

# Pan TRK [RM423]

Concentrated and Prediluted Rabbit Monoclonal Antibody  
902-3267-071321

**BIOCARE**  
M E D I C A L

Available Product Formats				
Format	Catalog Number	Description	Dilution	Diluent
Concentrate	ACR 3267 A, C	0.1, 1.0 mL	1:100	Renoir Red
Predilute	APR 3267 AA	6.0 mL	Ready-to-use	N/A
UltraLine – For BenchMark	AVR 3267 G	6.0 mL	Ready-to-use	N/A
Q Series– For Leica BOND-III	ALR 3267 G7	7.0 mL	Ready-to-use	N/A

## Intended Use:

For Research Use Only. Not for use in diagnostic procedures.

## Summary and Explanation:

Neurotrophic tyrosine receptor kinase (NTRK) proto-oncogenes NTRK1, NTRK2, and NTRK3 (that encode TRK A, TRK B, and TRK C proteins, respectively) may form gene fusions through their kinase domains, driving tumor development (1). TRK A is activated by nerve growth factor (NGF), TRK B by brain-derived neurotrophic factor (BDNF) or neurotrophin-4 (NT-4), and TRK C by neurotrophin-3 (NT-3) (2). NTRK fusions are characteristic of a few rare types of cancer, such as secretory carcinoma of the breast or salivary gland and infantile fibrosarcoma, but they are also infrequently seen in some common cancers, such as melanoma, glioma and carcinomas of the thyroid, lung and colon (3,4).

Pan TRK immunohistochemical staining to detect NTRK fusions has become increasingly important as TRK inhibitors, Larotrectinib and Entrectinib, have received regulatory approval and have demonstrated a high response rate in patients with NTRK fusions (3,5).

## Principle of Procedure:

Antigen detection in tissues and cells is a multi-step immunohistochemical process. The initial step binds the primary antibody to its specific epitope. After labeling the antigen with a primary antibody, a one-step or two-step detection procedure can be applied. A one-step procedure will feature an enzyme labeled polymer that binds the primary antibody. A two-step procedure will feature a linker antibody added to bind to the primary antibody. An enzyme-labeled polymer is then added to bind the linker antibody. These detections of the bound antibodies are evidenced by a colorimetric reaction.

**Source:** Rabbit monoclonal

**Species Reactivity:** Human, others not tested

**Clone:** RM423

**Isotype:** IgG

**Protein Concentration:** Call for lot specific Ig concentration.

**Epitope/Antigen:** Pan TRK

**Cellular Localization:** Cytoplasmic and axons

**Positive Tissue Control:** Brain

**Known Applications:**

Immunohistochemistry (formalin-fixed paraffin-embedded tissues)

**Supplied As:** Buffer with protein carrier and preservative

**Storage and Stability:**

Store at 2°C to 8°C. The product is stable to the expiration date printed on the label, when stored under these conditions. Do not use after expiration date. Diluted reagents should be used promptly; any remaining reagent should be stored at 2°C to 8°C.

## Staining Protocol Recommendations (intelliPATH FLX® and manual use):

**Peroxide Block:** Block for 5 minutes with Peroxidized 1.

**Pretreatment:** Perform heat retrieval using Borg Decloaker. Refer to the Borg Decloaker data sheet for specific instructions.

**Protein Block (Optional):** Incubate for 5-10 minutes at RT with Background Punisher.

**Primary Antibody:** Incubate for 60 minutes at RT.

**Probe:** N/A

**Polymer:** Incubate for 30 minutes at RT with a tertiary polymer.

**Chromogen:** Incubate for 5 minutes at RT with Biocare's DAB – OR – Incubate for 5-7 minutes at RT with Warp Red.

**Counterstain:** Counterstain with hematoxylin. Rinse with deionized water. Apply Tacha's Bluing Solution for 1 minute. Rinse with deionized water.

## Technical Note:

This antibody, for intelliPATH FLX and manual use, has been standardized with MACH 4 detection system. Use TBS for washing steps.

## Staining Protocol Recommendations (Ventana BenchMark ULTRA):

AVR3267 is intended for use with the BenchMark ULTRA. Refer to the User Manual for specific instructions for use. Recommended protocol parameters are as follows:

**Template/Detection:** OptiView DAB IHC

**Pretreatment Protocol:** CC1 88 minutes

**Peroxidase:** Pre Primary Peroxidase Inhibitor

**Primary Antibody:** 16 minutes, 36°C

## Staining Protocol Recommendations (Q Series – For Leica BOND-III):

ALR3267 is intended for use with the Leica BOND-III. Refer to the User Manual for specific instructions for use. Recommended protocol parameters are as follows:

**Protocol Name:** IHC Protocol F

**Detection:** Bond Polymer Refine

**HIER:** 40 min with ER2

**Peroxide Block:** 5 min

**Marker (Primary Antibody):** 15 min

**Post Primary:** 8 min

**Polymer:** 8 min

**Mixed DAB Refine:** 10 min

**Hematoxylin:** 5 min

## Performance Characteristics:

Sensitivity, specificity and cross-reactivity are summarized in Tables 1 and 2, respectively.

