proven

PD-L1 IHC 22C3 pharmDx is the one assay clinical trial-proven with KEYTRUDA^{1,2}

- PD-L1 IHC 22C3 pharmDx is the only assay used to assess PD-L1 across KEYTRUDA clinical trials*
 - FDA-approved in 2015 based on its use in the pivotal KEYNOTE-001 KEYTRUDA trial in NSCLC
 - Used in every subsequent KEYTRUDA trial that assessed PD-L1 expression



Every **ONE** of the pivotal KEYTRUDA KEYNOTE trials that assessed PD-L1 expression have used PD-L1 IHC 22C3 pharmDx

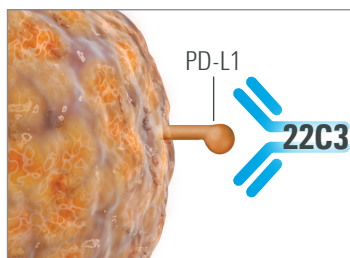
PD-L1 IHC 22C3 pharmDx offers the assurance of the only PD-L1 test clinical trial-proven as a companion diagnostic for KEYTRUDA

*The clinical-trial assay (CTA) version of PD-L1 IHC 22C3 pharmDx was used in KEYNOTE-001 and KEYNOTE-010.

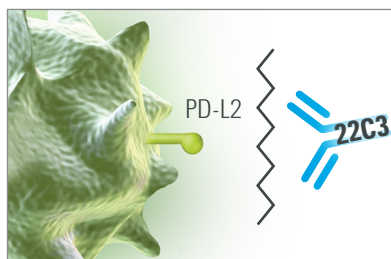
en with KEYTRUDA® (pembrolizumab)

PD-L1 IHC 22C3 pharmDx delivers high specificity and sensitivity^{1,11}

High specificity for accurate clinical results



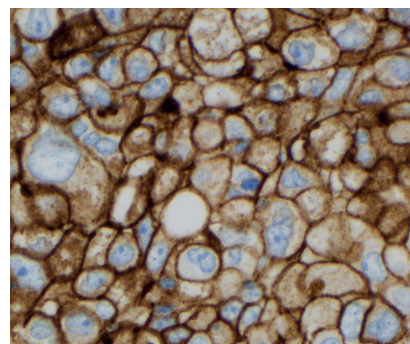
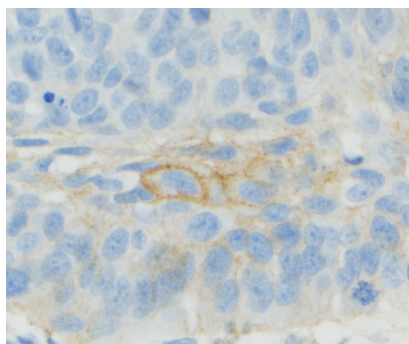
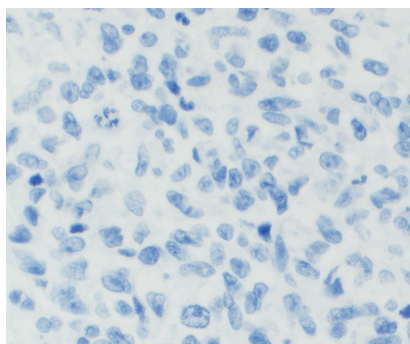
22C3 specifically binds to PD-L1
on the cell membrane of tumor cells, immune cells,
and cells of epithelial origin



22C3 does not cross-react with
Programmed Death-Ligand 2
(PD-L2) protein

High sensitivity for precise PD-L1 detection

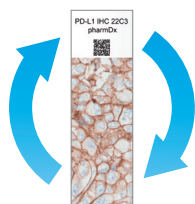
- Assessment of PD-L1 expression in NSCLC demonstrated staining across the dynamic range of 0–100% positive tumor cells and 0–3+ staining intensities



The stains above are of NSCLC specimens stained with PD-L1 IHC 22C3 pharmDx.

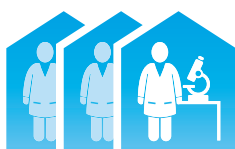
Dependable performance in a convenient,

PD-L1 IHC 22C3 pharmDx delivers repeatable and reproducible results to elevate your diagnostic confidence^{1,11}



Repeatable

- Agilent performed rigorous repeatability testing to ensure reliable results
- **100%** overall agreement across inter-instrument, inter-operator, inter-day, and intra-run tests*



Reproducible

- Reproducibility testing performed at three external testing sites demonstrated **> 85%** overall agreement across all tests*
- Inter-site, intra-site, inter-observer, and intra-observer tests were all performed

Agilent PD-L1 assays are pre-validated for efficient, reliable implementation in your lab^{1,11}

- Pre-validated assays place less burden on individual labs to establish accurate and reliable results
 - Lab-developed tests require time-intensive set-up, protocol development, validation, and continuous cross-batch verification
 - “Single-vial” assays still require time-consuming stock management of components



Validated

- PD-L1 IHC 22C3 pharmDx comes pre-validated, including validated scoring guidelines and on-site product demonstrations
- All necessary components for a complete staining run are validated together and included in each kit

*Overall agreement is based on average negative and average positive agreements. Tests were performed using NSCLC tissue.

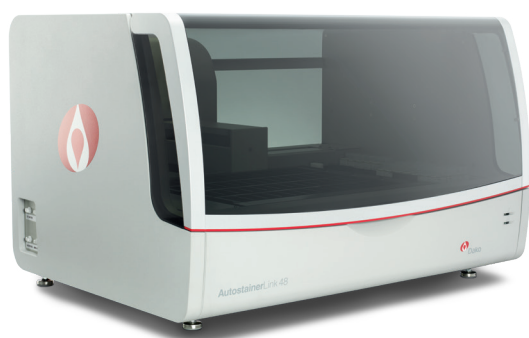
all-in-ONE kit

PD-L1 IHC 22C3 pharmDx is a standardized IHC assay with all necessary components for 50 tests in one kit¹

- Includes all reagents for a complete staining run, minimizing stock management
- All components are cross-validated and quality-controlled, eliminating time-intensive testing
- Includes positive and negative control cell line slides to validate staining runs and verify reagent performance, ensuring reliable results

PD-L1 IHC 22C3 pharmDx is designed for an automated process for enhanced operational efficiency^{1,11}

- PD-L1 IHC 22C3 pharmDx is designed for use on Autostainer Link 48, which comes preprogrammed with a validated staining protocol in the DakoLink software
 - Minimizes time from biopsy to diagnosis
 - Results can be available within one working day



Ordering PD-L1 IHC 22C3 pharmDx is easy—contact your local Agilent representative today