## Limitations:

This product is provided for Research Use Only (RUO) and is not for use in diagnostic procedures. Suitability for specific applications may vary and it is the responsibility of the end user to determine the appropriate application for its use.

## Precautions:

1. This antibody contains less than 0.1% sodium azide. Concentrations less than 0.1% are not reportable hazardous materials according to U.S. 29 CFR 1910.1200, OSHA Hazard communication and EC Directive 91/155/EC. Sodium azide (NaN<sub>3</sub>) used as a preservative is toxic if ingested. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. Upon disposal, flush with large volumes of water to prevent azide build-up in plumbing. (Center for Disease Control, 1976, National Institute of Occupational Safety and Health, 1976) (6)

2. Specimens, before and after fixation, and all materials exposed to them should be handled as if capable of transmitting infection and disposed of with proper precautions. Never pipette reagents by mouth and avoid contacting the skin and mucous membranes with reagents and specimens. If reagents or specimens come into contact with sensitive areas, wash with copious amounts of water. (7)

3. Microbial contamination of reagents may result in an increase in nonspecific staining.

4. Incubation times or temperatures other than those specified may give erroneous results. The user must validate any such change.

5. Do not use reagent after the expiration date printed on the vial.

6. The SDS is available upon request and is located at <http://biocare.net>.

## Technical Support:

Contact Biocare's Technical Support at 1-800-542-2002 for questions regarding this product.

## References:

1. Hechtman JF, Benayed R, Hyman DM, et al. Pan-Trk immunohistochemistry is an efficient and reliable screen for the detection of NTRK fusions. *Am J Surg Pathol.* 2017;41(11):1547-1551.

2. Cocco E, Scaltriti M, Drilon A. NTRK fusion-positive cancers and TRK inhibitor therapy. *Nat Rev Clin Oncol.* 2018;15(12):731-747.

3. Solomon JP, Linkov I, Rosado A, et al. NTRK fusion detection across multiple assays and 33,997 cases: diagnostic implications and pitfalls. *Mod Pathol.* 2020;33(1):38-46.

4. Solomon JP, Benayed R, Hechtman JF, Ladanyi M. Identifying patients with NTRK fusion cancer. *Ann Oncol.* 2019;30(Suppl\_8): viii16-viii22.



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## References Cont'd:

5. Drilon A. TRK inhibitors in TRK fusion-positive cancers. *Ann Oncol*. 2019;30(Suppl\_8): viii23-viii30.
6. Center for Disease Control Manual. Guide: Safety Management, NO. CDC-22, Atlanta, GA. April 30, 1976 "Decontamination of Laboratory Sink Drains to Remove Azide Salts."
7. Clinical and Laboratory Standards Institute (CLSI). Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline-Fourth Edition CLSI document M29-A4 Wayne, PA 2014.

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**Table 1:** Sensitivity and specificity were determined by testing formalin-fixed, paraffin-embedded diseased tissues.

Tissue	Positive Cases	Total Cases
Astrocytoma	36	37
Glioblastoma	6	7
Ovary Cancer	0	2
Breast Cancer	4	27
Colon Cancer	0	39
Lung Cancer	11	50
Prostate Cancer	3	42
Adrenocortical carcinoma	1	1
Bladder Cancer	0	2
Meningioma	3	3
Squamous Cell carcinoma (esophagus)	1	3
Adenocarcinoma (stomach)	0	3
Adenocarcinoma (small intestine)	1	1
Adenocarcinoma (colon & rectum)	3	6
Kidney Cancer	0	2
Liver Cancer	2	4
Lymphoma	1	3
Adenocarcinoma (head & neck, oral cavity, hard palate)	1	1
Squamous Cell carcinoma (head & neck, oral cavity, tongue)	0	1
Nasopharyngeal carcinoma	1	1
Adenocarcinoma (pancreas)	0	1
Adenocarcinoma (prostate)	2	2
Adenoid Cystic carcinoma	0	1
Squamous Cell carcinoma (skin)	0	1
Head & neck nasal cavity (melanoma)	1	1
Seminoma	1	2
Thyroid Cancer	2	2
Cervical Cancer	2	2
Endometrium Cancer	1	2

**Table 2:** Tissue cross-reactivity was determined by testing formalin-fixed, paraffin-embedded normal tissues.

Tissue	Positive Cases	Total Cases
Cerebrum	15	15
Cerebellum	4	4
Adrenal	2	4
Ovary	0	3
Pancreas	2	4
Testis	4	4
Thyroid	3	4
Breast	2	2
Spleen	2	3
Tonsil	0	2
Thymus	1	3
Bone Marrow	3	3
Lung	3	5
Heart	0	3
Esophagus	0	4
Stomach	1	4
Small Intestine	0	4
Colon	0	12
Liver	0	4
Salivary Gland	1	4
Kidney	4	4
Prostate	0	10
Uterus	2	4
Cervix	2	3
Skeletal Muscle	0	3
Skin	1	3
Peripheral Nerve	3	3
Pericardium	0	2
Eye (choroid, retinal & sclera)	2	3
Laryngopharynx	0	2
Bladder	0	1
Head, neck and salivary gland	0	1
Lymph node	0	4
Tracheal tissue	3	3



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