Product	Platform	Code
PD-L1 IHC 22C3 pharmDx	Autostainer Link 48	SK006

Your **ONE** source for diagnostic solutions

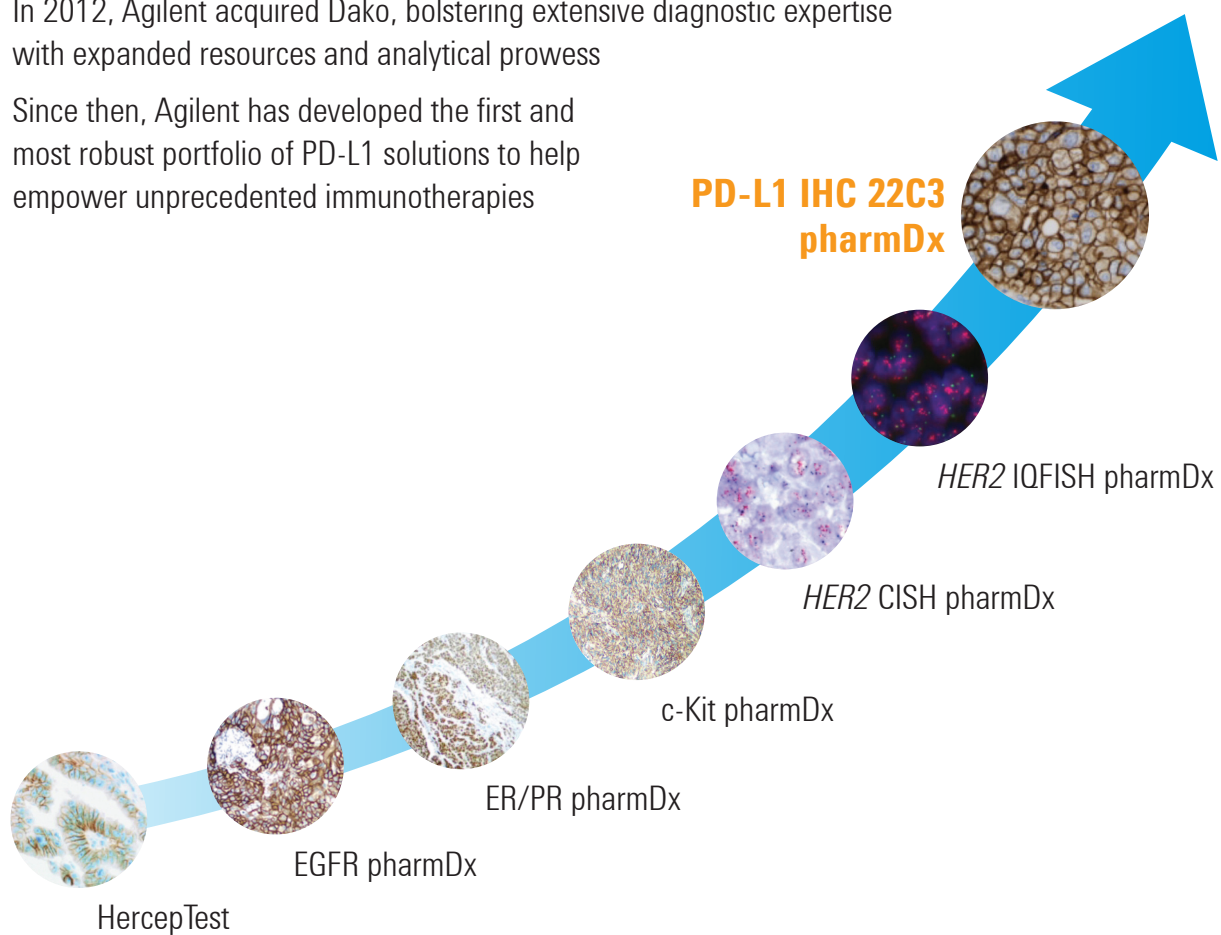
Agilent provides complete workflow solutions with custom packages of equipment, software, services, informatics, and consumables



The **ONE** you trust in CDx

Agilent has a legacy of pioneering diagnostic assay development to support the development, validation, and launch of landmark therapies

- In 1998, Dako developed HercepTest, the first ever companion diagnostic to support targeted therapy¹²
- In 2012, Agilent acquired Dako, bolstering extensive diagnostic expertise with expanded resources and analytical prowess
- Since then, Agilent has developed the first and most robust portfolio of PD-L1 solutions to help empower unprecedented immunotherapies

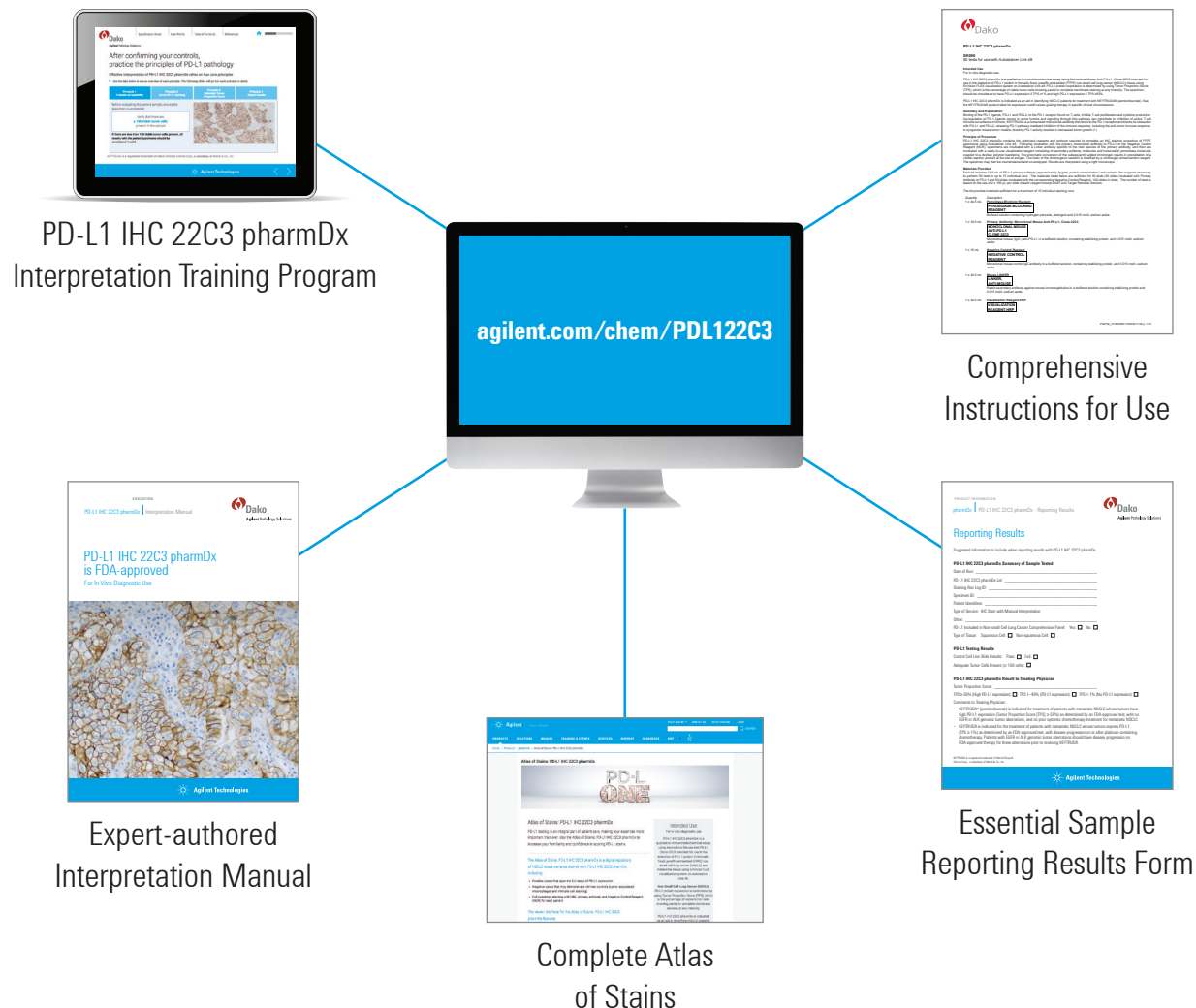


From developing the pioneer in companion diagnostics to introducing the latest in immuno-oncology biomarker testing, we continue to strive to bring you the best

ONE-stop comprehensive training

Comprehensive educational support and interpretation resources enhance your diagnostic certainty

- On-site product demonstrations provide hands-on experience with instruments and reagents prior to purchase
- Agilent supports accurate PD-L1 scoring and interpretation with a full suite of training resources available 24/7 at agilent.com/chem/PDL122C3*



* Availability of eLearning resources varies by country.



Agilent Technologies

Committed to continuing
to break new ground in
cancer diagnostics.

The Agilent CDx footprint is
broad and growing as we work
to advance the future of
CDx-empowered therapy.



Intended Use

For in vitro diagnostic use.

PD-L1 IHC 22C3 pharmDx is a qualitative immunohistochemical assay using Monoclonal Mouse Anti-PD-L1, Clone 22C3 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) non-small cell lung cancer (NSCLC) tissue using EnVision FLEX visualization system on Autostainer Link 48. PD-L1 protein expression is determined by using Tumor Proportion Score (TPS), which is the percentage of viable tumor cells showing partial or complete membrane staining at any intensity. The specimen should be considered to have PD-L1 expression if TPS $\geq$ 1% and high PD-L1 expression if TPS $\geq$ 50%.

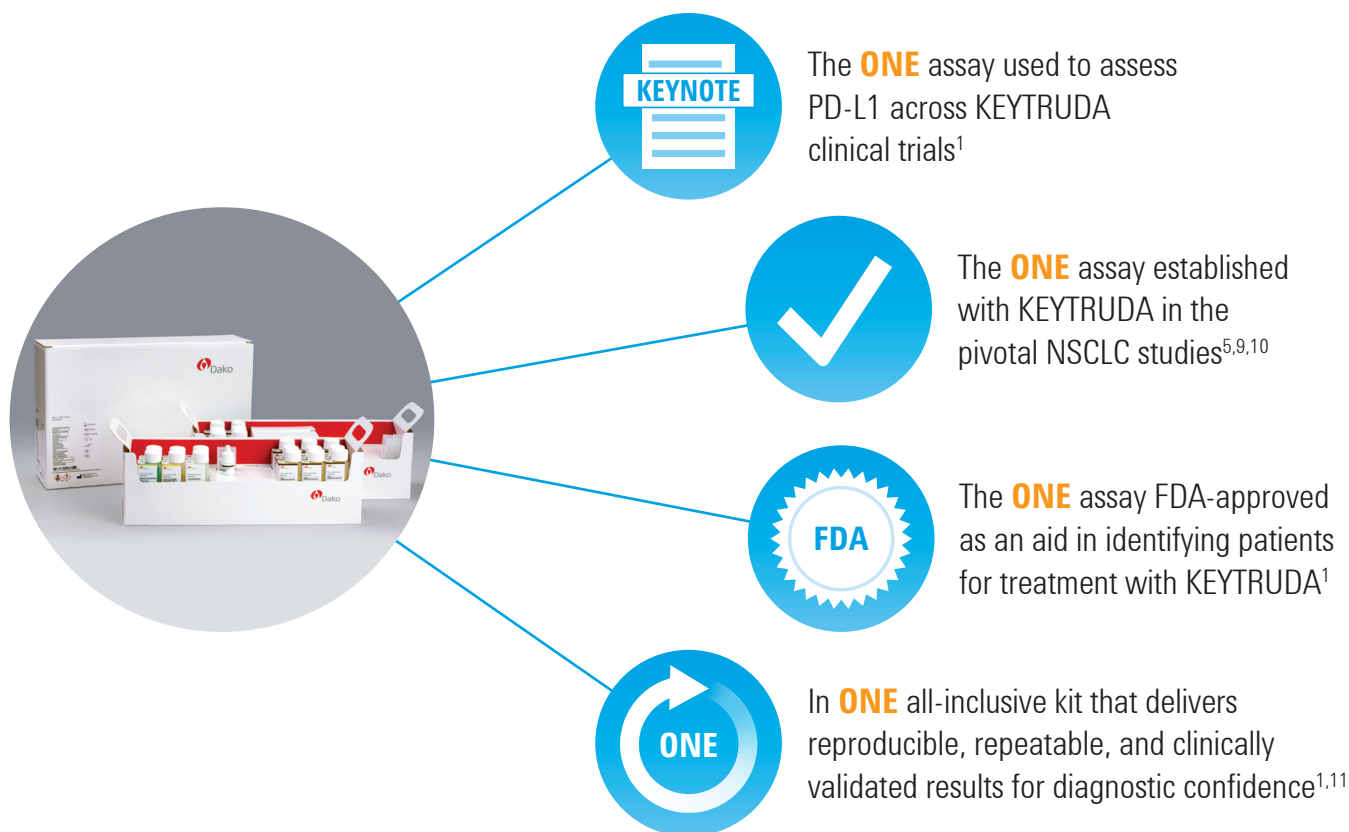
PD-L1 IHC 22C3 pharmDx is indicated as an aid in identifying NSCLC patients for treatment with KEYTRUDA® (pembrolizumab). See the KEYTRUDA® product label for expression cutoff values guiding therapy in specific clinical circumstances.

References: **1.** PD-L1 IHC 22C3 pharmDx [package insert]. Carpinteria, CA: Dako, Agilent Pathology Solutions; 2017. **2.** Keytruda [package insert]. Kenilworth, NJ: Merck & Co., Inc.; 2017. **3.** Berger KN, Pu JJ. PD-1 pathway and its clinical application: A 20 year journey after discovery of the complete human PD-1 gene. *Gene*. 2018;628:20-25. **4.** FDA approves Merck's KEYTRUDA® (pembrolizumab) in metastatic NSCLC for first-line treatment of patients whose tumors have high PD-L1 expression (Tumor Proportion Score [TPS] of 50 percent or more) with no EGFR or ALK genomic tumor aberrations [news release]. Kenilworth, NJ; Merck & Co., Inc.; October 24, 2016. <http://www.mrknewsroom.com/news-release/prescription-medicine-news/fda-approves-mercks-keytruda-pembrolizumab-metastatic-nsclc->. Accessed January 16, 2018. **5.** Garon EB, Rizvi NA, Hui R, et al. Pembrolizumab for the treatment of non-small-cell lung cancer. *N Engl J Med*. 2015;372(21):2018-2028. **6.** Drugs@FDA: FDA Approved Drug Products. Silver Springs, MD: U.S. Food and Drug Administration. <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm>. Accessed January 16, 2018. **7.** European Medicines Agency. http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/medicines/medicines_landing_page.jsp&mid=. Accessed January 16, 2018. **8.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.1.2018. © National Comprehensive Cancer Network, Inc. 2017. All rights reserved. Accessed January 16, 2018. To view the most recent and complete version of the guideline, go online to www.NCCN.org. National Comprehensive Cancer Network® (NCCN®) makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **9.** Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet*. 2016;387(10027):1540-1550. **10.** Reck M, Rodríguez-abreu D, Robinson AG, et al. Pembrolizumab versus chemotherapy for PD-L1-positive non-small-cell lung cancer. *N Engl J Med*. 2016;375(19):1823-1833. **11.** Roach C, Zhang N, Corigliano E, et al. Development of a companion diagnostic PD-L1 immunohistochemistry assay for pembrolizumab therapy in non-small-cell lung cancer. *Appl Immunohistochem Mol Morphol*. 2016;24:392-397. **12.** FDA Approves DAKO HercepTest for HER2 Overexpression. Carpinteria, CA; DAKO Corp.; September 29, 1998. <https://www.bioprocessonline.com/doc/fda-approves-dako-herceptest-for-her2-overexp-0001>. Accessed January 16, 2018.

PD-L1 ONE

For PD-L1 testing,

Choose PD-L1 IHC 22C3 pharmDx—
the **ONE** assay **clinical trial-proven**
with KEYTRUDA® (pembrolizumab)



Trusted Answers. Together.



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